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THE SOCIAL PEDIATRIC PROTECTION FUND

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Georgia (eu) Aim Social Pediatric Protection Fund is to execute programs of social pediatric development and maintain rights and healthcare of Children, Mothers and Adolescents. Fund has great organizational experience, technical equipment and skilled members.

Most of the members are Professors at TSMU, who have clinical and educational experience of 15-20 years and were one of the first, Before the independence, to read lectures about congenital infections, sexually transmitted diseases and prevention of HIV. Fund is also cooperating with physicians, psychologists, Lawyer (who operate in field of social assistance) and Public figures. By the joint forces of all the people above said SPPF is able to hold free medical examinations, juridicial consultations, charity events, informational lectures about healthy way of life, congenital infection, HIV, Social subjects and etc.

Since 1997 more than 93.000 Children and Hundreds of older people have been medically for free in the framework of charity events. Before Independence, The active members of SPPF and their consortium in 1980-1990 examined above 124 000 Children, all over Georgia.



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SIMEA was established in 1994 with the approval of the Shaanxi Provincial Department of Civil Affairs. It is a first-level social organization under the charge of the Shaanxi Provincial Health and Family Planning Commission. The concept of "seeking well-being" will give full play to the advantages and characteristics of the gathering of experts, a wide range of disciplines, and a sound network, aiming to build a platform for international medical exchanges and mutual learning.

2. Children's Hospital of Shaanxi Provincial People's Hospital

Date of establishment: 1950

Address: No. 256, Youyi West Road, Beilin District, Shaanxi Province

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Since its establishment in 1950, the Children's Hospital of Shaanxi Provincial People's Hospital has experienced more than 70 years of development. It is now the Children's Hospital of the Third Affiliated Hospital of Xi'an Jiaotong University. It is a children's hospital integrating medical treatment, teaching, and scientific research. Shaanxi Province Kawasaki Disease Diagnosis and Treatment Center, Shaanxi Province Pediatrics Clinical Medicine Research Center, National Drug Research Institute (Children Neuromedicine Specialty), Shanghai Cooperation Organization Hospital Cooperative Alliance International Exchange Center, and China Kawasaki Disease Website (www.chinakd.org) have been established.), European Center for Traditional Chinese Medicine (Prague). Insist on innovating the "send out and invite in" communication methods for academic exchanges and scientific research cooperation.

3. The Institution of Shaanxi Province Clinical Medicine Demonstration International Science and Technology Cooperation

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The Shaanxi Provincial Clinical Medicine Demonstration International Science and Technology Cooperation Base was established in 2020. It is an organization approved by the Shaanxi Provincial Department of Science and Technology to promote international cooperation and exchanges in clinical medicine and guide the province to carry out international cooperation and exchanges in clinical medicine. The cooperation base is set up in Shaanxi Provincial People's Hospital. Actively expand foreign medical resources, and provide a lasting communication channel for domestic medical and health institutions and public health service units to learn international advanced management experience and strengthen the training of talent teams.

THE SOCIAL PEDIATRIC PROTECTION FUND

**Shaanxi International Medical Exchange Promotion Association (SIMEA)
Children's Hospital of Shaanxi Provincial People's Hospital
Institution of Shaanxi Province Clinical Medicine Demonstration International
Science and Technology Cooperation**

№1

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PREFACE

Children is the hope of society, the future of world and mankind!

Strong children make the world strong! In order to strengthen international medical academic exchanges and improve the diagnostic and therapeutic skills of pediatricians, nurses and general practitioners around the world, the international Journal of Pediatrics was organized by the joint efforts of pediatricians and general practitioners from China, Georgia, Poland, The Czech Republic, Turkmenistan and India et al . This journal is of great clinical significance and academic value to promote international communication among pediatric medical staff and improve the diagnostic and treatment technology level of pediatric diseases. We hope that with our joint efforts and hard work, this journal will take root, sprout and grow in the world, bringing good news to the health of children around the world and benefiting children all over the world!

GEORGE CHAKHUNASHVILI (Georgia) and FUYONG JIAO (China)

INTERNATIONAL JOURNAL OF PEDIATRICS

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ADVANCED ARTICLE

SECURITY SCIENCE
IN PEDIATRICS

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(Tbilisi, Georgia)

ABSTRACT:

In the XXI century a great attention should be devoted to the problems of global heating, resulting in natural calamities and spread of different diseases. Therefore, measures against expected epidemic should be taken.

Science and security must be determined together with social-economic and ecological environment. Together with each of these two factors science may have both positive and negative sides. Thus, in my opinion, science of the XXI century should serve the mankind at high level of urbanization, safety of each citizen of this country and carry on preventive measurements against possible negative influence. Introduction of high technologies in investigations, existence of precise medical statistical database, creation of modern computer programs and their usage (prognosis of disease course, establishment of risk factors and groups, etc) – that is all on the basis of which it will be possible to solve many problems existing in the XXI century.

Keyword: Pediatrics, Security, Disease, Preventive measurements Children's rights.

Secondly, science and security must be determined together with social-economic and ecological environment. Together with each of these two factors science may have both positive and negative sides. Thus, in my opinion, science of the XXI century should serve the mankind at high level of urbanization, safety of each citizen of this country and carry on preventive measurements against possible negative influence. Introduction of high technologies in investigations, existence of precise medical statistical database, creation of modern computer programs and their usage (prognosis of disease course, establishment of risk factors and groups, etc) – that is all on the basis of which it will be possible to solve many problems existing in the XXI century.

Proceeding from the above-said, development of sciences and monitoring on them appear to be a main task, which takes into account creation of safe environment for human health, improvement of life conditions. At the same time it is necessary to carry out possible ecopathological preventive measures, which should be considered as a principal strategy of the XXI century.

At present it is doubtful that development of science is approaching its top heights. Particularly usage of gene engineering makes it possible to create a new human being. Today there exists a method for artificial fertilization and the newborns are already in evidence. In the XX century we became witnesses of human being's stepping out of the rocket into the space and even visiting other planets.

However it does not mean that science is developing in such a way, that every one can equally understand its development in different branches.

Let me explain how I personally interpret science and security.

First of all development of science should be based on the maintenance of bioethical standards.

Secondly, science and security must be determined together with social-economic and ecological environment. Together with each of these two factors science may have both positive and negative sides. Thus, in my opinion, science of the XXI century should serve the mankind at high level of urbanization, safety of each citizen of this country and carry on pre-

ventive measurements against possible negative influence.

Proceeding from the above-said our intention was to discuss several important topics regarding health care in order to carry on necessary preventive measurements.

A necessary condition for carrying on preventive measurements is a fundamental knowledge of the problem and striving for meaningful strategic directions, which of course is based on: a) precise medical statistics; b) higher medical technologies; c) modern computer treated analysis (on prognosis and new programs), which underlie our conclusions.

Each region of the world is characterized by peculiar situation-state in the sphere of public health care. In order to estimate this it is necessary to discuss:

- general situation in the region
- expected life span and death-rate
- expected span of healthy life
- classes of diseases, such as:

a) infectious diseases – tuberculosis passing through sexual way (including HIV/AIDS), malaria, diseases which might be prevented by means of vaccine prophylaxis (diphtheria, hepatitis, poliomyelitis)

b) non-infectious diseases (cardiovascular diseases, tumors, obesity, diabetes mellitus)

c) psychic health

d) accidents and traumas

And the most important thing today is Covid infections and fighting them.

For estimation of situation in public health in the region it is necessary to analyze data of separate groups of population: the I group comprises data about children's health. In this group death-rate of newborns and children aged 5 years are important. Neonatal mortality, especially at earlier stage, determines a general level of newborns' mortality. It is

clear, that in those countries, where mortality of newborns is high, its decrease may be achieved by reduction of mortality level in newborns, while decrease of mortality in newborns is achieved by attenuating of neonatal mortality level. While estimating children's health it is necessary to consider children's nutrition, including nursing during the first year of life and deficit of microelements in children's feeding; children's diseases (their course). All above mentioned indices depend on amount of the needed bed-places for children in hospitals, which should be considered together with social-economic and ecological conditions of the region.

At the same time, mortality rate in mothers, children immunization, carrying out preventive measures against tuberculosis and HIV/AIDS stipulate state of infant health.

Currently our research group conducts the project "Role of viral pathogens among infants with systemic infections" supported by the Georgian Research and Development Foundation (GRDF). Our US partner is the research group at the Department of Microbiology, Virology, Immunology and Molecular Diagnostics of the School of Medicine, University of Pittsburgh at Magee-Women's Hospital.

Political events of the last ten years adversely affected child health in Georgia. Currently the infant mortality rate in the country is very high and varies from 15 to 25 deaths per 1000 live births. In Georgia one of the most important causes of the infant death is the development of generalized infections. In the majority of such cases the causative agents are not being identified. As a rule, all newborns with a generalized infection with wide range of non-specific symptoms; including hyperthermia or hypothermia, jaundice, bleeding with associated coagulopathy, respiratory insufficiency, vascular instability, hepatomegaly, splenomegaly; are diagnosed as "neonatal sepsis" (without identification of etiology) and treated with broad-spectrum antibiotics. Despite this "empiric" treatment, the mortality rate for neonates with generalized infections of unknown origin is high, estimated to be over 65%. In addition, the "neonatal sepsis" is frequently associated with infections of central nervous system - meningitis and encephalitis, which makes prognosis even poorer.

Until now testing for viral infections in pediatric patients was ultimately rare, and included only serological testing, leaving physicians to treat patients with limited clinical information. Yet, some patients with generalized infection are likely to have a viral infection, a subset of whom has a treatable viral infection. Early identification of preventable or treatable viral infections is a key to reducing the low survival rate seen in this high-risk population.

Among the viral pathogens, members of the herpes viruses and enteroviruses play the most important role in the development of generalized infections in newborns.

Through our project we have estimated the prevalence of herpes viruses and enteroviruses among neonates with generalized infections, described clinical and immunological status of the infants by infection type; estimated survival, by infection type and clinical/immunological status; piloted the rapid and simple PCR based methods for screening and typing of viruses in neonates, which are based on the ultramodern molecular diagnostic methodology.

In parallel we are implementing the diagnostic and preventive measures for such an important infection as one induced by Human Immunodeficiency Virus (HIV). Until now in Georgia this infection was not seriously considered in paediatric clinical practice. Our activities in this field give us opportunity to perform the early diagnostics of this infection and through this contribute to the prevention of the HIV epidemic in our country.

Thus, all above mentioned is closely connected with social, economic and ecological factors, which will be discussed below. At the same time we can't avoid the problem of defence of children's rights, although all above mentioned indices concern this problem.

Since coming into force of convention of children's rights up today there has been some progress in the defence of children's rights. Some important steps have been made. A new legislation was developed with more refined international standards, such as additional proceedings of the convention of children rights about trade with children, children prostitution and pornography, use of children

Table 1

Indices of sick rate and morbidity degree among forced displaced persons from Abkhazia

	Total		Including 14 years old children	
	Total	New cases	Total	New cases
Infectious and parasitic diseases	5823	2935	14178	8432
Tumors	223	63	-	-
Diseases of endocrine system, nutrition disorders and metabolism	2048	706	946	604
Blood and hemopoietic diseases, separate disorders involving immune mechanism	933	339	1242	592
Psychical and behavioral disorders	1056	170	113	3
Diseases of nervous system	5921	1955	1346	542
Diseases of blood circulation system	10418	1835	318	39
Diseases of respiratory organs	14132	5662	19688	9825
Diseases of digestive organs	5564	1304	2995	1186
Diseases of genitourinary system	4522	1362	1219	505
Skin and subcutaneous cellular tissue diseases	2319	1066	1914	995
Diseases of osteomuscular system and conjunctive tissues	921	340	208	80
Congenital anomalies, deformations and chromosomal diseases	11	3	23	3
Some states induced in perinatal period	35	24	121	80
Symptoms, signs and divergence from the norm	84	74	72	42
Traumas, intoxications	924	790	523	374
In all	54955	18645	44905	23303

Source: Data of Health Care Ministry of Abkhazian Autonomic Republic

in armed conflicts. Highly important are the rights of children in conflict zones and I can't help dealing with it on the example of Georgia.

Demolition of the USSR and regaining of independence of Georgia have brought to its population political disorders, civil war and disorganization of economics. As a result of conflicts and separative movements in South Osetia and Abkhazia there took place fierce struggles and processes of forced migration. At present, as is known, Abkhazia and South Osetia are governed by de facto separative governments, which are not recognized by the International Commonwealth.

While considering data given in Table 1, it is clear that in 2002 as compared to 2001, sick rate among forced displaced persons decreased by 5,8%, and morbidity degree - by 33,6%. In spite of such a reduction among forced displaced persons sick rate is 1,93-fold greater, while degree of morbidity - 1,6-fold greater. In 2006 these indices were the same.

Especially high indices of sick rate and morbidity degree are observed according to the main following classes: in case of infectious and parasitic diseases sick rate is 3,6 fold and morbidity degree - 2,9 fold greater as compared to analogous medium indices of the country; blood and hemopoietic diseases - correspondingly 2,5 and 1,9 fold greater; diseases of nervous system and sense organs - correspondingly 2,4 and 2 fold greater; diseases of respiratory organs - correspondingly 2,4 and 1,3 fold greater; diseases of digestive organs - correspondingly 2,5 and 1,6 fold greater; diseases of genitourinary system - correspondingly 3,4 and 2,4 fold greater; skin and subcutaneous cellular tissue diseases - correspondingly 3,7 and 2,7 fold greater; traumas and intoxications - correspondingly 1,2 and 1,2 fold greater.

As regard the children, in 2002 sick rate of forced displaced children was 1,4 fold and morbidity degree 1,1 fold greater than those of analogous indices in the country, among them: infectious and parasitic diseases - correspondingly was 3,9 and 3,3 fold greater; blood and hemopoietic diseases - correspondingly 1,5 and 1,3 fold greater; diseases of nervous system and sense organs - correspondingly 2,6 and 3,7 fold greater; diseases of respiratory organs - correspondingly 1,4 fold greater; diseases of digestive organs - correspondingly 1,9 and 1,2 fold greater; skin and subcuta-

neous cellular tissue diseases - correspondingly 1,9 and 1,3 fold greater.

It is important that problems concerned with health, nutrition, education, as well as to defence and development of children are more acute in the zones of conflicts than in other regions of Georgia. The International Commonwealth had better expand its own role in these zones for solving the problems of defence of children's rights.

And indeed "Child has the right to be defended since embryo".

Let me come back to the following:

Several important International Meetings were held, such as: Yokohama World Congress held in 2001, which was directed against sexual exploitation of children for commercial reasons and a special session of General Assembly of UNO held in 2002 devoted to children. Obligations of governments and civil communities of different countries concerning defence of children's rights were corroborated at these meetings and measures for their fulfillment were taken.

Let me finish the above said by the words of Anders Johns (Secretary general, Interparliament Union) and Carol Belam (Executive director, Children Fund of UNO):

"In spite of the mentioned obligations and promises, children still suffer from violence, cruel treatment and exploitation. It is clear that our efforts are as necessary today as fifteen years ago. We will be able to create a suitable world for children in case if each child is protected from exploitation, violence, cruel treatment and ignorance.

Besides the above discussed problem of children's state, in order to estimate situation in the regions it is necessary to characterize groups of adults, women's health and aging, as well as groups of healthy persons.

While considering science and security, main determinants of health, particularly social-economical, should be noted. Health and development of the country, poverty, psycho-social factors, employment of population, education, general factors - these are the topics, which in cumulation creates one of the basic social-economic determinant of regions and separate states.

One of the main determinants of health is also a way of life, which consists of feeding, physical activity, smoking, alcoholism, drug addiction-toxemia.

With the support of UNICEF we have fulfilled a project "Social-psychological, medical-prophylactic and rehabilitation measures of children and adults in Penitentiary Institutions", one of the main goals of which was the study of drug addiction and toxemia problems in above mentioned contingent.

Data of clinical-laboratory and instrumental investigation in 417 children and adults have been analyzed. Questionnaire for Darvy and Bass aggression investigation, Shind test, Loosher colour test were used which permit to create a perfect "psychological portrait" of under age criminals with recommendations having proper practical significance. In future the latter will be a basis for creation of behavioral prophylactic model having a harmful influence on the society and on themselves.

Results of investigations carried out were analyzed by means of modern computer programs, involving psychological test-questionnaires and drawings in crayons.

Analysis of data obtained has shown that:

1. In children and adults of such category we deal with yet unformed person, subjected to definite changes.

2. While considering obtained results the I, II and III necessary stages were outlined, where:

The I stage stipulates pretrial period.

The II stage stipulates measures to be taken during trial.

The III stage - after being sentenced.

Most children formally refuse the fact of smoking, hashish and glue tasting, but it is not true. The majority of them before the arrest used different toxic substances (glue, petroleum), which need a great attention at the I-II-III stages.

Thus, investigations carried out have shown that there is a necessity of taking prophylactic measures against toxemia and drug addiction in children and adults in order to avoid formation of groups of persons committing a criminal offence.

An important determinant of health is physical environment, hygienic plan of action at present must be a strategic direction for all regions and countries. During last years quite new approaches and principles in health defence sphere were formulated in the documents and programs of WHO, including European Conferences on environment and health defence - Frankfurt (1989), Helsinki (1994) and London (1999).

According to these principles, sectors of environment and health defence were

imposed responsibility for elaboration and fulfillment of such mechanisms in human health and environment defence policy and spheres of its management, which in respect of ecology should provide a stable development, effective prevention of harmful environmental factors on human health and control on it.

Taking into account the fact, that the way and conditions of life, environmental and genetic factors have a great effect on human health, while share of health defence is only 12-14%, a great attention of WHO to the problems of environmental and health defence becomes more comprehensible.

Taking into account the fact that in every state above mentioned principles and initiatives must be recognized, the laws "About environmental defence" and "About health defence" should determine competencies of corresponding ministries in the sphere of provision of safe environment for human health.

At present considering current demands in many countries elaboration of sanitary-hygienic norms and rules determining safe environment has begun and main standard documents have already been prepared, including norms of radiation safety, hygienic standards of electromagnetic irradiation influence, hygienic standards determining safety of drinking and recreation water, atmospheric air, soil and food-stuffs, hygienic standards of pesticide content in environmental objects, hygienic requirements for labor conditions and safety, etc. By fulfillment of demands of these documents it will be possible to prevent an influence of harmful factors on health of country population.

At the same time, to create a safe environment for human health appears to be an important task for the economics of all countries, especially for countries with transitional economics. To solve this problem is possible only by joint efforts of different ministries and organizations, as well as by self-governmental institutions and board of administration.

That's why their goal must be the elaboration and fulfillment a national project for environmental hygiene, study and estimation of problems existing in the spheres of health-care and environmental defence, as well as determination of priority directions and actions in order to solve them.

It should be considered a complete aspect of environment and health de-

fence taking into account: policy in the sphere of environment and health defence, management of environment improvement, quality of water and air, quality and safety of food-stuffs, stable residues and soil contamination, ionizing and non-ionizing irradiation, natural calamities, industrial accidents, etc.

While considering each of these questions one should take into account social-economic, climate-geographical, demographic and other factors of the country, particularly: estimation and analysis of health risk connected with environmental harmful factors; determination of priority problems to improve environmental defence; formulation and accomplishment of concrete measures for prevention of harmful environmental factors affecting human health and sanitary and epidemic situation.

All above-said follows from the conception of interconnections between human activities of different kinds, its action on biosphere, as well as environmental influence on human health.

Besides, there must be elaborated and accomplished such a policy in the sphere of environmental and health defence, which, in regard to ecology, provides a stable development, effective prophylaxis of environmental factors having a harmful effect on human health and its control, as well as creation of available safe environment based on principles of justice.

The following indices should be studied which will elucidate:

a) effect of environmental factors on indices of human health state; b) reveal territories and regions, which are distinguished by a high level of pollution and harmful influence on human health.

It is necessary to consider and estimate the following:

a) systems of management of environment hygiene;

b) resources for accomplishment of policy of environmental and health defence

c) besides, concrete priority factors of the environment, particularly:

Water. Problems of improvement of water-supply of populated places as well as questions of sanitary state and measures for prevention from pollution of seaside regions and other recreation objects.

Air. Degree of atmospheric air pollution of populated places and sanitary defence measurements.

Stable debris and soil contamination. Questions of chemical safety and defence of the environment (soil, air, water) of inhabited places from domestic agricultural and industrial toxic debris.

Food-stuffs. Measures for reducing risk of influence on health; state conception of safe feeding of population is presented.

Ionizing and non-ionizing irradiation. Radiation background. Sources of ionizing and non-ionizing irradiation existing in the country. Measures to be taken.

Natural calamities and industrial accidents. Topics of readiness for expected natural calamities and industrial accidents as well as readiness for prophylaxis and their liquidation.

Industrial and domestic environment. Labor conditions of employed population, prophylactic measures for professional diseases, traumatism and poisoning; Creation of physical, social and psychological environment desirable for health in inhabited places.

Towns and large populated places. Hygienic-ecological problems created in big towns, ecopathology with preventive measures.

Temperature of the environment - In the XXI century a great attention should be devoted to the problems of global heating, resulting in natural calamities and spread of different diseases. Therefore, measures against expected epidemic should be taken.

Accomplishment of above said may be possible only on the strength of cooperation and intersector cooperation of relevant ministries, departments, institutions, self-governmental institutions and boards of administration and non-governmental organizations with a broad participation of population. A special role must be played by self-governmental institutions and boards of administration, which according to recommendations of WHO must elaborate and accomplish plans for regions and towns, separate projects for improvement the environment and public health. In order to realize concrete priority measures in most countries (especially, in the post soviet space) taking into account a complicated social-economic situation, it will be necessary to search different sources for financing, including assistance of international organizations, funds and donor countries. As to our region, it is necessary to have close contacts with South Caucasus and the Black Sea

Basin countries, first of all to solve such problems as water and health, contamination of the Black Sea, problems of the Mtkvari river basin, etc.

Introduction of high technologies in investigations, existence of precise medical statistical database, creation of modern computer programs and their usage (prognosis of disease course, establishment of risk factors and groups, etc) – that is all on the basis of which it will be possible to solve many problems existing in the XXI century.

Proceeding from the above-said, development of sciences and monitoring on them appear to be a main task, which takes into account creation of safe envi-

ronment for human health, improvement of life conditions. At the same time it is necessary to carry out possible ecopathological preventive measures, which should be considered as a principal strategy of the XXI century.

Let me finish my report by the words of Catholicos-Patriarch of All Georgia, His holiness and Beatitude, Ilia II:

“Life of human-being is an examination. It is suffering and we must endure it with dignity. Every human being created by the God is an image (icon) of Him, but we must remember that human being is always followed by a sin

committed by Adam and Eve. A human being is helpless and he needs the grace of holy spirit; he needs help of church as it is the strongest ecclesiastical force; church is the abode where a human being gets grace of holy spirit. That’s why our ancestors blessed each other so “Rejoice on earth and in heaven“. The only condition of this appears to be closeness to the Lord, fulfillment of His supreme will. We must hasten to do good, as nobody knows about that wonderful and secret day when a man will appear before the Lord, kindness done by us goes to the Lord”.

“CHILDREN’S RIGHTS MUST BE DEFENDED SINCE EMBRYO”

ORIGINAL ARTICLES AND SCIENTIFIC ACTIVITIES IN PEDIATRICS

EFFECTIVE TREATMENT AND RECOVERY OF SARS-COV-2 INFECTED INFANT/CHILDREN IN A FAMILY CLUSTER OUTBREAK

SHORT TITLE: TREATMENT OF SARS-COV-2 INFECTION IN FAMILY CLUSTER OUTBREAK

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ABSTRACT

Purpose: This study aimed to diagnose coronavirus infection in children based on clinical, laboratory, imaging features and its treatment. **Methods:** Design: Diagnosis and treatment. Setting: Henan Provincial Children's Hospital, Henan Zhengzhou 450018, China. **Subjects:** Five patients including 2 males and 3 females aging between 5 days to 8.6 years. **Intervention:** All patients underwent throat swabs and blood nucleic acid tests, chest radiography and computed tomography (CT) examinations. The patients were treated with interferon nebulization, oral Chinese medicine, ribavirin and lopinavir/ritonavir orally (1.5ml, 2 times / d×5d). **Main outcome measure:** We considered gender, age, and epidemiology and laboratory examination data. **Results:** Patient 1 showed reduction in hemoglobin and erythrocytes with 22 time increased dose of D2-polymer compared with other four patients. The blood cell sedimentation rate in patient 1 was 40 while in others it was normal. The C-reactive protein, calcitonin and influenza-A, B virus were normal, while SARS-CoV-2 nucleic acid by throat swab and blood tests were positive in all patients. Three of the chest radiographs showed rough lung texture, but CT case 1 showed small patchy shadows in multiple sites, cases 2 and 3 showed patchy shadows of the right lung, and cases 4 and 5 were normal. All five patients cured, discharged, and followed up were normal. **Conclusions:** Other than critical case, the symptomatic treatment was given with a good prognosis. Attention should be paid to avoid transmission among family members, and timely monitoring and evaluation of the pediatric status of infected families for early detection and diagnosis.

Keyword: Children, Novel coronavirus, Infection, Diagnosis

INTRODUCTION

The data on epidemiological and clinical characteristics in pediatric patients are limited. The cluster infection of COVID-19 in a family of five including 10-year children was reported from Wuhan in late January[1].

Compared to adults, the clinical manifestations and lung CT abnormalities of patchy opacities are more modest in children[2]. In China, as of 7 February 2020, this new form of COVID-19 pneumonia was reported in 285 children, including 10 newborns[3, 4].

The new coronavirus (SARS-CoV-2) has caused huge losses to human life and the economy. The number of confirmed COVID-19 cases and deaths has been increasing in the many countries of the world, but data on the epidemiological and clinical characteristics of pediatric patients are limited. Children have become susceptible to SARS-CoV-2 infection due to immature immune function. As of 24: 00 on February 7, 2020, 285 children with new-type coronavirus pneumonia were reported nationwide, including 10 new-

borns. Epidemiological investigations suggest that the population is generally susceptible to the new coronavirus, and some children have a clear family gathering history [3, 4].

National Health Commission of the People's Republic of China, 'Notice on Issuing a COVID-19 Infected Pneumonia Diagnosis and Treatment Plan (Trial Version 7)' on 3 March 2020, mentions that children, infants, and neonates are also susceptible to the new coronavirus. They may present with atypical symptoms of malaise, shortness of breath, and the gastrointestinal manifestation of vomiting and diarrhea. Yet, most of the affected children presented with mild disease with low fever and fatigue without clinical features of pneumonia[5].

In this paper, we aim to share our experience of clinical course and management of COVID-19 in newborn and children treated at the specialized referral children hospital in Henan, China.

METHODS

Subject Retrospective case summary
Five children who were diagnosed with SARS-CoV-2 new coronavirus infection through nucleic acid testing and other treatment in Henan Provincial Children's Hospital (Children's Hospital Affiliated to Zhengzhou University) from January to February 2020 were enrolled as research subjects. Five patients including 2 males and 3 females aging between 5 days to 8.6 years were treated. Among them, one was asymptomatic, three were mild, and one was of critical illness. This study was ap-

Table 1

Clinical profile of Children with COVID-19 treated at Henan Children's Hospital, China, during January to March 2020.

No.	Gender	Age	Adm.	Clinical category	Epidemiology			Main Clinical Manifestations				Fever (d)	Hospitalized (d)
					Family +ve	Wuhan related	Exp. to Diag. (d)	Fever (°C)	Sneeze	Cough	Vomiting/diarrhea		
1*	M	5D	2/2	Critical	5	Y	5	38	N	Y	N	18	29
2	F	6M	30/1	Mild	3	Y	4	38.1	N	Y	N	5	16
3	M	7Y6M	19/2	Mild	2	Y	20	Normal	N	N	N	N	16
4**	F	6Y7M	2/2	Mild	5	Y	8	38.6	N	N	N	2	15
5**	F	8Y6M	2/2	Mild	5	Y	9	37.4	N	N	N	2	15

No.= case number, Adm= admission date, family +ve= family members tested positive for COVID-19, expo to diag= exposure to diagnosis days, Vom/diarr= vomiting and diarrhea, Fevr=fever persisting for days, Stay=hospital stay in days, Y=yes, N=no.

*Case 1. The parents lived in Wuhan, Hubei and returned to Xinyang, Henan on 22 January 2020. Same day in afternoon of returning, mother felt cold and lethargic but took it at exertion from travel. She had cesarean delivery on 31 January, G1P1, 38+5 weeks. She had positive nucleic acid test for COVID-19 on 1st February.

** were siblings

proved by the Ethics Committee of Zhengzhou Children's Hospital and informed consent was obtained from the children's families.

METHOD

1. Diagnostic criteria. (1) Both throat swabs and blood nucleic acid tests were positive. (2) The diagnostic criteria were conducted following the first edition of the Chinese Journal of Pediatrics "Children's 2019 New Coronavirus Infection Diagnosis and Prevention Suggestions" on a trial basis.

2. According to the ICD-10 number, query and retrieve clinical data through electronic medical records.

The gender, age, epidemiology, laboratory examination, and imaging data (chest X-ray and CT) of the children were collected and analyzed.

3. Clinical types according to the infection status of children and the clinical characteristics of a confirmed diagnosis, they are divided into five types [5,6]: asymptomatic infection, mild, common, severe, critical.

Statistical methods

Descriptive analysis, measurement data are expressed as M (range).

RESULTS

General Information

There were five children from four families, 3 girls and 2 boys, age minimum of 5 days (case 1) to a maximum of 8 years and six months (case 5). Case 4 and 5 were siblings both female, Table 1. Epidemiological findings revealed cluster infection in families involving 20 members in total, including grandparents, parents, and sisters of the infected child who presented to the hospital. Fever was seen in four children (except case 3), with a maximum of 38.6 °C. None had runny nose, vomiting, or diarrhea. The median hospital stay was 16 days, highest of 29 days (case 1) and lowest 15 days (case 4 and 5), Table 1. The minimum age is 5 days after birth. The parents lived in Wuhan until the child was born. Department G1P1, born 38 +5 weeks after cesarean section, A's score, and other unknown. Before admission, the parents of the child returned to Xinyang, Henan from Wuhan on January 22, and the mother of the child felt cold and lethargic in the afternoon. A cesarean section was performed on January 31, and a new coro-

Table 2
Laboratory examination of 5 children COVID-19 treated at Henan Children's Hospital, China, during January to March 2020

№	Blood Tests					
	WBC ($\times 10^9/L$)	N (%)	L (%)	RBC ($\times 10^{12}/L$)	HGB (g/L)	PLT ($\times 10^9/L$)
1	12.95	0.505%	0.495	3.07	101 g/L	356
2	4.79	0.175%	0.772	5.05	127 g/L	451
3	9.02	0.613%	0.319	5.23	148 g/L	447
4	4.82	0.427%	0.247	4.52	126 g/L	283
5	5.02	0.388%	0.271	4.60	135 g/L	261

No.= case number, WBC= White blood cells, N= lymphocytes, L= neutrophils RBC= Red blood cells, PLT= Platelets

navirus infection was confirmed on February 1 with a positive nucleic acid test, indicating that the mother had a new coronavirus infection during childbirth.

Although the new coronavirus infection occurred only five days after birth, it suggested that it was not caused by vertical infection of mothers and infants. Because the mother was infected with the new coronavirus before cesarean section.

Table 1.

Clinical Manifestations and Laboratory Tests

Laboratory data are shown in Table 2 & 3, WBC was highest $12.41 \times 10^9/L$ (case 1) and lowest 4.79 (case 2). The lymphocyte percentage was high in case 1 and 2, and low in the other three cases ranging from 24.7-31.9%.

Hemoglobin was lowest at 10.1g/L and red blood cells $3.07 \times 10^{12}/L$ in case 1. Platelet was $>440 \times 10^9/L$ (in two cases: case 2 and 3). Alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and creatine kinase isoenzymes (CK-MB) were normal or not requested in all five cases. The D-dimer (D-2 polymer) was high at 22.48 ug/L in case 1 more than 50 times than others (lowest 0.2 in case 3).

Chest x-ray showed increased lung markings in case 1, 2, and 3. Chest CT showed multiple small patches in both lungs in case 1, Figure 1. In case 2 and 3, patches were seen in the right lungs on chest CT. The siblings, case 4 and 5 had normal CT and chest x-ray findings, Table 4.

TREATMENT

The treatment, heart failure was seen in the 5-day age neonate, case 1, requiring ICU care with mechanical ven-

tilation and immunoglobulin. Remaining 4 cases were mild and managed in a high dependency unit without ICU or ventilation. Supportive care with nebulization containing interferon α -2b was given to all five children. Oral Chinese medicine was used in all. Ribavirin was used in four children. Case 1 and 2 received lopinavir /ritonavir oral 1.5ml, 2 times/d for 5d. Glucocorticoid and oseltamivir were not used in any children, Table 5.

The outcome was the full recovery in all five children. Before discharge, all tested negative for the COVID-19 nucleic acid test, Table 6. The family was advised to continue to separate the child and observe at home for two weeks after the discharge. At two weeks regular follow all were doing well.

DISCUSSION

Familial cluster infection 5 children from four family epidemiology suggest a family cluster infection, of which 20 family members were involved in the infection. Including grandparents, grandma, father, mother, and sister. Among them, the neonates were critically ill only 5 days after birth. Before birth, his parents were in Wuhan. After the mother became infected with the new coronavirus pneumonia, she had a fever and then had a cesarean section. A positive checkup confirmed the diagnosis.

Clinically, fever is the main manifestation. Four children (80%) had a fever ranging from cough, asthma, vomiting, and diarrhea. This shows that fever is the most common manifestation of neonatal coronavirus infection in children. It's also a signal and a clue. It is the first performance that should be taken seriously. Italian studies report that fever is the most common manifestation of 83% - 98%, while cough and shortness of

Table 3

Laboratory examination of 5 children COVID-19 treated at Henan Children's Hospital, China, during January to March 2020.

No	CRP (mg/L)	PCT (ng/dL)	ESR (mm/h)	flu virus A/B	ALT (U/L)	AST (U/L)	LDH (U/L)	CK MB (U/L)	D-2 polymer	Chest radiograph	Chest CT
1	<0.5	0.092	40	NA	46.7	37.8	NA	48.3	22.48	Rough lung texture	Multiple small patches
2	0.5	0.11	11	-	21.8	55.3	NA	NA	0.4	Rough lung texture	Multiple small patches
3	<0.5	0.039	12	-	48.4	32.8	261.3	14.7	0.2	Rough lung texture	Patchy shadow of right lung
4	NA	NA	NA	NA	NA	NA	NA	NA	NA	Normal	Normal
5	NA	NA	NA	NA	NA	NA	NA	NA	NA	Normal	Normal

No.= case number, CRP= C-reactive Protein, PCT= Procalcitonin, ESR= erythrocyte sedimentation rate, ALT= Alanine aminotransferase, AST= aspartate aminotransferase, LDH= lactate dehydrogenase, CK-MB: Creatine kinase- myocardial band, D-2= D-dimer (D-2 polymer), NA= not applicable.

breath account for 31% - 55%. None of the 5 children had congenital, genetic, and metabolic diseases[6, 7, 8, 9].

According to its symptoms and clinical manifestations, it is divided into an asymptomatic infection, mild, common, severe, and critical. Studies suggest that children with a new type of coronavirus infection have five clinical characteristics. First, the number of infections is smaller than that of adults. Second, symptoms and clinical manifestations are lighter than those of adults. Third, there are fewer complications than adults. Fourth, recovery is faster than that of adults, and fifth have a better prognosis. This may be related to less exposure of children than adults, pediatric immune function is not yet fully developed, pediatric infections are mild and inaccurate, and therefore, the diagnosis cannot be found in time and is easily missed.

Five cases had family members with a history of infection. Fever is the main symptom of most children. Except for Example 3, fever is low to moderate, with a maximum body temperature of 38.6. The clinical and immunological characteristics of children need attention, and further research and discussion are needed. One patient in this group had no clinical manifestations despite a nucleic acid test and a family member who was

diagnosed with a new coronavirus infection. It should be noted that children with asymptomatic infection should be vigilant because those with no symptoms or mild symptoms are likely to become a hidden source of infection that should be paid attention to. It has been reported that most of the early lymphocytes were reduced in adults and lower in 4 cases. Leukocytes in children under 5 years of age have two crosses. Lymphocytes are normally higher than neutrophils. So if the lymphocytes decrease, it may be related to viral infection.

Increased D-dimer is an indicator of serious infection. The D-dimer in this group of cases was as high as 22.248. It was 22 times higher than in other cases, but there was no significant difference between C-reactive protein(CRP), procalcitonin(PCT) in mild and critical illness. In adult patients, AST, ALT, LDH, isoenzymes, etc. increased, but no significant increase in children in this group. A positive nucleic acid test is an important basis for the diagnosis of new crown infection. In this group of 5 children, throat swabs, blood nucleic acid tests were positive twice, and no negative children. The patient was discharged from the hospital with a negative secondary test and continued to be separated and observed at home for two weeks after discharge [3, 7].

It has been reported that the nucleic acid test may be negative in the early stage, so the chest radiograph and CT of epidemiological history and symptoms suggest that children with new crowns should be repeatedly tested for nucleic acid to avoid missed diagnosis. Negative throat swabs but positive anal swabs have been reported to indicate a long period of exclusion of the virus from the intestinal tract. Chest radiographs of 3 patients in this group showed rough lung texture, but CT examination showed patchy consolidation shadows in multiple parts of both lungs and right lung.

It shows that chest CT is earlier and more diagnostic value than chest radiograph. Given the low sensitivity of nucleic acid detection, to prevent missed diagnosis, epidemiological and clinical manifestations should be combined, and combined diagnosis of nucleic acid examination and chest CT should be used to reduce missed diagnosis [8].

In terms of treatment. Because children with neo-crown infections are less ill and have a better prognosis, they are mainly family-gathered. For ordinary, asymptomatic, mild cases, a special medication is not emphasized. Except for case 1 who was treated in the ICU in the group, the remaining 4 cases were closely observed after hospitalization, and they were cured after being supported by symptomatic treatment. No special changes were observed after two weeks of follow-up. Example 1, the patient recovered and was discharged from the hospital despite the onset of disease on 5 days after birth and treatment with mechanical ventilation. The application of antiviral drugs such as ribavirin in children with new crown infec-

Table 4

Imaging (chest X-ray, chest CT) of 5 children with COVID-19 treated at Henan Children's Hospital, China, during January to March 2020

No	Sex	Age	Chest x-ray increased lung marking	Chest CT multiple small patches
1	M	5d	Y	Y both lungs
2	F	6m	Y	Y right lung
3	M	7y6m	Y	Y right lung
4*	F	6y7m	Normal	Normal
5*	F	8y6m	Normal	Normal

No.= case number, M= male, F= female, Y= yes, * were sibling

tion suggests that further studies on efficacy, safety, and toxic side effects are needed. Patients 1 and 2 orally took lopinavir/ritonavir orally (1.5ml, 2 times/d×5d)antiviral treatment. None of the 5 patients received oseltamivir phosphate [4, 6, 8, 10, 11].

Except for neonates in this group, the remaining four cases were not treated with antibiotics, and emphasis was placed on avoiding blind or incorrect use of antibacterial drugs. Reasonable selection of antibiotics should be based on bacterial infection and bacterial culture and drug sensitivity tests. For critically ill patients, a short course of small doses of gamma ball and glucocorticoid can be given. The application of traditional Chinese medicine should be treated with individualized syndromes according to the age, physique, and condition of the child. It is recommended to take traditional Chinese medicine instead of injecting traditional Chinese medicine preparations.

α-2b interferon nebulization, as a medication for respiratory diseases, is currently widely used, but the clinical efficacy of novel coronavirus infection is still lacking theoretical and clinical evidence of rigorous scientific research such as randomized double-blind placebo control. Therefore, further clinical rigorous scientific research is needed to provide scientific theoretical and experimental evidence for clinical applications. Moreover, atomization may increase the risk of aerosol infection, which deserves further discussion and discussion.

CONCLUSION

Conclusions: Other than critical case, the symptomatic treatment was given with a good prognosis. Attention should be paid to avoid transmission among family members, and timely monitoring

and evaluation of the pediatric status of infected families for early detection and diagnosis.

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Declaration of Interest:

None

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None

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Table 5

Treatment of 5 children with COVID-19 treated at Henan Children's Hospital, China, during January to March 2020

No	Heart failure	ICU	Mechanical ventilation	Supportive oxygen therapy	Nebulized inhaled interferon alpha-2b	Rib-avirin	Lopinavir / ritonavir	Oseltamivir	Cefoperazone	Glucocorticoid	Immunoglobulin (IVIG)	Chinese herbal medicine
1	N	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y
2	N	N	N	N	Y	N	Y	N	N	N	Y	Y
3	N	N	N	N	Y	Y	N	N	N	N	N	Y
4	N	N	N	N	Y	Y	N	N	N	N	N	Y
5	N	N	N	N	Y	Y	N	N	N	N	N	Y

No.= case number, ICU= intensive care unit, Y=yes, N=no

CORONAVIRUS DISEASE (COVID-19) SITUATION IN MONGOLIA

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SUMMARY

As a developing country, the government takes various actions to combat COVID-19 successfully. All imported cases are under control. But because of the expectation of more people returning from overseas, it's still a great threat to our population. And the economic situation is getting worse because of all kinds of lockdown.

OVERVIEW

Mongolia is located between Russia to the north and China to the south, where it neighbors the Inner Mongolia Autonomous Region. Total population in Mongolia is about 3.3 million and nearly half of the people live in the capital, Ulaanbaatar, and in other provincial centers. About two-thirds of the total population is under age 30, 36% of whom are under 141.

It is imperative for Mongolia to take COVID-19 seriously because of its vulnerability. The rate of infection of COVID-19 pose a great threat to Mongolia medically, economically, and socially. The first case of COVID-19 in Mongolia confirmed on March 10, was a French company employee who traveled into Mongolia from Russia.

As of May 18, 2020, there have been no confirmed cases of community transmission and there are 1623 people in quarantine²; however, the numbers are expected to grow as Mongolians are expected to return home from abroad.

SITUATION OF COVID-19

TOTAL CASES: 140 (March, 10-May, 18)
RECOVERED: 24
DEATH: 0
IMPORTED CASES: 140
NO LOCAL CASES REPORTED.

Majority of cases (about 80%) are university students who returned from overseas. They are often healthy and with no other comorbidities. 5 children (aged 8-16) and 2 pregnant women are confirmed for COVID-19.

About 28% of cases are mild or with no symptoms, 50% are moderate, and 21% of cases are severe².

Government strategies for combating COVID-19:

- Closed all schools and kindergartens starting from January 25. The closures were originally intended to last a month but were later extended to May 31. All classes are now conducted via TV and the internet.

- All public events including conferences, sports, and festivals have been canceled across the country, while all ed-

ucational institutes are to remain closed until 31 May.

- All sport clubs, night clubs, karaoke are closed and only restaurants, stores close at 22: 00 pm.

- Stores and public places don't serve if a person didn't wear a mask.

- The government closed the border with China and all air traffic was stopped. All passengers who arrived to Mongolia on special chartered flights from other countries were screened and stay into a 21-day quarantine.

- Canceled the national holiday Tsagaan Sar, the Mongolian lunar new year.

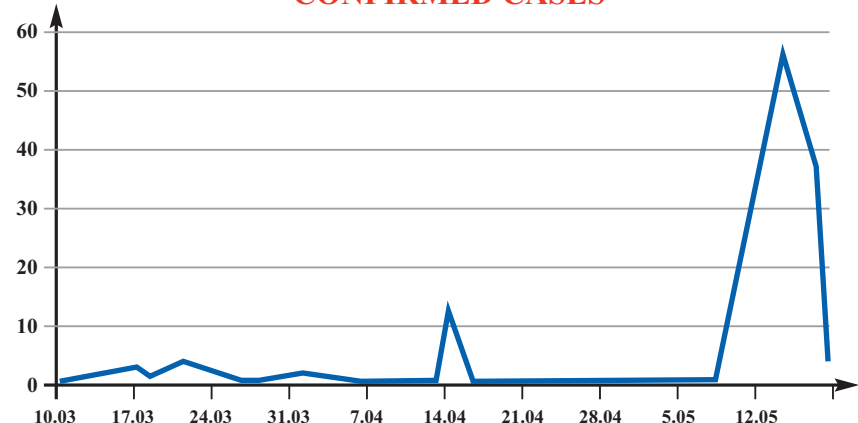
- Readiness for COVID-19 transmission, all stages of hospitals preparing for medicine, medical staffs and other supplies.

- For health emergency preparedness, organized 2 days of simulation exercise.

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CONFIRMED CASES



CLINICAL MANAGEMENT OF CHILDREN WITH KAWASAKI DISEASE DURING THE SITUATION OF PREVENTION AND CONTROL OF COVID-19

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SUMMARY

In December 2019, a new coronavirus (2019-nCoV) infection outbreak in Wuhan, Hubei Province, China has spread to all parts of the country. Epidemiology shows that the population is generally susceptible to the virus, and patients with basic diseases are severe, High-risk groups of critically ill patients, and the number of children and adolescent infection cases is increasing. Children with Kawasaki disease have poor basic conditions. After 2019-nCoV infection, they will bring serious challenges to the diagnosis and treatment of these children. Combining the clinical characteristics of children with 2019-nCoV infection and the diagnosis and treatment of children with Kawasaki disease, the clinical management recommendations for children with Kawasaki disease 2019-nCoV infection are presented here for clinical reference.

Keyword: Kawasaki disease; new coronavirus pneumonia; children

1. OVERVIEW:

In December 2019, an outbreak of new coronavirus pneumonia (COVID-19) broke out in Wuhan, Hubei Province, China, and quickly spread to all parts of the country. The "Diagnosis and Treatment Plan for New Coronavirus Infected Pneumonia (Trial Version 4)" issued by the National Health Commission For the first time, children were included in the susceptible population, and it was mentioned that the symptoms of children's cases were relatively mild. Chinese Journal of Pediatrics also published "Diagnosis and Prevention of Children's 2019 New Type of Filling Virus Infection/Pneumonia (Trial First Edition)". With the increase in the number of infection cases, reports of children's illnesses have gradually increased, and the prevention and control situation for children groups is still grim. It has been reported that 10% of COVID-19 patients are accompanied by Kawasaki disease and even the formation of coronary aneurysms.

Since April this year, there have been cases of multi-system inflamma-

tory syndrome (also known as "MIS-C") similar to Kawasaki disease in children in the United Kingdom, Italy, the United States, and South Korea.

Italy's Bergamo is a severely affected area with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic. In the past month, there has been a concentrated outbreak of Kawasaki disease in this area. Recently, researchers have evaluated SARS-CoV-2 The incidence and characteristics of Kawasaki-like diseases during the epidemic. Studies suggest that during the epidemic of New Coronary Pneumonia, the incidence of Kawasaki disease in Bergamo, Italy increased by 30 times, and that during the epidemic, the children were older, had a higher rate of cardiac involvement and were characterized by macrophage activation syndrome.

2. THE DISCOVERY AND DEVELOPMENT OF KAWASAKI DISEASE

Kawasaki Tosaku (Tomisaku Kawasaki) reported KD in Japan for the first

time in 1967 through descriptive statistics on the clinical manifestations of 50 children, but the etiology and pathogenesis of KD are still unclear. According to reports, children of almost all ethnicities have KD, and it has increased year by year in recent years. In the long run, undiagnosed and untreated KD in childhood may affect health care delivery systems in developing countries [1]. Coronary artery injury is the most serious complication of KD. The incidence of coronary artery injury in children with untreated or untreated KD is as high as 20% to 25% [2]. In developed countries, KD has replaced rheumatic fever as the main cause of acquired heart disease in children. This study retrospectively analyzed the clinical data of children with KD combined with coronary aneurysms and summarized their clinical features to improve clinicians' understanding of KD in coronary aneurysms.

3. BRIEF INTRODUCTION OF KAWASAKI DISEASE

1) Concept and clinical performance

Kawasaki disease (KD), also known as mucosal skin lymph node syndrome, is an acute febrile rash disease characterized by systemic vasculitis, which mainly occurs in children under 5 years of age. The diagnostic criteria mainly include fever lasting more than 5 days, and have 4 or more of the following 5 main clinical manifestations: 1. Abnormal lips or oral mucosa, including lip congestion and chapped, diffuse mucosa of the oral mucosa, protruding tongue, hyperemia Strawberry tongue". 2. Bilateral conjunctival hyperemia occurs within 3-4 days after the onset

of the disease. The purulent discharge is dissipated after heat remission. 3. Cervical lymph nodes are swollen, which can be unilateral or bilateral, greater than 1.5cm, hard and tender, but the surface is not red and there is no suppuration. It appears at the beginning of the disease and dissipates when the fever subsides. 4. Abnormal limbs, acute edema and palmar-plantar erythema in the hands and feet during the acute phase, membranous peeling occurs at the junction of the finger, toe, and skin at the recovery stage, and there is a transverse groove in the finger and toenails. In severe cases, the finger and toenails can also fall off. 5. Abnormal skin. Polymorphic skin spots and scarlet fever-like rashes often appear in the first week, and redness and peeling of the perianal skin may also occur [16]

2) Review of Kawasaki disease:

Kawasaki disease generally occurs in all seasons. It is necessary to master and learn the relevant professional knowledge about the disease, and make timely preventive and nursing measures to reduce the troubles and injuries caused by the disease to children. So, should Kawasaki disease be reviewed forever? Kawasaki disease is a manifestation of vasculitis, the most common acute multi-system inflammatory disease affecting infants and young children. The disease may be characterized by high fever, red rash on the mouth and throat, inflammation of the mucous membranes, and swelling of the lymph nodes (lymph nodes). In addition, individuals with Kawasaki disease may develop arteries that carry blood to the affected coronary arteries, heart muscle (myocarditis), the inflammatory wall of the heart muscle (coronary arteritis), and associated widening or bulging (aneurysm) Inflammation [12], and/or other symptoms and findings.

3) Kawasaki disease review schedule:

① Review of no coronary artery disease

Children with normal coronary arteries in the acute phase of Kawasaki disease undergo a comprehensive examination (including physical examination, electrocardiogram, and echocardiography, etc.) at 1, 3, 6 months, and 1 to 2 years after discharge.

In the first three months of Kawasaki disease, you need to review whether the erythrocyte sedimentation rate, C-reactive protein, and myocardial en-

zymes are normal. At the same time, you need to check the head and other hemangiomas for physical examination.

② Review of coronary aneurysm lesions

Coronary aneurysms occur in 15% to 25% of children with Kawasaki disease who have not been effectively treated. Long-term follow-up should be followed closely, once every 6 to 12 months, monthly review, and coronary angiography if necessary.

Coronary aneurysm disappears spontaneously more than 2 years after the disease, but often has abnormalities such as thickening of the wall and weakening of the elasticity.

Large aneurysms are often not easy to completely disappear, often causing thrombosis or stenosis.

4) After recovery from Kawasaki disease

After the recovery of Kawasaki disease, the heart problems must be reviewed regularly within two to seven months [5]. It is necessary to check the electrocardiogram and electrocardiogram. This is necessary because many Kawasaki diseases are caused by incomplete treatment. Late complications [14].

In particular, cardiovascular complications: coronary artery dilation, severe aneurysm prolongation for several years. After recovery, it is normal three times in a row, and it is checked again in 3 to 5 years to check whether there are sequelae.

4. BRIEF INTRODUCTION OF NEW CORONAVIRUS

At the end of 2019, since the emergence of a new coronavirus (SARS-CoV-2, previously known as 2019-nCoV) infection in China, the development of the epidemic has attracted worldwide attention. The World Health Organization (WHO) has paid close attention to it, and many expert meetings have finally concluded that the epidemic is an "emergency public health event of international concern." Since the epidemic situation was determined, the whole country has made prevention and control of the epidemic situation and protection of the people's lives the top priority of the entire party and the country. China has taken serious and responsible positive measures, even at all costs, to strictly prevent and control, and to control the spread of the epidemic to the smallest extent.

The latest World Health Organization epidemic report focuses its technology on the zoonotic component of the new coronavirus. There is increasing evidence that the 2019 new coronavirus is associated with other known coronaviruses circulating in bats, proving that it is associated with the bat subspecies *Phinolophus* bat. The International Committee on Taxonomy of Viruses (ICTV) stated that the new coronavirus was named "SARS-CoV-2" (Severe Acute Respiratory Syndrome Coronavirus 2). The zoonotic transmission of SARS-CoV and SARS-CoV-2 and the clinical manifestations of human infection with SARS-CoV-2 have yet to be confirmed, highlighting the need to study the entire virus group. [3].

1) Epidemiological characteristics of new coronary pneumonia:

Source of infection: The source of infection seen so far is mainly patients infected with new coronavirus. Invisible infections and asymptomatic infections may also become the source of infection.

Transmission route: droplets and contact transmission through the respiratory tract are the main transmission routes. In many places, new coronaviruses have been detected in the stool of diagnosed patients, and there is a risk of fecal-oral transmission. Aerosol transmission refers to the nucleus composed of the protein and pathogens left by the water droplets lost in the air suspension process, forming the nucleus of the aerosol, which can float to a distance through the form of an aerosol, causing long-distance transmission. There is currently no evidence that the new coronavirus is transmitted by aerosol. Mother-to-infant transmission has reported that the mother is a patient diagnosed with new coronavirus pneumonia, and the throat swab virus nucleic acid is positive in the newborn 30 hours after birth, suggesting that the new coronavirus may cause neonatal Gan Ruo-nan through mother-to-child transmission. Of course, more are needed. Scientific research confirmed. The transmission routes such as the digestive tract have yet to be clarified. [11]

Susceptible crowd: The crowd is generally susceptible. The elderly and those with underlying diseases such as asthma, diabetes, and heart disease may be at increased risk of contracting the virus.

5. PROTECTION, DIAGNOSIS AND TREATMENT OF CHILDREN WITH KD DURING THE EPIDEMIC:

1) Protective measures for children

① Hand hygiene should be done first, the key is to wash hands frequently and wash hands correctly. Older children and adolescents can wash their hands independently, but under parental supervision; young children need to wash their hands with parental assistance. Parents should wash their hands first, and after helping children wash their hands, they should clean their hands again. Avoid touching your eyes and nose with dirty hands. Wash your hands before eating, after defecation, after contact with secretions, before wearing a mask, and after taking off a mask. Wash your hands according to the seven-step hand washing method. Finally, dry your hands with a disposable dry tissue, and then use it to turn off the faucet. (2) Wear the mask correctly [14]. Children's masks are children's N95 masks, children's surgical masks, children's medical masks, disposable children's masks and cotton masks in order of protection level. Children over the age of 1 need to wear a mask when going out. It is recommended to wear a N95 mask or a disposable surgical mask for children in high-risk areas. Disposable masks can be worn in non-high-risk areas. The mask should completely cover the mouth and nose, and should not be exposed to the nasal cavity. Do not touch the outside of the mask while wearing the mask or when removing the mask to avoid infection. Parents should pay attention to children's breathing when wearing masks to avoid suffocation. Parents also need to wear masks correctly and wear masks themselves before wearing masks for children [9]. (3) Pay attention to personal hygiene. Take frequent showers, manicures, change clothes frequently, and keep them clean and tidy. Children and adolescents should be informed in detail to avoid direct contact with human secretions, especially oral or respiratory secretions, urine and feces. Educate children and adolescents not to cover them directly with their hands when sneezing or coughing. Instead, use correct arm bends to cover them. Try to cover the nose and mouth with paper

towels or towels. Pay attention to food hygiene, ensure adequate sleep, keep warm and prevent cold. (4) Avoid gathering activities and minimize the risk of exposure to the source of infection. When you have to go out, you should wear a mask, try not to take public transportation, and go out to minimize the exposure of the elevator. [7]

2) Protection guidance for family members

Minimize outing activities, do not visit patients with suspected or confirmed COVID-19; if you must go out, you need to wear a mask; and wash your hands first after going out home. Persons who go out to contact with COVID-19 suspected or diagnosed patients must be strictly isolated for at least 14 days, while avoiding contact with children. It is recommended that families try not to accept visitors. Children and all family members should observe fever, cough, chest tightness, shortness of breath, vomiting, diarrhea, fatigue and other symptoms; if the above symptoms should be treated in time, and should not be observed at home. Maintain regular ventilation and cleanliness of home windows. Surfaces of objects with high frequency contact, such as elevator buttons, door handles, light switches, TV remote controls, mobile phones, etc., should be cleaned and disinfected if necessary. [8]

3) Protection and monitoring of children with suspected or confirmed COVID-19 cases of KD

The similarity between KD and children's COVID-19 poses new challenges to the diagnosis and treatment of children with KD during the epidemic. Since the outbreak of new coronavirus pneumonia (COVID-19) in Wuhan in mid-December 2019, we have diagnosed and treated 156 children with KD, including 95 boys and 61 girls, mainly children from 1 month to 17 years old, Of which more are 1-year-old children, less are 8-year-old, 10-year-old and 17-year-old children;

During COVID-19, we jointly investigated the diagnosis and treatment of children with KD in six centers, including Zhengzhou, Xi'an, Baoji, Hebei, Xianyang, Shenzhen, and Yulin. According to the following standards [4]:

Expansion: diameter ≥ 2.5 SSD;

Small aneurysm: localized dilation shows an inner diameter ≤ 4 mm (5-year-

old children: the inner diameter of one segment is 1.5 times the adjacent segment) Z score ≥ 2.5 to < 5 ;

Moderate aneurysm: aneurysm inner diameter > 4 mm and < 8 mm (children ≥ 5 years: the inner diameter of the segment is 1.5 to 4 times that of the adjacent segment) z score ≥ 5 to < 10 ;

Giant aneurysm: an aneurysm with an inner diameter of 8 mm (children ≥ 5 years old: the inner diameter of one segment is more than 4 times the adjacent segment) z score ≥ 10 .

In this special case, children with fever need to undergo layer-by-layer screening to exclude COVID-19. The diagnosis and treatment of children with fever in China is divided into three steps:

(1) Sub-inspection: All children need to be sub-inspected by professional nurses. After the sub-inspection, they are divided into 2 major categories. Those without fever can go to ordinary outpatient clinics; those with fever should go to hot clinics;

(2) Children's fever clinic: ①. First, the nucleic acid test needs to be improved to exclude COVID-19; ②. Children with cough symptoms need to improve chest CT examination if necessary;

(3) Re-examination patients: Because children with KD need to regularly review cardiac ultrasound, but the hospital takes preventive and control measures during the epidemic, so these patients who need to be re-examined should adopt:

- ①. Online appointment;
- ②. Treat in the nearest local hospital;
- ③. Video remote consultation;
- ④. Online outpatient appointments;
- ⑤. Inpatient diagnosis and treatment in non-scheduled hospitals [13];

According to the above-mentioned triage methods, KD patients who were newly diagnosed and re-diagnosed were promptly diagnosed and treated, and the cure rate was greatly improved, and there was no delay in the treatment of KD patients due to the epidemic. Therefore, during the epidemic, we should also formulate a reasonable plan for the treatment of non-COVID-19 children, so as not to delay the optimal treatment time [13].

4) Continued medication during Kawasaki disease:

Kawasaki disease (KD) is vasculitis in children associated with severe coro-

nary artery disease. It is the most common cause of pediatric acquired heart disease in developed countries, and many rapidly industrializing developing countries have reported this situation more and more. The incidence varies greatly between countries and is the highest in Northeast Asia. In Japan, nearly 100 children under five years of age suffer from the disease, while sub-Saharan Africa has the lowest incidence. The cause of KD is still uncertain. Suppose there is an interaction between genetic susceptibility and several environmental and immune factors. Several susceptibility genes have been identified to be associated with the development of KD and increased risk of coronary artery disease. Gene-gene association and changes in DNA methylation have also been found to play a key role in the pathogenesis and prognosis of KD.

During the epidemic, the first diagnosis of Kawasaki disease should be intravenously infused with large doses of gamma globulin (IVIG), 2g/(kg•time), oral aspirin 50~80mg/(kg•d), dipyridamole 3~5mg/(kg • D); Vitamin D 800u/time, once/day; after the condition is stable, can be discharged from home to continue oral medication, 3 days after fever or the disappearance of acute symptoms, aspirin reduction, 3 ~ 5mg/(kg•d), Lasts from February to March [6, 16].

6. SUMMARY

At this particular moment of the outbreak, the management of different populations, especially the proper management of basic diseases, will significantly affect the outcome and prognosis of the disease. KD is a common basic disease of children and adolescents. This disease is mucosal skin lymph node syndrome. It is necessary to grasp the principles of its comprehensive prevention and control and individual treatment, to block the deterioration of the disease as early as possible, and to avoid the occurrence of severe COVID-19. To achieve a better prognosis. Up to now, the disease caused by 2019-nCoV infection is still in the stage of continuous recognition. Therefore, this management recommendation will be continuously improved based on the deepening of the medical workers' knowledge of the disease.

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STUDIES OF VIBRATIONAL PROPERTIES OF PATHOGENIC NANOBIOSYSTEMS BY SPECTROSCOPIC METHODS OF INVESTIGATION

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ABSTRACT

Diseases caused by viral infections are one of the biggest problems for global health, and as methods involved in diagnostics are getting faster and more efficient, methods of their therapy are still need to be stronger. This retrospective study aimed to explore nano biospectroscopy research and technology in the field of virology in order to provide a theoretical and computer modeling and experimental support for the techniques used, and to suggest the applying tools that have not been used previously.

Keywords: *virology, spectroscopy, computer modeling, radiation resonance therapy*

1. INTRODUCTION

Medical disasters prediction, management and control are one of the main parts medical planning and preparation. The term “disaster medicine” first appeared in the medical lexicon in the post - World War II era [1]. The term “disaster medicine” would continue to appear sporadically in both the medical and popular press until the 1980s when the first concerted effort to organize a medical response corps for disasters becomes

the part of the National Disaster Medical System.

Viruses are assembled in the infected host cells of human, animals, or plants. Because of viral breeding the, host cell dies. There are especially viruses which are breeding in the cell of the bacteria. Viruses spread in many different ways. Just as many viruses are very specific as to which host species or tissue they attack, each species of virus relies on a particular propagation way.

The interdisciplinary collaboration (Biomedicine and Biophysics, Physical Research, Information Technologies and Systems) is an engine of strengthen the abilities of researchers in development of new biophysical and biomedical methods and tools. Those works which are based on novel achievements in optical spectrometry, laser and molecular physics as well as information technologies and systems are critically important for study of common properties of nano-scale virus-like particles, and elaboration of basic concepts and new revolutionary method for estimation unique vibration/oscillation properties, determine the unique “fingerprints” of pathogenic micro-organisms, especially viruses.

Farther development of new methods of pathogens treatment is greatly facilitated by an improved understanding of the pathophysiology of epidemic diseases. There is therefore a need to ad-

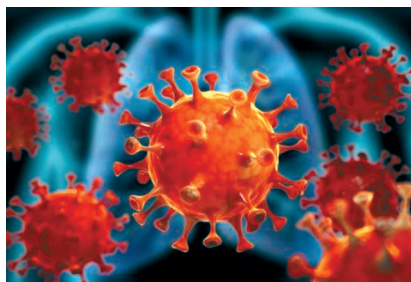


Fig. 1 Corona virus. <https://www.google.com/url?sa=i&url=https%3A%2F%2Fthe-conversation.com%2F4-unusual-things-weve-learned-about-the-coronavirus-since-the-start-of-the-pandemic>

dress the current knowledge gaps in disease aetiology in order to support innovation in evidence-based therapy. In this context, a better understanding of the mechanisms that are common to several diseases, in particular of those leading to co-morbidities, constitutes an important challenge. The special attention must be focused on the integration of pre-clinical and clinical studies for the identification of mechanisms common to several diseases. Performing activities should assess and validate the relevance of these common mechanisms and of their biomarkers (where relevant) on the development of disease-specific pathophysiology, as well as their role in the development of co-morbidities in both males and females. The expected impact should provide: A better understanding of disease pathways and / or mechanisms common to a number of diseases; new directions for clinical research for better disease prevention, health promotion, therapy development, and the management of co-morbidities. In this direction the multidisciplinary development of ability to detect rapidly, directly and selectively individual virus particles has the potential to significantly impact healthcare, since it could enable diagnosis at the earliest stages of replication within a host's system. Simultaneous acquisition of the vibrational and electronic fingerprints of molecular systems of biological interest, at the interface between liquid media, or at the air/solid, air/liquid interfaces is difficult to achieve with conventional linear optical spectroscopy due to their rather poor sensitivity to the low number of molecules or their maladjustment to water environment (infrared absorption). It relies on inelastic scattering of monochromatic light, usu-

ally from a laser in the visible, near infrared, or near ultraviolet range. The laser light interacts with molecular vibrations, phonons or other excitations in the system, resulting in the energy of the laser photons being shifted up or down. The shift in energy gives information about the vibrational modes in the system. Infrared spectroscopy yields similar, but complementary, information. Spontaneous scattering is typically very weak, and as a result the main difficulty of this kind of spectroscopy is separating the weak non-elastically scattered light from the intense Rayleigh scattered laser light.

Current paper presents some information about studies carried out in the last decade using spectroscopic methods as a research tool in the field of virology. Spectroscopic analyses are sensitive to variations in the biochemical composition of the sample, are non-destructive, fast and require the least sample preparation, making spectroscopic techniques tools of great interest in biological studies. Herein important chemometric algorithms that have been used in virological studies are also evidenced as a good alternative for analyzing the spectra, discrimination and classification of samples. Techniques that have not yet been used in the field of virology are also suggested. This methodology emerges as a new and promising field of research, and may be used in the near future as diagnosis tools for detecting diseases caused by viruses.

2. THEORETICAL AND EXPERIMENTAL STUDIES

With the advancement of technology and consequently advanced spectroscopy, the interest of researchers in spectroscopic techniques in biological studies has grown. This field of science is known as biospectroscopy, and means the use of spectroscopy to analyze biological objects. Several studies have been conducted involving identification of bacteria [3,4], viruses [5,6], cancer diagnosis [7], and even in the field of forensic entomotoxicology [8], demonstrating that spectroscopic techniques are capable of detecting biochemical changes in biological matrices.

Viruses are submicroscopic infectious agents and obligate intracellular parasites. They are totally dependent on a

host cell because they are not able to generate energy to conduct all biological processes (fig.1). Virus particles (virions) come in a variety of sizes and shapes.

However, approximately spherical shapes with diameters in the range between 50nm and 100nm are especially common. Many nearly spherical viruses are revealed by X-ray crystallography to have icosahedral symmetry. A typical virus particle contains genetic material, RNA or DNA, surrounded by a protein coat (capsid). Such an object should have reasonably distinct vibrational frequencies, the study of which may be of interest. Excitation of these vibrations could have applications in either the diagnosis or treatment of viral diseases. The sole discussion of these vibrational modes conjectured that ultrasound in the GHz range could be resonantly absorbed by HIV virus particles, leading to their destruction [9]. The two methods most commonly used in clinical diagnoses of viruses are enzyme-linked immunosorbent assay, with the best known being the ELISA method and real-time polymerase chain reaction (PCR). These methods have brought benefits such as high levels of repeatability and reproducibility, ease in handling and robustness [10]. However, they have also some negative points. As example, both methods requires high quality reagents; in some situations they are not suitable for identifying specific viral species/strains and they are also destructive to the samples. Thus, there is a need for techniques that are as advantageous as ELISA and PCR techniques, and which have fewer disadvantages.

The potential of spectroscopic techniques in the detection and identification of virus-infected cells has been studied using statistical methods as a sensitive, rapid and reliable methodology. The ability to discriminate between contaminated and non-contaminated objects in a short time with high sensitivity which characterized biospectroscopy determine its high prospect for studying viruses and similar pathogens [11,12].

An expected difficulty in the use of biospectroscopy in virology is related to the fact that humans have a great diversity of virus circulating in their organism, and each human has a unique microbiome. Because of it, obtaining a fin-

gerprint would be more difficult in view of the specificity of each organism. The solution to this problem seems to be the use of a broad and well-trained database, and changes obtained by multivariate statistical analysis, differentiating these alterations [13,14].

The main spectroscopic techniques that have been used in virological studies are nuclear magnetic resonance spectroscopy (NMR) [15], Raman spectroscopy [16], infrared spectroscopy (IR) [17] and molecular fluorescence spectroscopy [18]. These techniques are known to provide rapid responses and reliable data, as well as having powerful structural elucidation capability.

Such advantages highlight the possibility of identifying and classifying different types of virus using spectroscopic techniques. In this paper, studies using biospectroscopy coupled to statistical methods of classification in virological investigations are emphasized. First, we will discuss the most commonly used spectroscopic techniques, and then we will discuss the computational processes used to extract useful information from the obtained spectra (spectral preprocessing, multivariate classification algorithms, performance evaluation).

3. CONVERSATION

In order to understand the possible pathway of biospectroscopy development it is necessary to use the new science and technology tool calls bionanotechnology. The main objective of this modern discipline is cellular uptake of nanosize molecules functioning within the cell. If the size of molecules is bigger than 10nm are taken by the cell through a clathrin-assisted mode of endocytosis called pinocytosis, while particles of size greater than 200 nm in diameter are usually phagocytosed by the macrophages.

In comparison with cellular molecules (nano-ensembles) the size of viruses varies from 20 to 300 nanometers. Practically all viruses by the sizes are smaller, than bacteria. Viruses are masterpieces of nanoengineering with a basic common architecture that consists of the capsid – a protein shell made up of repeating protein subunits- which packs within it the viral genome. Nanosized biological agents and pathogens such as viruses are known to be respon-

sible for a wide variety of diseases such as flu, AIDS and herpes, and have been used as bioreagents [19,20]. For today there are experimentally certified data that Viral nanoparticles are emptied virus cells that can carry drugs directly to cancer cells to kill them [21]. Scientists have engineered viral nanoparticles from plant viruses, insect viruses, and animal viruses [22]. Viral nanoparticles could revolutionize cancer treatment, acting not only as a safer, more specific form of cancer treatment, but also as a new imaging tool. The nanoparticles could create a type of drug delivery that is extremely tumor specific with greatly reduced side effects. The viral nanoparticles would be more soluble and have higher drug efficacy than current treatments [23,24].

Oscillations are generated by biochemical oscillators that incorporate the periodic variation in a parameter over time to generate an oscillatory output. Spatial oscillators incorporate the periodic variation in the localization of a protein to define subcellular positions such as the site of cell division and the localization of DNA. There are some data which are focuses on the mechanisms of oscillators and the design principles of temporal and spatial oscillatory systems [25].

Current optical detection methods which are well developed for single micrometer size particles, cannot be applied to nanoparticles due to a strong signal dependence on particle size. Typically, such sensors consist of a light source which illuminates a sample volume of an aerosol or a liquid flow containing the particles of interest. An off-axis detector measures power of scattered light. The latter is a function of particle properties such as size, concentration, and optical density. In the tens of nanometers size regime particles act as dipoles, therefore the power of scattered light is proportional to the sixth power of particles size. Lowering the detection size limits for the existing detectors places an impossible requirement on noise optimization. Therefore, a signal which has weaker particle size dependence can allow access to smaller particles [26]. There are several virus quantification techniques available to virologists, such as the quantitative PCR (polymerase chain reaction) method [27], the plaque titer method [28] and the

image enhanced microscopy (IEM) technique [29]. However, a problem common to most of these techniques is that the analysis of a sample involves several tedious steps, which can take several hours to multi plays to complete. The fast detection and characterization of nanoparticles, such as viruses or environmental pollutants, are important in fields ranging from biosensing to quality control. However, most existing techniques have practical throughput limitations, which significantly limit their applicability to low concentration analysis.

A wide range of potential applications can be foreseen, including real-time analysis of clinically relevant virus samples and contamination control of processing fluids used in the semiconductor industry [30]. For nanoparticle structures identification a rather interesting method is Vibrational Spectroscopy (VS), which provides the most definitive means of identifying the surface species generated upon molecular adsorption and the species generated by surface [31, 32].

The experimental results are compared with theoretical calculations based on an elastic continuum model and appropriate Raman selection rules derived from a bond Polaris ability model. The observed Raman mode is shown to belong to one of the Raman-active axial modes of the M13 phage protein coat. It is expected that the detection and characterization of this low-frequency vibrational mode can be used for applications in biomedical nanotechnology such as for monitoring the process of virus functionalization and self-assembly. Recently, a technique which departs radically from conventional approaches has been proposed. This novel technique utilizes biological objects such as viruses as nano-templates for the fabrication of nanostructure elements. Low wave number ($\leq 20 \text{ cm}^{-1}$) acoustic vibrations of the M13 phage have been studied using Raman spectroscopy [33].

The experimental results are compared with theoretical calculations based on an elastic continuum model and appropriate Raman selection rules derived from a bond polarizability model. Aside from serving as a protective layer, capsids are involved with various other aspects of their respective virus life cycles including timely viral genome en-

capsulation (self-assembly and genome packaging), cell-to-cell virus transport, entry into host-cell (e.g., via cell receptor binding), genome release into host cell, etc.

The utility of the class system is not entirely lost, however; specific angle patterns within the capsid ensures the existence of distinct hexamer shapes (each shape is colored distinctly in. Evidence indicates that capsid formation is nucleated, often starting with a single

capsomer species (e.g., pentamers; for the purposes of this paper, a capsomer is a generally symmetric cluster of either five or six subunits), which then proceeds to completion by the addition of small subunit clusters (or single subunits). In T~1 capsid, where subunits are in identical/equivalent environments, nucleated assembly will be possible with no additional machinery. However, the formation of two or more capsomers from a single interaction site will require the employment of additional machinery to ensure high yields of the native state. For example, quasi-equivalent switches are required for the proper assembly of capsids containing two distinct capsomers: a pentamer and one type of hexamer. The addition of a second hexamer shape necessitates the requirement of a second mechanism such as auxiliary proteins for proper assembly. For spherical virus capsids requiring more distinct hexamer shapes. Additional mechanisms to stabilize those new shapes at exactly the right positions within the forming capsid are likely to be also needed dominantly form.

Because capsids from different classes display markedly different geometries, they are bound to display different physical properties. The periodic nature of capsid hexamer contents also useful in understanding „T-switching“: a process that permits canonical capsid subunits to more easily sample capsids containing similar hexamer shapes. This allows for a segue to understanding currently intractable and deadly pleomorphic viruses like Ebola and arenaviruses. For example, from the above T-switching rule, the available diversity of an arena virus may only be explained if we assume that the biologically relevant form of the arenavirus is the T~12 capsid. Non-icosahedral capsids. Although the framework presented

doesn't appear to readily explain non-icosahedral capsids (some are just „slightly“ non-icosahedral, such as the natively prolate phi29 capsids, while others are wildly different in form, such as Ebola with its natively filamentous shape), those capsids, like their icosahedral counterparts, also display capsomer sub-structures.

In light of this, the geometric constraints analogous to endo angles that affect capsomer shape may be useful in obtaining insights into non-icosahedral capsid morphology, behavior, and classification. It will be exciting to see whether incorporating the non-icosahedral capsids into an expanded capsid periodic table will be possible. All canonical capsids (made up of trapezoidal subunits) may be built from a single type of pentamer and a repertoire of distinct hexamer shapes (colored distinctly only once in each capsid. The hexamer shape is described by the number of endo angles it displays.

Yet, the ability to detect rapidly, directly, and selectively individual virus particles has the potential to significantly impact healthcare, since it could enable diagnosis at the earliest stages of replication within a host's system. One promising approach for the direct electrical detection of biological macromolecules uses semi-conducting nano-wires or carbon nano-tubes configured as field-effect transistors, which change conductance upon binding of charged macro-molecules to receptors linked to the device surfaces. One of the simplest medical nanomaterials is a surface perforated with holes, or nanopores. These pores are large enough to allow small molecules to pass but are small enough to impede the passage of much larger virus particles. The next step was cylindrical gold nano-tubules with inside diameters as small as 1.6 nm. When tubules were positively charged, positive ions were excluded and only negative ions were transported through the membrane. With a negative voltage, only positive ions could pass. The combining voltage gating with pore size, shape, and charge constraints allows achieving precise control of ion transport with significant molecular specificity. Lieber's group has reported direct, real-time electrical detection of single virus particles with high selectivity using nano-wire field-effect tran-

sistors to measure discrete conductance changes characteristic of binding and unbinding on nano-wire arrays modified with viral anti-bodies [34].

The integrity of such devices allows increasing the number of the detection viruses. The analysis of the manifold literature shows, that task of the detection pathogenic micro-organisms is timely. Therefore, our available method would be one brick in the solution of the problems like that. Simultaneous acquisition of the vibrational and electronic fingerprints of molecular systems of biological interest, at the interface between liquid media, or at the air/solid, air/liquid interfaces in conditions similar to those encountered in nature or in model environments requires the use of sensitive and specific spectroscopic probes. One of the promising solutions of this problem is the use of the nonlinear Two-Color Sum-Frequency Generation Spectroscopy (2C-SFG) that meets the desired spectroscopic requirements.

The goal of this approach is to probe membrane models of various forms and in various environments: (i) lipid monolayers and bilayers; (ii) deposited on substrates, floating on water as Langmuir layers and at a liquid-liquid interface; (iii) alone and in interaction with molecules, including peptides and proteins; (iv) submitted to controlled stress(chemical, pH, electrochemical potential).The increasing amount of available data of protein three-dimensional atomic structures, determined mostly by X-ray crystallography (related to the fast expansion of that field around third generation synchrotron storage rings) and NMR, has given much information about role of many proteins in biological processes. However, it has been pointed out that knowing the structure does not directly lead to the knowledge of the function, and that the protein alone, without its environment or its partners of interaction, is not totally informative. Additionally, some proteins cannot be satisfactorily crystallized and thus cannot be accessed by X-ray crystallographic methods. Among them, membrane proteins need their membrane partners to fully play their role and are often not able to crystallize. In situ studies, and their according investigation techniques, are therefore favored for such objects. In the following, in situ should not be under-

stood as *in vivo*, but imply rather that the objects are designed and studied in an environment mimicking what they experience *in vivo*.

Specific *in situ* techniques allow direct investigation of key functional behaviors of synthetic membrane models (lipid mono and bilayers in an aqueous environment interacting either with selected proteins, ions or organic molecules) [35-36]. The strong absorption of the water vapor and the poor detection properties of conventional FTIR spectroscopy led to the discarding of this technique for the study of such interfacial systems. This evidence for the limited range of infrared spectroscopic tools dedicated to the study of such fragile objects in their specific environment was written only about ten years ago. From that time, there has been a lot of progress from the spectroscopic point of view.

In addition to IR absorption spectroscopy (conventional or attenuated total reflection (ATR) configuration), three other IR-based spectroscopies have been able to address the issue of a molecular layer on water with a signal-to-noise ratio sufficient to extract scientific information from experimental data. Raman spectroscopy is often used on biological environment, although the low count rate on monolayers requires long acquisition times. It has been recently reported the detection of viruses by acoustic oscillations [37,38].

However, the process of “rupture event scanning”, which was reported, involves the separation of a virus particle from antibodies by ultrasound. This is distinct from the excitation of the vibrational modes of the virus particle itself, and occurs at much lower frequencies. There have also been some experimental studies of ultrasonic absorption by empty viral capsids [39, 40]. These experiments reveal an enhanced absorption in the MHz range as proteins re-assemble into a capsid, but do not find a resonant peak in this frequency range. At the same time, it was emphasized that these and other results show that viral capsids are flexible and change size or shape in response to vibrations or to changes in temperature or pH [41].

One of the most promising methods of biospectroscopy is SFG. These ultrashort pulsed lasers based optical measurement method is unique for investigation of vibrational modes of different viruses

and other pathogenic microorganisms as well as study of nature of their oscillation processes and parameters of oscillation. Non-linear optics and its resonance technologies is possible direction of organization of treatment of pathogenic microorganisms in their different living media. Contrary to the previous ones, this second order nonlinear process is intrinsically specific to an interface, and involves no contribution from molecules in a centrosymmetric bulk, i.e., in solution or in gas phase. It has been extensively applied to solid interfaces in vacuum, controlled atmosphere and electrochemical conditions.

For a few years, technological development of picosecond and femtosecond tunable laser sources have led both to an increase of the number of SFG experimental setups around the world and to a progressive application to fragile or buried interfaces. In addition to unique SFG setup is research based on usage of the CLIO Free Electron laser [42,43]. This latter allows probing specific vibrations located in the near and far infrared, which is again unique

to date. Although molecular fluorescence spectroscopy has been little used in studies in the field of virology, it is also an interesting approach with great potential in this perspective. This technique analyzes the fluorescence capacity of a sample [44], where a beam of high energy light (usually in the ultraviolet region) is irradiated on the sample to be excited into a higher electronic energy level; then the fluorophore molecule will rapidly lose energy to this environment through non-radiative

modes (called internal conversion) and will return to the lowest vibrational level of the lowest electronic excited state. The molecule persists at this vibronic level for a period of time known as the fluorescence lifetime, and then returns to the fundamental electronic state by emitting a photon with energy lower than the irradiated one [45].

The excitation and emission spectrum are recorded by the instrument and is generally used to build excitation-emission (EEM) fluorescence matrices. Another commonly-employed form of fluorescence technique is fluorescence correlation spectroscopy (FCS), which is used for temporal and spatial analysis of molecular interactions of biomolecules present in solution at extremely low concentrations. This technique is based on the principle that a fluorophore molecule has a specific free diffusion rate that is directly related to its size. This basic principle, for example, can be used to study protein interactions. As with other spectroscopic techniques, molecular fluorescence spectroscopy provides rapid results with high sensitivity and specificity, and is non-destructive, making this technique a tool of interest in the field of virology.

Spectroscopically interrogating biological samples analyze definitely needs to use computational tools which facilitate the information collection and extraction. For this, it is necessary to address the different computational methods and tools and among them there are employed the methods:

- Preprocessing and multivariate analysis techniques, which consists the

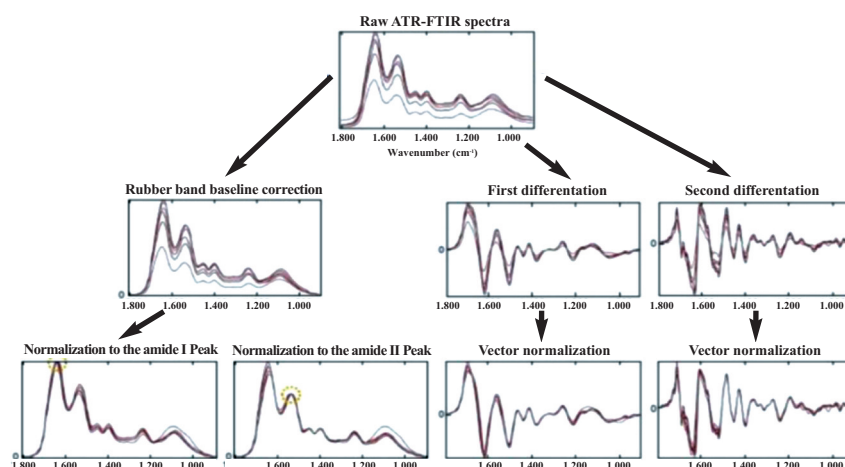


Fig.2. Visual effect of different pre-processing on a set spectrum. Source: Baker M.J., Trevisan J., Bassan P., et al. Using Fourier transform IR spectroscopy to analyze biological materials. Nat. Protoc. 2014; 9:1771–1791.

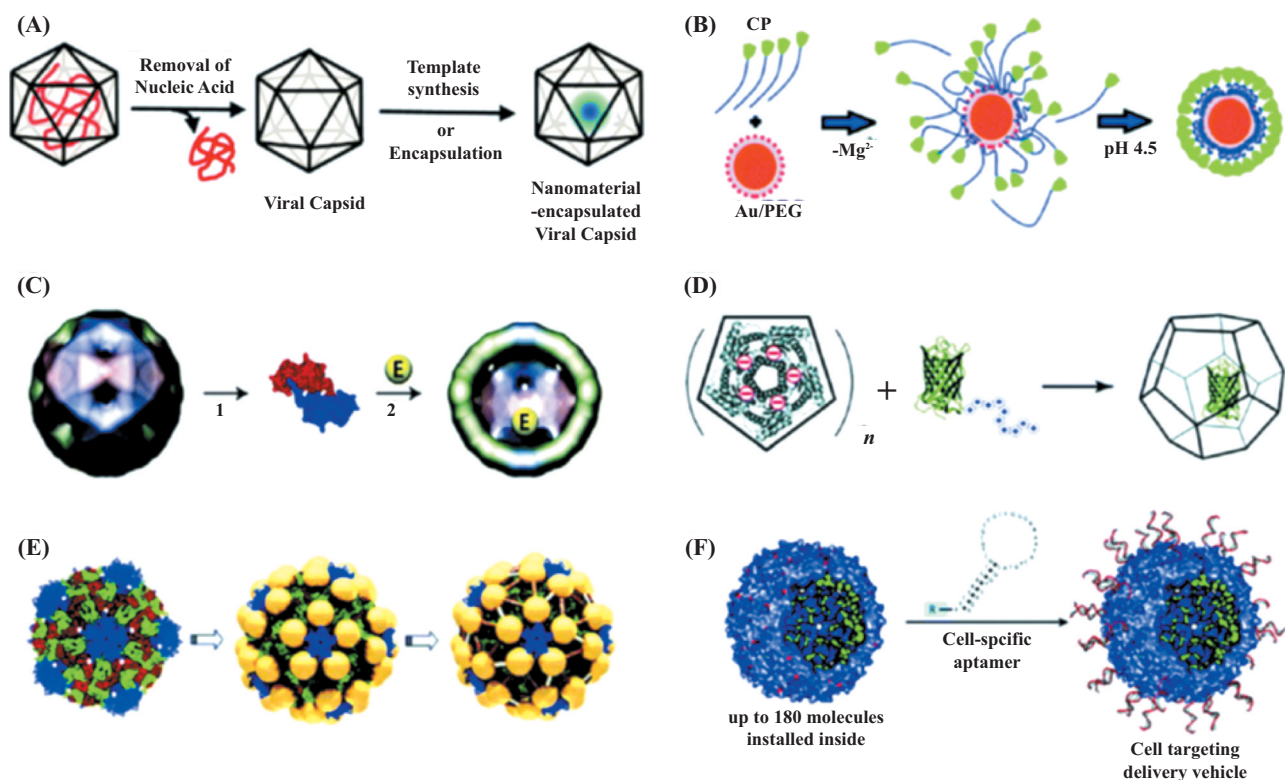


Fig. 3. Viral Capsids and their forms

correction and improvement of the signal-to-noise ratio of the spectrum, commonly employed before data analysis. [fig.2].

- Spectral cut and Baseline correction, which include determination of exact region of interest and diminish of the wavenumbers which are not absorbed and light scattering occurs due to the non-homogenous particle size [46].

- Spectral normalization techniques are used when it is necessary to remove spectral changes responsible for the thickness or concentration of the sample, making the normalized spectra become comparable to each other. [47].

- Multivariate analysis techniques are employed to analyze multivariate data, meaning data having two or more variables per object. Examples are first-order data (such as IR, Raman spectrum) and second-order data (such as fluorescence).

- Principal component analysis (PCA) is an unsupervised multivariate analysis technique widely used in biological studies. This technique is used to reduce the dimensionality of the sample's data and generate a new visualization.

- Cluster analysis (CA) techniques are unsupervised methods of pattern

recognition that aim to group the spectra into groups when there is no information about the classes. [48].

- Partial least squares (PLS) is a multivariate calibration technique that finds factors (latent variables, LVs) in the spectra set that explain the maximum variance in the reference variables set, using the simultaneous decomposition of the two.

- Linear discriminant analysis (LDA) is a supervised technique widely used for class discrimination..

- Successive projections algorithm (SPA) is a progressive variable selection technique. This means that it starts with a variable (wavelength or wavenumber, for example) and adds new variables in each interaction until an optimal number is selected.

- The genetic algorithm is a technique that mimics Darwin's theory of evolution, where evolution occurs by natural selection in which the more adapted organisms have a greater chance of survival. In the case of GA, the variable selection process begins with a randomly formed population of variables [49].

- Sensitivity (SENS) can be defined as the confidence that a positive result for a sample of the labeled class is obtained [50].

- Diagnostic virology continues to evolve rapidly. Viral testing is now essential for the care of a number of patient groups, including hospitalized patients with acute respiratory infections; transplant recipients and other immunocompromised patients; patients infected with human immunodeficiency virus (HIV), hepatitis C virus (HCV), and hepatitis B virus (HBV); and infants with possible congenital infection. Multiple test methods continue to be used, but molecular tests are emerging as the dominant technology. A variety of commercial molecular assays have been or are in the process of being approved or cleared as in vitro diagnostic tests by the Food and Drug Administration (FDA) [51].

During the last years in response of global spraying the new structural types of corona viruses the method of estimation unique vibration/oscillation properties, determine the unique "fingerprints" of pathogenic micro-organisms, especially viruses. The main task of the works done by international group including Georgian, French, German British and Greek researcher-swas elaboration of optical resonance spectrometry method of detection and treatment of pathogenic nanobiostuc-

tures including corona type viruses [52-53].

Viruses and their genomes are mostly enclosed and protected by spherical capsids - symmetric coats or shells composed primarily of multiple copies of protein subunits (Fig.3). Aside from serving as a protective layer, capsids are involved with various other aspects of their respective virus life cycles including timely viral genome encapsulation (self-assembly and genome packaging), cell-to-cell virus transport, entry into host-cell (e.g., via cell receptor binding), genome release into host cell, etc. Despite their central importance to the life cycle, the various evolutionary pressures acting on spherical capsids are not well known. Half a century of empirical data has uncovered a large array of capsid sizes that range from tens to many thousands in subunit composition. Spherical capsids of all observed sizes may be obtained from a grouping of twelve pentamers (symmetric clusters of five subunits) separated by a variable number of hexamers (clusters of six subunits). For spherical virus capsids requiring more distinct hexamer shapes. Additional mechanisms to stabilize those new shapes at exactly the right positions within the forming capsid are likely to be also needed dominantly form.

Because capsids from different classes display markedly different geometries, they are bound to display different physical properties. The periodic nature of capsid hexamer contents also useful in understanding „T-switching“: a process that permits canonical capsid subunits to more easily sample capsids containing similar hexamer shapes. This allows for a segue to understanding currently intractable and deadly pleomorphic viruses like Ebola and arenaviruses. All canonical capsids (made up of trapezoidal subunits) may be built from a single type of pentamer and a repertoire of distinct hexamer shapes (colored distinctly only once in each capsid. The hexamer shape is described by the number of endo angles it displays. It is necessary to underline that effect of destroy of enveloped viruses is based on the highly symmetric structure (e.g. icosahedral and others) of many viruses, which leads to a well-defined resonant frequency which may be specifically absorbed by these structures and may subsequently lead to their ir-

reversible damage. Modeling and Simulation of oscillation effects in different viruses including corona like ones is based on studies of biostructure's physical characteristics, scattering and absorption properties. Estimation of electromagnetic (EM) spectrum and resonance wave length ranges is important for characterization of nano-microscaled particles and determination of biostructures unique spectral signatures, essential in bio-agents detecting and identification systems, and becoming as a great challenge in real systems investigations. Method of estimation of spectral response on EM field & particle interaction is based on solutions of electrodynamic two (2D) or three (3D) dimensional boundary tasks. Analytical expressions of EM fields are derived from rigorous solutions of Maxwell's and Helmholtz's equations and defined through the dimensionless parameters, diameters over an excitation wavelength. It makes possible to apply the classical well-known approach to sub-micro particles characterization. One of the ways for estimation of resonance frequencies range is the method determining the eigenvalues and corresponding eigenvectors obtained by algebraic system of functional equations which could be written based on the solution of electrodynamic task considering EM wave-VL particle scattering [54]. Algebraic system has more complicated form when VL particle is of core-shell biostructure with different electric parameters. Resonant wavelength range is predicted theoretically in the vicinity of values corresponding the maximums of intensity of particular scattered partial waves. Estimation of resonant wavelength range based on determination of far-field characteristics such as scattering or absorption cross sections, the intensity of energy, wholly representing the response on wave-particle interaction is considered as the reasonable and decisive solution preferable for studying the spectroscopic properties and determination of possible spectral signatures of bioparticles, viruses. Method of studying spectroscopic characteristics based on elaborated physical models of viruses represents the new possibility for estimation of spectroscopic properties and resonance wavelength range of viral nanoparticles, virions. Thus, two main mediums of different structures

and properties constitute the virion: capsid of protein capsomeres and nucleic acids into the capsid. Type, number and arrangement of capsomeres and length of nucleic acid are essential in defining the size of capsid designed mostly in near-symmetrical geometry, having the unique self-assemble mechanism. A simple calculation shows, that the ratio of inner (core) and outer spherical volumes of icosahedral capsid of bacteriophage T7 (of diameters inner $1 d = 42.6 \text{ nm}$ and outer $2 d = 56.6 \text{ nm}$) is approximately 0.426 [55], so quite a large portion (0.57) of volume in virion is occupied by the capsid proteins. Capsid's size is large enough than the „discrete“ nature of protein subunits, therefore the influence of that on capsid whole geometry could probably be less significant. This fact allows virion to be modelled as a spherical core-shell particle of smooth inner or outer surfaces. Core-shell VLP model of spherical geometry could be used as the first approximation of shape-structure of icosahedral unenveloped virion. The structure and geometry of capsids as well as processes happening inside a layer probably dominate in determination of physical, spectroscopic properties of nano-sized particles, virions.

Theoretical approach of studying spectroscopic properties of VLPs is based on classical Maxwell's EM theory, separation of variables method for solving Helmholtz's (wave) equation. Solution of Helmholtz's equation leads to the Bessel's and/or Legendre's equations [56]. EM fields in different areas of VLP are written as the sums of multipole-waves with unknown multipole coefficients. Application of boundary conditions to EM field components on core-shell surfaces and labor consuming mathematical transformations leads to rigorous theoretical solution of EM scattering problem on single VL particle. Analysis of EM field expressions show that arguments of functions determining the multipole coefficients and scattered fields depend only on relative values of particles diameters over wavelength. Therefore, it makes possible to expand the research area, and the findings of well-established Mie theory [57] considering the light scattering on a homogeneous sphere be applied to nanoparticles of core-shell morphology and particles of biological origin as well.

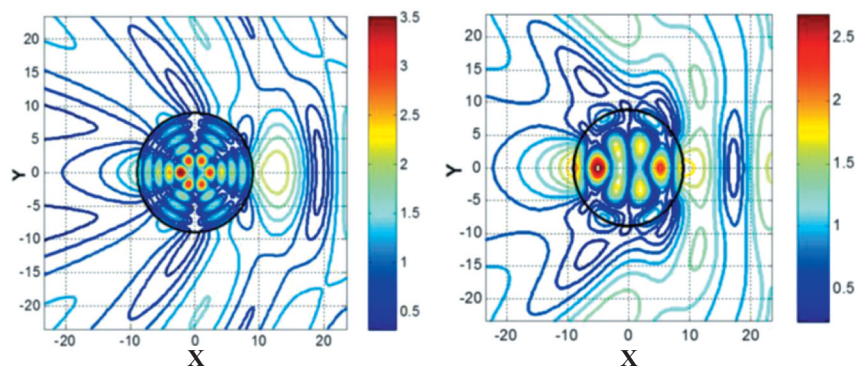


Figure 4. 3 Isolines of EM field amplitudes for cylindrical model of TMV virion, in the range of $(-,+)$. Diameter of cylinder: ≈ 18 nm; dielectric permittivity: of cylindrical particle - (a), 12 (b), surrounding medium -, excitation wave length = 23.5 nm, (X,Y) plane is perpendicular to the axis of cylinder.

Spectral response on EM wave-VLP interaction is determined by estimation of far-field ($r \ll 2d/\lambda$) characteristics representing the angular distribution of scattered (absorbed) energy. Scattering properties are characterized via expressions such as: the total scattering cross section.

Proposed theoretical solution, analytical expressions of EM fields make possible to estimate the fields in the areas of core, shell and surrounding areas of VLPs. based on machine learning and modeling techniques have been used for generating a simulated spectrum of nanoparticle of given size and available literature optical constants. Computer simulation (based on MatLabR2013b software) was carried out for TMV particles characterization. Parameters of TMV particle are obtained from scientific publications based on different measuring technics. Length of TMV virion is 280-300 nm, outer (d_2) and inner (d_1) diameters of capsid are 18 nm and 4 nm, correspondingly. Two models - homogeneous cylindrical (of diameter) and homogeneous of core-shell structure (of diameters - outer and inner), are used for simulation study of TMV virion. Computer simulation shows, that expected resonant spectral response is observable on far-field characteristics, resonant vibrational frequencies of whole TMV particle may be associated to scattering cross-section maximums. Values and locations of maximums strongly depend on dielectric and magnetic parameters, distance between the neighbor maximums increases the longer wave lengths range is.

Cylindrical model of TMV virion: diameter ≈ 18 nm, dielectric permittivity

of particle and surrounding medium, magnetic permeabilities of particle and surrounding medium. Near-field distribution presented in a form of isolines of EM field amplitudes (Fig. 4), indicates the locations of energy maximums inside and outside of particle. Investigation of EM field distribution makes possible to have insight vision of nanobioparticles [59-61].

Proposed computing model is useful for investigation of spectroscopic properties of nanobioparticles and appreciation of possible resonant wave length ranges correlating with scattering/absorbing efficiency of VLP.

Experimental data obtained by applying exquisite techniques and outcomes of theoretical or simulation models should complement each other and verify factors such as possible anisotropy of core-shell areas of virion, surface roughness and inhomogeneity unforeseen in simplified approaches.

4. CONCLUSIONS

Spectroscopic methods have the characteristic of providing fast results and reliable information related to the composition of the samples. The studies presented here have shown promising results in a field of science that needs to be better explored. It has been shown that multivariate analysis techniques are of great importance to analyze spectroscopic data, providing the potential to identify and classify biological samples. We do hope that with advancement in this field of study, spectroscopic methods and tools will be used in bio medicine in the near future. Methods of light therapy of different diseases based on estimation of EM field characteristics

and resonant wave ranges based on computer simulation of nanobioparticles characterization will be widely implemented, and possibility of determination of resonant (own) frequencies of entire system of molecules including virions will be a key point for that.

It is a well-known fact that the yogis of ancient times practiced meditational techniques to get rid of diseases and stay healthy. Meditations induce the positive vibrations which are known to kill many of the harmful microorganisms which get into our body. Recent frontiers in technology are exploring the possibility of using external excitations to vibrate a virus to its death.

The genetic material of virus is DNA/RNA enclosed within the protective protein shell (Capsid). Every cell in human body has a natural tendency to vibrate at frequency known as the natural frequency, and so the virus. Natural frequency values of these vibrations are very high compared to healthy cells, and depend on the molecular structure and differ from virus to virus.

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INVESTIGATIONS OF VIBRATIONAL PROPERTIES OF VIRUSES AND VIRUS-LIKE PARTICLES BY COMPUTING METHODS

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Diseases caused by viral infections are one of the biggest problems for global health, and as methods involved in diagnostics are getting faster and more efficient, methods of their therapy are still need to be stronger. This retrospective study aimed to explore nano bio spectroscopy research and technology in the field of virology in order to provide a theoretical and computer modeling support for the techniques used, and to suggest the applying tools that have not been used previously.

Keywords: *virology, spectroscopy, computer modeling, radiation resonance therapy*

1. INTRODUCTION

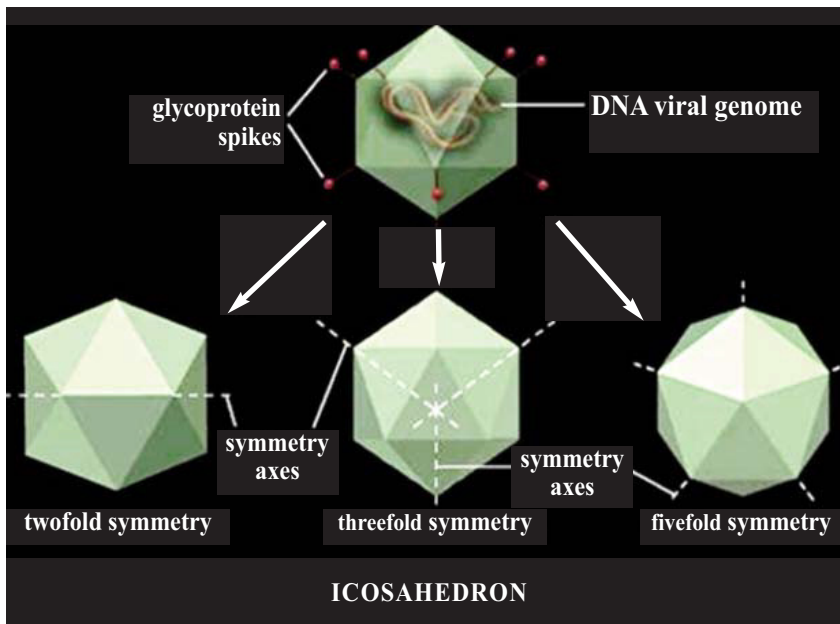
Viruses are assembled in the infected host cells of human, animals, or plants. Because of viral breeding the, host cell dies. There are especially viruses which are breeding in the cell of the bacteria. Viruses spread in many different ways. Just as many viruses are very specific as to which host species or tissue they attack, each species of virus relies on a particular propagation way.

The interdisciplinary collaboration (Biomedicine and Biophysics, Physical Research, Information Technologies and Systems) is an engine of strengthen the abilities of researchers in development of new biophysical and biomedical methods and tools. Those works which are based on novel achievements in optical spectrometry, laser and molecular physics as well as information technologies and systems are critically important for study of common properties of nano-scale virus-like particles, and elaboration of basic concepts and new revolutionary method for estimation unique vibration/oscillation properties, determine the unique “fingerprints” of pathogenic micro-organisms, especially viruses. Farther development of new methods of pathogens treatment is greatly facilitated by an improved understanding of the pathophysiology of epidemic diseases. There is therefore a

need to address the current knowledge gaps in order to support innovation in evidence-based therapy. In this context, a better understanding of the mechanisms that are common to several diseases, in particular of those leading to co-morbidities, constitutes an important challenge. The special attention must be focused on the integration of pre-clinical and clinical studies for the identification of mechanisms common to several diseases. Performing activities should assess and validate the relevance of these common mechanisms and of their biomarkers (where relevant) on the development of disease-specific pathophysiology, as well as their role in the development of co-morbidities in both males and females. The expected impact should provide: A better understanding of disease pathways and / or mechanisms common to a number of diseases; new directions for clinical research for better disease prevention, health promotion, therapy development, and the management of co-morbidities. In this direction the multidisciplinary development of ability to detect rapidly, directly and selectively individual virus particles has the potential to significantly impact healthcare, since it could enable diagnosis at the earliest stages of replication within a host’s system. Simultaneous acquisition of the vibrational

and electronic fingerprints of molecular systems of biological interest, at the interface between liquid media, or at the air/solid, air/liquid interfaces is difficult to achieve with conventional linear optical spectroscopy due to their rather poor sensitivity to the low number of molecules or their maladjustment to water environment (infrared absorption). It relies on inelastic scattering of monochromatic light, usually from a laser in the visible, near infrared, or near ultraviolet range. The laser light interacts with molecular vibrations, phonons or other excitations in the system, resulting in the energy of the laser photons being shifted up or down. The shift in energy gives information about the vibrational modes in the system. Infrared spectroscopy yields similar, but complementary, information. Spontaneous scattering is typically very weak, and as a result the main difficulty of this kind of spectroscopy is separating the weak non-elastically scattered light from the intense Rayleigh scattered laser light.

Current paper presents some information about studies carried out in the last decade using spectroscopic methods as a research tool in the field of virology. Spectroscopic analyses are sensitive to variations in the biochemical composition of the sample, are non-destructive, fast and require the least sample preparation, making spectroscopic techniques tools of great interest in biological studies. Herein important chemometric algorithms that have been used in virological studies are also evidenced as a good alternative for analyzing the spectra, discrimination and classification of samples. Techniques that have not yet been used in the field of virology are



Example of Virion: Virus icosahedron A virus icosahedron (20-sided structure) shown in the (left) twofold, (centre) threefold, and (right) fivefold axes of symmetry. Edges of the upper and lower surfaces are drawn in solid and broken lines, respectively. Encyclopaedia Britannica'

also suggested. This methodology emerges as a new and promising field of research, and may be used in the near future as diagnosis tools for detecting diseases caused by viruses.

THEORETICAL AND EXPERIMENTAL STUDIES

With the advancement of technology and consequently advanced spectroscopy, the interest of researchers in spectroscopic techniques in biological studies has grown. This field of science is known as biospectroscopy, and means the use of spectroscopy to analyze biological objects. Several studies have been conducted involving identification of bacteria [1,2], viruses [3,4], cancer diagnosis [5], and even in the field of forensic entomotoxicology [6], demonstrating that spectroscopic techniques are capable of detecting biochemical changes in biological matrices.

Viruses are submicroscopic infectious agents and obligate intracellular parasites. They are totally dependent on a host cell because they are not able to generate energy to conduct all biological processes. Virus particles (virions) come in a variety of sizes and shapes.

However, approximately spherical shapes with diameters in the range between 50nm and 100nm are especially

common. Many nearly spherical viruses are revealed by X-ray crystallography to have icosahedral symmetry. A typical virus particle contains genetic material, RNA or DNA, surrounded by a protein coat (capsid). Such an object should have reasonably distinct vibrational frequencies, the study of which may be of interest. Excitation of these vibrations could have applications in either the diagnosis or treatment of viral diseases. The sole discussion of these vibrational modes conjectured that ultrasound in the GHz range could be resonantly absorbed by HIV virus particles, leading to their destruction [7].

The two methods most commonly used in clinical diagnoses of viruses are enzyme-linked immunosorbent assay, with the best known being the ELISA method and real-time polymerase chain reaction (PCR). These methods have brought benefits such as high levels of repeatability and reproducibility, ease in handling and robustness [8]. However, they have also some negative points. As example, both methods requires high quality reagents; in some situations they are not suitable for identifying specific viral species/strains and they are also destructive to the samples. Thus, there is a need for techniques that are as advantageous as ELISA and PCR techniques, and which have fewer disadvan-

tages. The potential of spectroscopic techniques in the detection and identification of virus-infected cells has been studied using statistical methods as a sensitive, rapid and reliable methodology. The ability to discriminate between contaminated and non-contaminated objects in a short time with high sensitivity which characterized biospectroscopy determine its high prospect for studying viruses and similar pathogens [9, 10].

An expected difficulty in the use of biospectroscopy in virology is related to the fact that humans have a great diversity of virus circulating in their organism, and each human has a unique microbiome. Because of it, obtaining a fingerprint would be more difficult in view of the specificity of each organism. The solution to this problem seems to be the use of a broad and well-trained database, and changes obtained by multivariate statistical analysis, differentiating these alterations [11, 12].

The main spectroscopic techniques that have been used in virological studies are nuclear magnetic resonance spectroscopy (NMR) [13], Raman spectroscopy [14], infrared spectroscopy (IR) [15] and molecular fluorescence spectroscopy [16]. These techniques are known to provide rapid responses and reliable data, as well as having powerful structural elucidation capability.

Such advantages highlight the possibility of identifying and classifying different types of virus using spectroscopic techniques. In this paper, studies using biospectroscopy coupled to statistical methods of classification in virological investigations are emphasized. First, we will discuss the most commonly used spectroscopic techniques, and then we will discuss the computational processes used to extract useful information from the obtained spectra (spectral preprocessing, multivariate classification algorithms, performance evaluation).

DISCUSSION AND ANALYZE

In order to understand the possible pathway of biospectroscopy development it is necessary to use the new science and technology tool calls bionanotechnology. The main objective of this modern discipline is cellular uptake of nanosize molecules functioning with-

in the cell. If the size of molecules is bigger than 10nm are taken by the cell through a clathrin-assisted mode of endocytosis called pinocytosis, while particles of size greater than 200 nm in diameter are usually phagocytosed by the macrophages. Phagocytosis occurs in specialized cells called phagocytes, which includes macrophages, neutrophils, and other white blood cells, which destroys the molecular association. Invagination produces so called phagosome which usually fuses with one or more lysosomes containing hydrolytic enzymes.

In comparison with cellular molecules (nano-ensembles) the size of viruses varies from 20 to 300 nanometers. Practically all viruses by the sizes are smaller, than bacteria. However, the largest viruses, for example a virus of cow smallpox, have the same sizes, as well as the smallest bacteria (hlamidiya and rikketsiya) who too are obligate parasites and breed only in living cells. Therefore, as distinctive features of viruses in comparison with other microscopic causative agents of infections the sizes or obligatory parasitism, and features of a structure and unique mechanisms of replication (reproduction themselves) serve not. Viruses are masterpieces of nanoengineering with a basic common architecture that consists of the capsid – a protein shell made up of repeating protein subunits- which packs within it the viral genome.

Nano-sized biological agents and pathogens such as viruses are known to be responsible for a wide variety of diseases such as flu, AIDS and herpes, and have been used as bioreagents [17, 18].

For today there are experimentally certified data that Viral nanoparticles are emptied virus cells that can carry drugs directly to cancer cells to kill them [19]. Scientists have engineered viral nanoparticles from plant viruses, insect viruses, and animal viruses [20]. Viral nanoparticles could revolutionize cancer treatment, acting not only as a safer, more specific form of cancer treatment, but also as a new imaging tool. The nanoparticles could create a type of drug delivery that is extremely tumor specific with greatly reduced side effects. The viral nanoparticles would be more soluble and have high-

er drug efficacy than current treatments [21,22].

Viruses and other biological species can be characterized according to size, shape, and optical/spectroscopic properties. These properties allow them to be distinguished from other biological species and from other particulates such as dust particles.

In response to new tasks which face medicine development of a rapid and efficient diagnostic test is considered a high priority. In this direction the decisive word belongs to development of nanotechnologies which have a great potential for use in methods of detection, diagnosis and treatment. The gold nanorods (AuNR) are of particular interest, especially considering their optical properties and chemistry of the surface, which allows easy connection to organic molecules adapted to specific needs. For research of mechanisms of action of viruses and pathogenic microorganisms the study of their properties is very important including oscillations pervade biological systems at all scales. In bacteria, oscillations control fundamental processes, including gene expression, cell cycle progression, cell division, DNA segregation and cell polarity. Oscillations are generated by biochemical oscillators that incorporate the periodic variation in a parameter over time to generate an oscillatory output. Spatial oscillators incorporate the periodic variation in the localization of a protein to define subcellular positions such as the site of cell division and the localization of DNA. There are some data which are focuses on the mechanisms of oscillators and the design principles of temporal and spatial oscillatory systems [23].

Current optical detection methods which are well developed for single micrometer size particles, cannot be applied to nanoparticles due to a strong signal dependence on particle size. Typically, such sensors consist of a light source which illuminates a sample volume of an aerosol or a liquid flow containing the particles of interest. An off-axis detector measures power of scattered light. The latter is a function of particle properties such as size, concentration, and optical density. In the tens of nanometers size regime particles act as dipoles, therefore the power of scattered light is proportional to the

sixth power of particles size. Lowering the detection size limits for the existing detectors places an impossible requirement on noise optimization. Therefore, a signal which has weaker particle size dependence can allow access to smaller particles [24]. In the field of virology, for example, it is critical to accurately quantify virus particles to study the effects of drug therapy in patients; and also, to study viral fitness, replication, and inhibition. There are several virus quantification techniques available to virologists, such as the quantitative PCR (polymerase chain reaction) method [25], the plaque titer method [26] and the image enhanced microscopy (IEM) technique [27]. However, a problem common to most of these techniques is that the analysis of a sample involves several tedious steps, which can take several hours to multi plays to complete.

The fast detection and characterization of nanoparticles, such as viruses or environmental pollutants, are important in fields ranging from biosensing to quality control. However, most existing techniques have practical throughput limitations, which significantly limit their applicability to low concentration analysis. There are some experimental dates that an integrated nanofluidic scheme for preconcentration and subsequent detection of nanoparticle samples within a continuous flow-through system. In These experiments using a Brownian ratchet mechanism increase the nanoparticle concentration 27-fold. Single nanoparticles are subsequently detected and characterized by optical heterodyne interferometry. A wide range of potential applications can be foreseen, including real-time analysis of clinically relevant virus samples and contamination control of processing fluids used in the semiconductor industry [28].

For nanoparticle structures identification a rather interesting method is Vibrational Spectroscopy (VS), which provides the most definitive means of identifying the surface species generated upon molecular adsorption and the species generated by surface. In principle, any technique that can be used to obtain vibrational data from solid state or gas phase samples (IR, Raman etc.) can be applied to the study of surfaces - in addition there are a number of tech-

niques which have been specifically developed to study the vibrations of molecules at interfaces (EELS, SFG etc.) [29, 30].

There are, however, only two techniques that are routinely used for vibrational studies of molecules on surfaces - these are: IR Spectroscopy (of various forms, e.g. RAIRS, MIR) and Electron Energy Loss Spectroscopy (EELS). There are both advantages and disadvantages in utilizing EELS, as opposed to IR techniques, for the study of surface species. It offers the advantages of high sensitivity, variable selection rules, spectral acquisition to below 400 cm^{-1} but suffers from the limitations of use of low energy electrons. Raman spectroscopy is used to study low-wave-number ($\leq 20\text{cm}^{-1}$) acoustic vibrations of the M13 phage. A well-defined Raman line is observed at around 8.5cm^{-1} . The experimental results are compared with theoretical calculations based on an elastic continuum model and appropriate Raman selection rules derived from a bond Polarizability model. The observed Raman mode is shown to belong to one of the Raman-active axial modes of the M13 phage protein coat. It is expected that the detection and characterization of this low-frequency vibrational mode can be used for applications in biomedical nanotechnology such as for monitoring the process of virus functionalization and self-assembly.

Recently, a technique which departs radically from conventional approaches has been proposed. This novel technique utilizes biological objects such as viruses as nano-templates for the fabrication of nanostructure elements. For example, rod-shaped viruses such as the M13 phage and tobacco mosaic virus have been successfully used as biological templates for the synthesis of semiconductor and metallic nanowires. Low wave number ($\leq 20\text{cm}^{-1}$) acoustic vibrations of the M13 phage have been studied using Raman spectroscopy [31]. The experimental results are compared with theoretical calculations based on an elastic continuum model and appropriate Raman selection rules derived from a bond polarizability model. Aside from serving as a protective layer, capsids are involved with various other aspects of their respective virus life cycles includ-

ing timely viral genome encapsulation (self-assembly and genome packaging), cell-to-cell virus transport, entry into host-cell (e.g., via cell receptor binding), genome release into host cell, etc. Despite their central importance to the life cycle, the various evolutionary pressures acting on spherical capsids are not well known. Half a century of empirical data has uncovered a large array of capsid sizes that range from tens to many thousands in subunit composition. Spherical capsids of all observed sizes may be obtained from a grouping of twelve pentamers (symmetric clusters of five subunits) separated by a variable number of hexamers (clusters of six subunits). This is the case for the T~7d papilloma viruses where all capsomers are made up of five subunits but they are in both hexavalent and pentavalent configuration, and larger viruses whose "hexamers" are actually trimers of "fused" or covalently bonded dimers. Capsid size may be characterized by two integers, h and k , which describe the number of hexamers ($h\{k\}$) one would have to "walk over" to get from one pentamer to an adjacent pentamer within a completed capsid. The utility of the class system is not entirely lost, however; specific angle patterns within the capsid ensures the existence of distinct hexamer shapes (each shape is colored distinctly in. Evidence indicates that capsid formation is nucleated, often starting with a single capsomer species (e.g., pentamers; for the purposes of this paper, a capsomer is a generally symmetric cluster of either five or six subunits), which then proceeds to completion by the addition of small subunit clusters (or single subunits). In T~1 capsid, where subunits are in identical/equivalent environments, nucleated assembly will be possible with no additional machinery. However, the formation of two or more capsomers from a single interaction site will require the employment of additional machinery to ensure high yields of the native state. For example, quasi-equivalent switches are required for the proper assembly of capsids containing two distinct capsomers: a pentamer and one type of hexamer. The addition of a second hexamer shape necessitates the requirement of a second mechanism such as auxiliary proteins for proper assembly. For spherical

virus capsids requiring more distinct hexamer shapes. Additional mechanisms to stabilize those new shapes at exactly the right positions within the forming capsid are likely to be also needed dominantly form.

Because capsids from different classes display markedly different geometries, they are bound to display different physical properties. The periodic nature of capsid hexamer contents also useful in understanding "T-switching": a process that permits canonical capsid subunits to more easily sample capsids containing similar hexamer shapes. This allows for a segue to understanding currently intractable and deadly pleomorphic viruses like Ebola and arenaviruses. For example, from the above T-switching rule, the available diversity of an arena virus may only be explained if we assume that the biologically relevant form of the arenavirus is the T~12 capsid. Non-icosahedral capsids. Although the framework presented doesn't appear to readily explain non-icosahedral capsids (some are just "slightly" non-icosahedral, such as the natively prolate phi29 capsids, while others are wildly different in form, such as Ebola with its natively filamentous shape), those capsids, like their icosahedral counterparts, also display capsomer sub-structures. In light of this, the geometric constraints analogous to endo angles that affect capsomer shape may be useful in obtaining insights into non-icosahedral capsid morphology, behavior, and classification. It will be exciting to see whether incorporating the non-icosahedral capsids into an expanded capsid periodic table will be possible. All canonical capsids (made up of trapezoidal subunits) may be built from a single type of pentamer and a repertoire of distinct hexamer shapes (colored distinctly only once in each capsid. The hexamer shape is described by the number of endo angles it displays. It is necessary to underline that effect of destroy of human immunodeficiency virus (HIV) and other enveloped viruses is based on the highly symmetric structure (e.g. icosahedral and others) of many viruses, which leads to a well-defined resonant frequency of ultrasound in the GHz range and which may be specifically absorbed by these structures and may subsequently lead to their irreversible damage.

In order to clarify the possible role of nanoparticles in diseases recently associated with them (such as Crohn's disease, neurodegenerative diseases, autoimmune diseases, and cancer), nanoscale characterization techniques should be used to a larger extent to identify nanoparticles at disease sites in affected organs or tissues, and to establish pertinent interaction mechanisms. Rapid, selective, and sensitive detection of viruses is central to implement an effective response to viral infection, such as through medication or quarantine. Established methods for viral analysis include plaque assays, immunological assays and transmission electron microscopy. These methods have not achieved rapid detection at a single virus level and often require a relatively high level of sample manipulation that is inconvenient for infectious materials. Yet, the ability to detect rapidly, directly, and selectively individual virus particles has the potential to significantly impact healthcare, since it could enable diagnosis at the earliest stages of replication within a host's system. One promising approach for the direct electrical detection of biological macromolecules uses semiconducting nano-wires or carbon nanotubes configured as field-effect transistors, which change conductance upon binding of charged macro-molecules to receptors linked to the device surfaces. One of the simplest medical nanomaterials is a surface perforated with holes, or nanopores. These pores are large enough to allow small molecules to pass but are small enough to impede the passage of much larger virus particles. The next step was cylindrical gold nano-tubules with inside diameters as small as 1.6 nm. When tubules were positively charged, positive ions were excluded and only negative ions were transported through the membrane. With a negative voltage, only positive ions could pass. The combining voltage gating with pore size, shape, and charge constraints allows achieving precise control of ion transport with significant molecular specificity. Lieber's group has reported direct, real-time electrical detection of single virus particles with high selectivity using nano-wire field-effect transistors to measure discrete conductance changes characteristic of binding

and unbinding on nano-wire arrays modified with viral anti-bodies [32].

The integrity of such devices allows increasing the number of the detection viruses. The analysis of the manifold literature shows, that task of the detection pathogenic micro-organisms is timely. Therefore, our available method would be one brick in the solution of the problems like that. Simultaneous acquisition of the vibrational and electronic fingerprints of molecular systems of biological interest, at the interface between liquid media, or at the air/solid, air/liquid interfaces in conditions similar to those encountered in nature or in model environments requires the use of sensitive and specific spectroscopic probes. Such a characterization is difficult to achieve with conventional linear optical spectroscopies due to their rather poor sensitivity to the low number of molecules (Raman) or their maladjustment to water environment (infrared absorption), at the exception of PM-IRRAS in specific work conditions. In addition, these techniques are for most of them only partially surface specific. One of the promising solutions of this problem is the use of the nonlinear Two-Color or Sum-Frequency Generation Spectroscopy (2C-SFG) that meets the desired spectroscopic requirements. The goal of this approach is to probe membrane models of various forms and in various environments: (i) lipid monolayers and bilayers; (ii) deposited on substrates, floating on water as Langmuir layers and at a liquid-liquid interface; (iii) alone and in interaction with molecules, including peptides and proteins; (iv) submitted to controlled stress (chemical, pH, electrochemical potential).

The increasing amount of available data of protein three-dimensional atomic structures, determined mostly by X-ray crystallography (related to the fast expansion of that field around third generation synchrotron storage rings) and NMR, has given much information about role of many proteins in biological processes. However, it has been pointed out that knowing the structure does not directly lead to the knowledge of the function, and that the protein alone, without its environment or its partners of interaction, is not totally informative. Additionally, some proteins cannot be satisfactorily crystallized

and thus cannot be accessed by X-ray crystallographic methods. Among them, membrane proteins need their membrane partners to fully play their role and are often not able to crystallize. In situ studies, and their according investigation techniques, are therefore favored for such objects. In the following, in situ should not be understood as in vivo, but imply rather that the objects are designed and studied in an environment mimicking what they experience in vivo. On the other hand, due to their essential role as the barrier between the cell cytoplasm and the extracellular medium, membranes themselves also get a lot of attention regarding their shape, stability, structure, composition, modifications under stresses (pH, temperature, electric potential) and interaction with proteins, water and chemicals in solution. The electrical behavior of bilayers makes them good candidates as membrane biosensors when attached to a conducting surface (semiconductor or metal). There are lots of possibilities to get average information on a given parameter of a membrane and its evolution under a given stress (e.g. diffusion of light, electrochemical methods, microbalance measurements). Specific in situ techniques allow direct investigation of key functional behaviors of synthetic membrane models (lipid mono and bilayers in an aqueous environment interacting either with selected proteins, ions or organic molecules) [33, 34].

The strong absorption of the water vapor and the poor detection properties of conventional FTIR spectroscopy led to the discarding of this technique for the study of such interfacial systems. This evidence for the limited range of infrared spectroscopic tools dedicated to the study of such fragile objects in their specific environment was written only about ten years ago. From that time, there has been a lot of progress from the spectroscopic point of view. In addition to IR absorption spectroscopy (conventional or attenuated total reflection (ATR) configuration), three other IR-based spectroscopies have been able to address the issue of a molecular layer on water with a signal-to-noise ratio sufficient to extract scientific information from experimental data. PM-IRRAS, an IR absorption technique initially developed to study the nanosurface of met-

als, has been applied to that of liquids. Being less sensitive to IR radiation absorption and easier to detect, Raman spectroscopy is often used on biological environment, although the low count rate on monolayers requires long acquisition times. It has been recently reported the detection of viruses by acoustic oscillations [35, 36]. However, the process of “rupture event scanning”, which was report, involves the separation of a virus particle from antibodies by ultrasound. This is distinct from the excitation of the vibrational modes of the virus particle itself, and occurs at much lower frequencies. There have also been some experimental studies of ultrasonic absorption by empty viral capsids [37, 38]. These experiments reveal an enhanced absorption in the MHz range as proteins reassemble into a capsid, but do not find a resonant peak in this frequency range. At the same time, it was emphasized that these and other results show that viral capsids are flexible and change size or shape in response to vibrations or to changes in temperature or pH [39].

One the most promising methods of biospectroscopy is SFG. These ultrashort pulsed lasers based optical measurement method is unique for investigation of vibrational modes of different viruses and other pathogenic microorganisms as well as study of nature of their oscillation processes and parameters of oscillation. Non-linear optics and its resonance technologies is possible direction of organization of treatment of pathogenic microorganisms in their different living media. Contrary to the previous ones, this second order nonlinear process is intrinsically specific to an interface, and involves no contribution from molecules in a centrosymmetric bulk, i.e., in solution or in gas phase. It has been extensively applied to solid interfaces in vacuum, controlled atmosphere and electrochemical conditions. For a few years, technological development of picosecond and femtosecond tunable laser sources have led both to an increase of the number of SFG experimental setups around the world and to a progressive application to fragile or buried interfaces. In addition to unique SFG setup is research based on usage of the CLIO Free Electron laser [40, 41]. This latter allows probing specific vibrations located in

the near and far infrared, which is again unique to date.

Although molecular fluorescence spectroscopy has been little used in studies in the field of virology, it is also an interesting approach with great potential in this perspective. This technique analyzes the fluorescence capacity of a sample [42], where a beam of high energy light (usually in the ultraviolet region) is irradiated on the sample to be excited into a higher electronic energy level; then the fluorophore molecule will rapidly lose energy to this environment through non-radiative modes (called internal conversion) and will return to the lowest vibrational level of the lowest electronic excited state. The molecule persists at this vibronic level for a period of time known as the fluorescence lifetime, and then returns to the fundamental electronic state by emitting a photon with energy lower than the irradiated one [43]. The excitation and emission spectrum are recorded by the instrument and is generally used to build excitation-emission (EEM) fluorescence matrices.

Another commonly-employed form of fluorescence technique is fluorescence correlation spectroscopy (FCS), which is used for temporal and spatial analysis of molecular interactions of biomolecules present in solution at extremely low concentrations. This technique is based on the principle that a fluorophore molecule has a specific free diffusion rate that is directly related to its size. This basic principle, for example, can be used to study protein interactions. As with other spectroscopic techniques, molecular fluorescence spectroscopy provides rapid results with high sensitivity and specificity, and is non-destructive, making this technique a tool of interest in the field of virology.

COMPUTATIONAL METHODS OF INVESTIGATION

Spectroscopically interrogating biological samples analyze definitely needs to use computational tools which facilitate the information collection and extraction. For this, it is necessary to address the different computational methods and tools and among them there are employed the methods:

- Preprocessing and multivariate analysis techniques, which consists

the correction and improvement of the signal-to-noise ratio of the spectrum, commonly employed before data analysis.

- Spectral cut and Baseline correction, which include determination of exact region of interest and diminish of the wavenumbers which are not absorbed and light scattering occurs due to the non-homogenous particle size [44].

- Spectral normalization techniques are used when it is necessary to remove spectral changes responsible for the thickness or concentration of the sample, making the normalized spectra become comparable to each other. Among the possible normalizations, there is the min-max normalization, which can be applied when there is a known peak that is stable and consistent between the specimens; or scaling methods to equalize the importance of each variable in multivariate data. [45].

- Multivariate analysis techniques are employed to analyze multivariate data, meaning data having two or more variables per object. Examples are first-order data (such as IR, Raman spectrum) and second-order data (such as fluorescence).

- Principal component analysis (PCA) is an unsupervised multivariate analysis technique widely used in biological studies. This technique is used to reduce the dimensionality of the sample's data and generate a new visualization. Dimensionality reduction occurs through a linear transformation of the original variables, generating orthogonal variables called principal components (PC).

- Cluster analysis (CA) techniques are unsupervised methods of pattern recognition that aim to group the spectra into groups when there is no information about the classes. These techniques are exploratory therefore they group the samples based on their similarity between spectra. CA techniques include k-means clustering (KMC), fuzzy c-means cluster analysis (FCA) and hierarchical cluster analysis (HCA) [46].

- Partial least squares (PLS) is a multivariate calibration technique that finds factors (latent variables, LVs) in the spectra set that explain the maximum variance in the reference variables set, using the simultaneous decomposition of the two. For this, PLS finds a

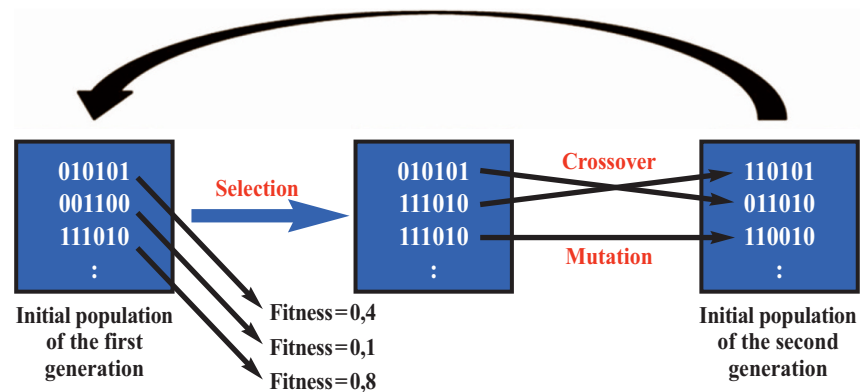
set of new maximally correlated variables orthogonal to each other, similar to PCA.

- Linear discriminant analysis (LDA) is a supervised technique widely used for class discrimination. It maximizes the between-class variance over the within-class variance in order to create a linear decision boundary between them.

- Successive projections algorithm (SPA) is a progressive variable selection technique. This means that it starts with a variable (wavelength or wavenumber, for example) and adds new variables in each interaction until an optimal number is selected. This technique uses multicollinearity minimization as a criterion for variable selection.

- The genetic algorithm is a technique that mimics Darwin's theory of evolution, where evolution occurs by natural selection in which the more adapted organisms have a greater chance of survival. In the case of GA, the variable selection process begins with a randomly formed population of variables [47]. Each chromosome is assigned an aptitude through a mathematical function called fitness function, where chromosomes with the highest fitness value are copied and the chromosomes with the lowest fitness value are eliminated in a step called the selection step. After the selection step, genetic operators are probabilistically applied. The mutation operator makes a variable that is selected to be unselected or vice-versa, and the crossover operator crosses the chromosomes.

- Sensitivity (SENS) can be defined as the confidence that a positive result for a sample of the labeled class is obtained; specificity (SPEC) is the confidence that a negative result for a sample of non-labeled classes is obtained; positive predictive value (PPV) measures the proportion of positives that are correctly assigned; negative predictive value (NPV) measures the proportion of negatives that are correctly assigned; Youden's index (YOU) evaluates the classifier's ability to avoid failure; positive likelihood ratio (LR+) represents the ratio between the probability of predicting a sample as positive when it truly is positive and the probability of predicting a sample as positive when it is actually not positive; and the negative likelihood ratio (LR-) represents the ra-



Operational scheme of the genetic algorithm (GA). In this scheme an initial population with 3 chromosomes is shown. A fitness value is assigned for each chromosome through the fitness function (F). Note that the chromosome with less fitness is discarded in the selection stage, while the larger one is doubly copied and the second largest fitness receives a copy. It is observed that the chromosome is mutated through the mutation operator in the second moment, and the other two chromosomes are crossed through the crossover operator.

tio between the probability of predicting a sample as negative when it is actually positive and the probability of predicting a sample as negative when it is truly negative [48].

- Diagnostic virology continues to evolve rapidly. Viral testing is now essential for the care of a number of patient groups, including hospitalized patients with acute respiratory infections; transplant recipients and other immunocompromised patients; patients infected with human immunodeficiency virus (HIV), hepatitis C virus (HCV), and hepatitis B virus (HBV); and infants with possible congenital infection. Multiple test methods continue to be used, but molecular tests are emerging as the dominant technology. A variety of commercial molecular assays have been or are in the process of being approved or cleared as in vitro diagnostic tests by the Food and Drug Administration (FDA) [49].

During the last years in response of global spraying the new structural types of corona viruses the method of estimation unique vibration/oscillation properties, determine the unique “fingerprints” of pathogenic micro-organisms, especially viruses.

The main task of the works done by international group including Georgian, French, German British and Greek researchers was elaboration of optical resonance spectrometry method of detection and treatment of pathogenic nanobiostructures including corona type viruses [50, 51].

Viruses and their genomes are mostly enclosed and protected by spherical capsids - symmetric coats or shells composed primarily of multiple copies of protein subunits. Aside from serving as a protective layer, capsids are involved with various other aspects of their respective virus life cycles including timely viral genome encapsulation (self - assembly and genome packaging), cell-to-cell virus transport, entry into host-cell (e.g., via cell receptor binding), genome release into host cell, etc. Despite their central importance to the life cycle, the various evolutionary pressures acting on spherical capsids are not well known. Half a century of empirical data has uncovered a large array of capsids sizes that range from tens to many thousands in subunit composition. Spherical capsids of all observed sizes may be obtained from a grouping of twelve pentamers (symmetric clusters of five subunits) separated by a variable number of hexamers (clusters of six subunits). This is the case for the T~7d papilloma viruses where all capsomers are made up of five subunits but they are in both hexavalent and pentavalent configuration, and larger viruses whose “hexamers” are actually trimers of “fused” or covalently bonded dimers.

Capsid size may be characterized by two integers, h and k , which describe the number of hexamers ($h \times k \{1\}$) one would have to “walk over” to get from one pentamer to an adjacent pentamer within a completed capsid. The utility of the

class system is not entirely lost, however; specific angle patterns within the capsid ensures the existence of distinct hexamer shapes (each shape is colored distinctly in. Evidence indicates that capsid formation is nucleated, often starting with a single capsomer species (e.g., pentamers; for the purposes of this paper, a capsomer is a generally symmetric cluster of either five or six subunits), which then proceeds to completion by the addition of small subunit clusters (or single subunits). In T~1 capsids, where subunits are in identical/equivalent environments, nucleated assembly will be possible with no additional machinery. However, the formation of two or more capsomers from a single interaction site will require the employment of additional machinery to ensure high yields of the native state. For example, quasi-equivalent switches are required for the proper assembly of capsids containing two distinct capsomers: a pentamer and one type of hexamer. The addition of a second hexamer shape necessitates the requirement of a second mechanism such as auxiliary proteins for proper assembly. For spherical virus capsids requiring more distinct hexamer shapes. Additional mechanisms to stabilize those new shapes at exactly the right positions within the forming capsid are likely to be also needed dominantly form.

Because capsids from different classes display markedly different geometries, they are bound to display different physical properties. The periodic nature of capsid hexamer contents also useful in understanding “T-switching”: a process that permits canonical capsid subunits to more easily sample capsids containing similar hexamer shapes. This allows for a segue to understanding currently intractable and deadly pleomorphic viruses like Ebola and arenaviruses. For example, from the above T-switching rule, the available diversity of an arena virus may only be explained if we assume that the biologically relevant form of the arenavirus is the T~12 capsid. Non-icosahedral capsids. Although the framework presented doesn't appear to readily explain non-icosahedral capsids (some are just “slightly” non-icosahedral, such as the natively prolate phi29 capsids, while others are wildly different in form, such as Ebola with its natively filamentous shape), those capsids, like their icosahedral counterparts, also display capsomer sub-structures. In light of this, the geometric constraints analogous to endo angles that affect capsomer shape may be useful in obtaining insights into non-icosahedral capsid morphology, behavior, and classification. It will be exciting to see whether incorporating the non-icosahedral capsids into an expanded capsid periodic table will be possible.

All canonical capsids (made up of trapezoidal subunits) may be built from a single type of pentamer and a repertoire of distinct hexamer shapes (colored distinctly only once in each capsid. The hexamer shape is described by the number of endo angles it displays. It is necessary to underline that effect of destroy of enveloped viruses is based on the highly symmetric structure (e.g. icosahedral and others) of many viruses, which leads to a well-defined resonant frequency which may be specifically absorbed by these structures and may subsequently lead to their irreversible damage.

Modeling and Simulation of oscillation effects in different viruses including corona like ones is based on studies of biostructure's physical characteristics, scattering and absorption properties. Estimation of electromagnetic (EM) spectrum and resonance wave length ranges is important for characterization of nano-micro-scaled particles and determination of biostructures unique spectral signatures, essential in bio-agents detecting and identification systems, and becoming as a great challenge in real systems investigations.

Method of estimation of spectral response on EM field & particle interaction is based on solutions of electrodynamics two (2D) or three (3D) dimensional boundary tasks. Analytical expressions of EM fields are derived from rigorous solutions of Maxwell's and Helmholtz's equations and defined through the dimensionless parameters, diameters over an excitation wavelength. It makes possible to apply the classical well-known approach to sub-micro particles characterization.

One of the ways for estimation of resonance frequencies range is the method determining the eigenvalues and corresponding eigenvectors obtained by algebraic system of functional equations

which could be written based on the solution of electrodynamic task considering EM wave-VL particle scattering [52]. Algebraic system has more complicated form when VL particle is of core-shell structure with different electric parameters. Resonant wavelength range is predicted theoretically in the vicinity of values corresponding the maximums of intensity of particular scattered partial waves. Estimation of resonant wavelength range based on determination of far-field characteristics such as scattering or absorption cross sections, the intensity of energy, wholly representing the response on wave-particle interaction is considered as the reasonable and decisive solution preferable for studying the spectroscopic properties and determination of possible spectral signatures of bioparticles, viruses.

Method of studying spectroscopic characteristics based on elaborated physical models of viruses represents the new possibility for estimation of spectroscopic properties and resonance wavelength range of viral nanoparticles, virions.

Thus, two main mediums of different structures and properties constitute the virion: capsid of protein capsomeres and nucleic acids into the capsid. Type, number and arrangement of capsomers and length of nucleic acid are essential in defining the size of capsid designed mostly in near-symmetrical geometry, having the unique self-assemble mechanism. A simple calculation shows, that the ratio of inner (core) and outer spherical volumes of icosahedral capsid of bacteriophage T7 (of diameters inner 1 $d = 42.6$ nm and outer 2 $d = 56.6$ nm) is approximately 0.426 [53], so quite a large portion (0.57) of volume in virion is occupied by the capsid proteins. Capsid's size is large enough than the “discrete” nature of protein subunits, therefore the influence of that on capsid whole geometry could probably be less significant. This fact allows virion to be modelled as a spherical core-shell particle of smooth inner or outer surfaces. Core-shell VLP model of spherical geometry could be used as the first approximation of shape-structure of icosahedral unenveloped virion. The structure and geometry of capsids as well as processes happening inside a layer probably dominate in determination

of physical, spectroscopic properties of nano-sized particles, virions.

Theoretical approach of studying spectroscopic properties of VLPs is based on classical Maxwell's EM theory, separation of variables method for solving Helmholtz's (wave) equation. Solution of Helmholtz's equation leads to the Bessel's and/or Legendre's equations [54]. EM fields in different areas of VLP are written as the sums of multipole-waves with unknown multipole coefficients. Application of boundary conditions to EM field components on core-shell surfaces and labour consuming mathematical transformations leads to rigorous theoretical solution of EM scattering problem on single VL particle. Analysis of EM field expressions show that arguments of functions determining the multipole coefficients and scattered fields depend only on relative values of particles diameters over wavelength. Therefore, it makes possible to expand the research area, and the findings of well-established Mie theory [55] considering the light scattering on a homogeneous sphere be applied to nanoparticles of core-shell morphology and particles of biological origin as well.

Spectral response on EM wave-VLP interaction is determined by estimation of far-field ($r \ll 2d/\lambda$) characteristics representing the angular distribution of scattered (absorbed) energy. Scattering properties are characterized via expressions such as: the total scattering cross section

$$\sigma_r = 2\pi \frac{1}{k_z^2} \sum_{s=-1}^{\infty} (|A_s^e|^2 + |A_s^m|^2) \frac{s^2(s+1)^2}{(2s+1)}$$

Proposed theoretical solution, analytical expressions of EM fields make possible to estimate the fields in the areas of core, shell and surrounding areas of VLPs. based on machine learning and modeling techniques have been used for generating a simulated spectrum of nanoparticle of given size and available literature optical constants.

Computer simulation (based on MatLabR2013b software) was carried out for TMV particles characterization. Parameters of TMV particle are obtained from scientific publications based on different measuring technics. Length of TMV virion is 280-300 nm, outer (d2) and inner (d1) diameters of

capsid are 18 nm and 4 nm, correspondingly. Two models - homogeneous cylindrical (of diameter) and homogeneous of core-shell structure (of diameters - outer and inner), are used for simulation study of TMV virion. Computer simulation shows, that expected resonant spectral response is observable on far-field characteristics, resonant vibrational frequencies of whole TMV particle may be associated to scattering cross-section maximums. Values and locations of maximums strongly depend on dielectric and magnetic parameters, distance between the neighbor maximums increases the longer wave lengths range is.

Near-field distribution presented in a form of isolines of EM field amplitudes), indicates the locations of energy maximums inside and outside of particle. Investigation of EM field distribution makes possible to have insight vision of nanobiotoparticles [56-59].

Proposed computing model is useful for investigation of spectroscopic properties of nanobiotoparticles and appreciation of possible resonant wave length ranges correlating with scattering/absorbing efficiency of VLP.

Experimental data obtained by applying exquisite techniques and outcomes of theoretical or simulation models should complement each other and verify factors such as possible anisotropy of core-shell areas of virion, surface roughness and inhomogeneity unforeseen in simplified approaches.

CONCLUSIONS

Spectroscopic methods have the characteristic of providing fast results and reliable information related to the composition of the samples. The studies presented here have shown promising results in a field of science that needs to be better explored. It has been shown that multivariate analysis techniques are of great importance to analyze spectroscopic data, providing the potential to identify and classify biological samples. We do hope that with advancement in this field of study, spectroscopic methods and tools will be used in bio medicine in the near future. Methods of light therapy of different diseases based on estimation of EM field characteristics and resonant wave ranges based on computer sim-

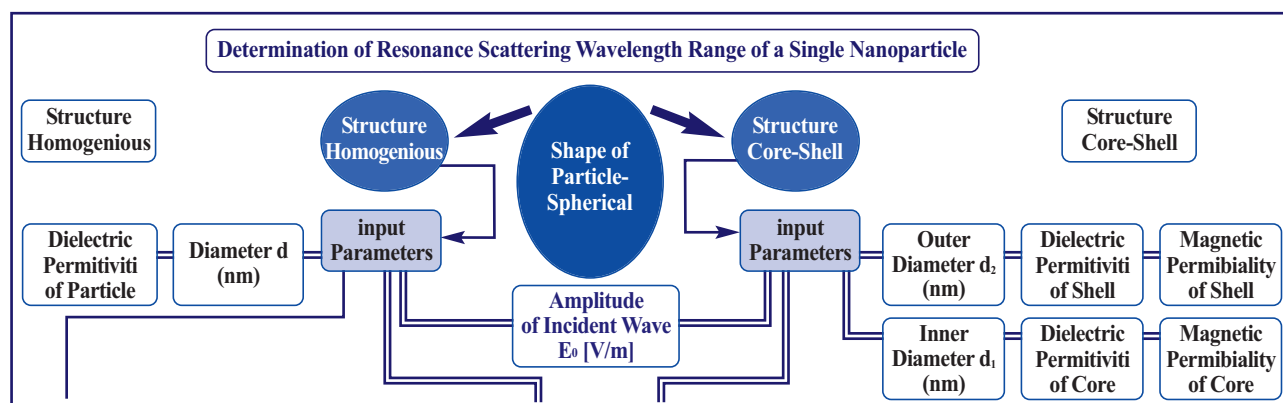
ulation of nanobiotoparticles characterization will be widely implemented, and possibility of determination of resonant (own) frequencies of entire system of molecules including virions will be a key point for that.

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RESEARCH PROGRESS OF KAWASAKI DISEASE IN SHOCK SYNDROME

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Kawasaki disease is a systemic vasculitis that often involves medium-sized arteries, especially coronary arteries [1]. More children under the age of five are seen. Coronary artery abnormalities (CAAs) include coronary artery dilatation and aneurysm in 15 ~ 25% of untreated children. In 2009, Kanegaye et al. [2] defined Kawasaki disease as Kawasaki disease shock syndrome (Kawasaki disease shock syndrome, KDSS). Kawasaki disease shock syndrome (KDSS) is a rare manifestation of Kawasaki disease (KD), but it can lead to serious sequelae and adverse results. The incidence of KDSS in KD patients was 1.9% ~ 7.0% [3-6]. The incidence of KDSS in China is lower than that in western countries. In acute phase, about 5% of KD children developed hypotension and shock. The main manifestations of this kind of children were tissue hypoperfusion and hemodynamic instability, accompanied by a clinical manifestation that systolic blood pressure was continuously lower than the normal systolic depression value of 20% or more in children of the same age. Compared with KD children without shock symptoms, KDSS children have a higher risk of cardiovascular complications, such as mitral valve regurgitation and myocardial systolic dysfunction, increased incidence of coronary artery disease; resistance to immunoglobulin therapy; often complicated with multiple organs

1. DIAGNOSIS OF KDSS

In 2009, Kanegaye et al put forward the diagnostic criteria of KDSS: persist-

ent blood pressure drop, systolic blood pressure below 20% of the normal mean blood pressure in the corresponding age group or peripheral circulation perfusion disorder in children with KD. Systolic blood pressure < 70 mmHg in children aged 1 ~ 12 months or systolic blood pressure < $[70 + 2x \text{ age (years)}]$ mmHg in children aged 1 ~ 12 months was hypotension [7]. In addition, there were KD manifestations of normal systolic blood pressure and decreased diastolic blood pressure in clinic. Xue Chaochao and others thought that it was between KD and KDSS, which was the transitional period of the course of disease [8]. Foreign literature reported that KDSS accounted for 1.9% ~ 7% of KD children [9]. About 1.78% ~ 1.90% of KD children in Taiwan had KDSS. Foreign statistics showed that KDSS was more common in women than in men [10] [11]. The error may be related to race, environment, sample number and atypical early manifestation of the disease, which leads to lack of clinical understanding and missed diagnosis.

2. EARLY RECOGNITION OF KDSS

The incidence of KDSS. There was no significant gender difference between men and women, although it was reported that men were slightly more than women [12]. Compared with non-shock KD, there was no significant difference in the age of onset of KDSS

[13], which could occur in any age group, including adults. In contrast, KDSS was more likely to occur in infants under 6 months of age and children over 10 years of age. The overall median age of onset was older than that of KD, and it was more likely to occur in patients with incomplete KD [14].

3. POSSIBLE MECHANISM OF KDSS

The mechanism of circulatory and hemodynamic disorders of KD in acute phase is not clear. It is generally believed that it is the result of multiple factors. The possible pathogenesis includes capillary leakage caused by vasculitis, myocardial systolic dysfunction and abnormal regulation of cytokines, which may affect each other to accelerate the occurrence of circulatory disturbance.

3.1 Capillaries leakage

Although KD is characterized by coronary artery damage, small and medium vessels can be involved in the whole body. Inflammatory factor storm, high expression of vascular endothelial growth factor and dysfunction of endothelial cells are the causes of vascular endothelial injury, and then the increase of vascular permeability. When the permeability of small blood vessels and capillaries continues to increase, resulting in plasma exosmosis and loss of small molecular proteins, followed by the decrease of plasma colloid osmotic pressure, the significant decrease of plasma albumin and the decrease of circulating blood volume [15]. The clinical manifestations were decreased blood

pressure, hypoperfusion of tissue, diffuse edema of the whole body and hydrops in the third space, such as chest cavity and abdominal cavity.

3.2 Myocardial systolic dysfunction

In patients with KD, in addition to coronary artery damage, there are also myocardial cell damage and myocardial ischemia and myocardial infarction caused by coronary artery disease. Endocardial biopsies confirmed that myocardial fibrosis caused by diffuse myocarditis injury is an important cause of left ventricular systolic dysfunction in patients with KD [16]. The decrease of left ventricular ejection fraction in KD is associated with the occurrence of KDSS [17]. It should be noted that most patients with KD are in subclinical cardiac insufficiency, rather than an independent factor leading to KDSS.

3.3 abnormal regulation of cytokines.

Many scholars believe that KDSS and septic shock have similar clinical characteristics and immunological mechanism. Abnormal cytokine regulation and activation of intracellular signal transduction pathway mediated by superantigen [18]. Continuous dilatation of microvessels leads to the decrease of peripheral vascular resistance and circulation congestion.

4. NURSING CARE

4.1 nursing care of fever.

Fever is a typical manifestation of Kawasaki disease. Children with Kawasaki disease shock syndrome have repeated fever in the course of disease. The body temperature is between 38°C and 39°C, and the body temperature is between 38°C and 39°C. Keep high fever and vital signs. Watch out for febrile convulsion. Take positive cooling measures: when the body temperature is not higher than 38.5°C, try to take physical cooling when the body temperature is not higher than 38.5°C, such as using antipyretic paste, warm water wipe bath, drinking the right amount of warm water, etc., when the temperature is more than 38.5°C. At the same time of physical cooling, antipyretic drugs can be used to cool down according to

the doctor's orders, and the body temperature can be measured every half hour after taking cooling measures. Children often have the performance of sweating when the heat recedes, wipe dry in time and change the clothes in time to avoid cold and aggravate the condition.

4.2 Emergency care

When KDSS occurs, nursing. The child was immediately moved to the rescue bed, the head raised 15°, the lower extremity raised 20°, in order to increase the amount of blood in the heart. Heart rate, heart rate, pulse, blood pressure, transcutaneous pulse oxygen saturation, capillary filling time were observed and related nursing records were made. Limb temperature-to a certain extent, reflects the limb circulation and perfusion, and can touch the limb to understand the shock during nursing. Maintenance of effective ventilation, mask oxygen inhalation (5L/min) and timely removal of oral secretions and foreign bodies in children, if can not improve ventilation, should be treated by mechanical ventilation. Rapid venous volume expansion can effectively increase the volume of circulating blood, which is the key to prevent shock deterioration and make children turn to crisis. In nursing care, two venous pathways suitable for volume expansion can be quickly established within 5 minutes, and the thick proximal vein is selected, and the best choice is for external jugular vein or external jugular vein. At the same time, the Department of Anesthesiology was invited to carry out deep venous puncture for the use of vasoactive drugs.

4.3 Monitoring of blood pressure

If the child has shock symptoms of hypotension on admission, it is important to correctly measure and record the changes in blood pressure. According to the age of the child, the cuff of different width should be $2 \leq 3$ of the length of the upper arm. The normal average value of blood pressure of different ages can be calculated by this formula, that is, systolic blood pressure (mmHg) = $80 + (\text{age} \times 2)$, diastolic blood pressure $2 \leq 3$ of systolic blood pressure. Blood pressure was measured once an hour

during the whole nursing process of the child, and when dopamine or dobutamine was used, blood pressure was measured every half hour if there was a fluctuation of blood pressure in order to adjust the dosage of the drug in a timely manner.

4.4 Nursing care for the use of expanded drugs

The principle of both crystal fluid and colloidal fluid was adopted in the expansion of shock. 20 ml of saline was the first choice in clinic, and the infusion was completed within 10 minutes. after rapid infusion of saline according to the doctor's orders, blood pressure and heart rate were monitored immediately. The molecular weight of colloidal solution is large, and the dilatation effect is longer than that of crystal solution, so normal saline continues to be infused with colloidal body fluid after expansion. Albumin is the first choice of colloidal fluid in clinical rescue. The dose of 20ml/kg is completed within 30 minutes. During volume expansion, attention should be paid to the wet sound of both lungs and the sudden enlargement of liver and spleen to avoid heart failure. After dilatation of lens and colloid, blood pressure gradually returned to normal, consciousness changed, and no heart failure such as pulmonary edema, hepatosplenomegaly and so on.

4.5 nursing care of vasoactive drugs

The combination of norepinephrine and dobutamine can play a synergistic role in improving systemic hemodynamics. However, both of them are high-risk drugs, the use process should be closely nursing and observation, first check whether the infusion pump is normal, in the syringe and infusion tube. Paste the red mark on it. According to the normal blood pressure value of children in this age group, the starting drug speed was set according to the normal blood pressure value, and the blood pressure, heart rate, blood oxygen saturation and other indexes were monitored every 30 minutes according to the principle of low concentration to high concentration. When changing drugs, nursing action should be quick. When norepinephrine

is used in peripheral veins, the local skin color changes should be closely observed to prevent venous leakage. If venous leakage occurs, infusion should be stopped immediately, and the infusion pathway should be changed in time to keep blood pressure stable. At the same time, phentolamine injection of 10mg should be given local closure immediately. The drug concentration should be gradually reduced when stopping the drug, and sudden withdrawal of the drug should be strictly prohibited. If the child appears blood pressure drop, drowsiness and even coma in the course of withdrawal, the doctor should be reported immediately.

4.6 Nursing Care of gamma globulin shock therapy

Gamma globulin is a blood product, before infusion, strict aseptic configuration operation should be carried out to evaluate the body temperature, if it reaches more than 38.5°C, the doctor should suspend the infusion. The children in this group were mentally soft and difficult to take oral administration. Ibuprofen suppository or paracetamol was given to embolize anus and antipyretic. The body temperature decreased to less than 38.5°C. Then configuration, first put gamma globulin at room temperature for 15 minutes after input, before and after infusion of saline flushing tube, to avoid mixing with other drugs to cause adverse reactions, at the beginning of about 10ml/min, 15 minutes later, if there is no adverse reaction, can speed up the infusion speed, but not more than 20ml/min [19]. In the course of medication, we should pay close attention to whether there are adverse reactions, once fever, rash and so on, immediately suspend infusion, notify doctors, and give antiallergic treatment.

4.7 corrective nursing care of hypoalbuminemia and hyponatremia

Children with KDSS have different degrees of hypoalbuminemia and hyponatremia, which are significantly correlated with vascular inflammation [20]. It should be corrected slowly in the course of antishock therapy. The children in this group were treated with albumin on the first day, and the albumin

(1g/kg) was infused twice every other day according to the doctor's orders. After 3 times, the albumin returned to the normal range. Because it was a blood product, the nursing should be infused within 4 hours. Because hyponatremia can cause nausea, vomiting, coma, convulsion and edema in children, sodium should be supplemented in time, usually 24 ~ 48 hours, and blood sodium and other electrolytes should be closely monitored in nursing.

4.8 Aspirin care

Aspirin is a necessary drug for the treatment of Kawasaki disease, and it is also the first choice. Aspirin has the effect of anti-infection and anticoagulant. Early combined with immunoglobulin can effectively control the process of acute inflammation and reduce coronary artery disease. Every day on time and according to the quantity to feed the child, in order to reduce the stimulation of the drug to the gastric mucosa and form a drug-induced ulcer, the children are taking medicine after meals, take proper amount of food before taking medicine at night, do not take medicine on an empty stomach. If you have symptoms of fever before and after taking aspirin, be sure to interval at least six hours with Merrill Lynch or tenolin, and ask the doctor in charge if you want to adjust the duration of aspirin use. During aspirin, attention should be paid to the occurrence of bleeding, hematuria and black stool in the nose, skin, mucous membrane or gums, and the liver function should be reviewed regularly. Tell the child not to pick his nose with his hand; when brushing his teeth and gargling, use a soft toothbrush to gently move, if necessary, use an oral protective bag to help the child clean his mouth; give the child a light and digestible diet to keep his stool unobstructed.

4.9 Nursing of coronary artery aneurysm

Children with coronary artery aneurysm (KDSS) are prone to sudden death caused by rupture. Nursing. The child was told to stay in bed and rest and reduce the work done by the heart. Closely observe whether the child has uncomfortable symptoms, pay attention

to whether the heart rate is normal, whether the heart rate is uniform, whether the heart sound has murmur during auscultation. For shock children, the action of turning over and patting the back should be gentle, and when defecation is difficult, the enema should be given to Keselu to avoid the rupture of coronary artery aneurysm. For children of different ages, personalities and psychological characteristics, take targeted nursing measures: for older children to communicate more, to encourage more language, to avoid increasing their psychological burden; for young children, because of pain, fear and other reasons often cry, can give toys, play cartoons to distract their attention, cooperate with treatment, if necessary to give drug sedation, in order to reduce the heart load.

4.10 Nutrition care

After the occurrence of KDSS, the children should suspend eating, carry out total intravenous nutrition, and replenish the amount of 60 ~ 80ml/kg solution every day. Due to fever, rash, skin erosion and other reasons, children need to supplement water-soluble vitamins every day to facilitate skin repair. After stable blood pressure and recovery of consciousness, the children were given a fluid or semi-fluid diet with high calorie, high protein and high vitamin content to avoid eating raw, cold, hot, hard, sour, spicy and other foods, so as not to affect the recovery process of the disease.

4.11 skin and mucous membrane nursing

Children with KD had conjunctival congestion in both eyes. When there were more eye secretions, the eyes were washed with saline 1 ~ 2 times a day, and erythromycin eye ointment was applied twice a day to avoid strong light irradiation in the eyes. When the oral mucosa is chapped and erosive, gargle with sodium bicarbonate solution or saline every day, and apply the mouth lip evenly after the vitamin E capsule is crushed every day. For finger end peeling, use disinfection scissors to cut off, tell children not to tear, avoid infection. Change sheets and clothes every day to avoid skin infec-

tion. Norepinephrine can cause strong contraction of arterioles and venules of the whole body, and the contraction of superficial vessels is more significant, resulting in dry and cold skin temperature, which can be covered with blankets, warm and dry towels applied to the foot and other thermal insulation measures. There was no serious skin infection in all the children.

4.12 Psychological nursing

The child is relatively young, irritable and irritable during the acute period, and gives more comfort and encouragement. When in contact with the child, there should be more limb contact, such as hugging, shaking hands and so on. Safe physical contact can increase the child's sense of security. Children can also be prepared for favorite toys, books, or organize children and parents to carry out some feasible and meaningful activities to enrich the child's life during hospitalization and reduce the mental stress of the child [8]. In addition, try to concentrate on the operation, the action is gentle, reduce the stimulation to the child. Parents are worried about the prognosis because of the child's condition, explain the disease, explain the disease knowledge, give psychological support and spiritual comfort, and establish confidence in treatment.

4.13 Health education

Explain the condition to the family in time and give psychological support, do a good job of discharge guidance, including taking medicine as directed by the doctor, do not increase or decrease the amount of medicine at will and observe whether there are digestive tract symptoms; give children easy to digest high vitamins, high protein food supplementary nutrition; regular outpatient review; pay attention to rest, do not exercise violently; need to be vigilant for coronary artery disease, 1 month, 3 months, 6 months, 1 year after discharge.

5. SUMMARY

In a word, KDSS is a serious complications of Kawasaki disease. Some of the early clinical symptoms of KDSS are not typical and are easy to be missed or

misdiagnosed. Therefore, early identification and timely and appropriate treatment can quickly correct shock, reduce coronary artery damage and multiple organ injury and other serious complications. It is also very important to pay attention to the popularization of nursing knowledge in hospitalized children. It will also improve the prognosis of children with KDSS.

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CLINICAL ANALYSIS OF 3 NEONATAL WITH PNEUMOTHORAX

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ABSTRACT

Objective: To analyze the common causes, clinical features and treatment measures of neonatal pneumothorax, and further reduce the incidence of pneumothorax. **Methods:** A total of 30 neonatal pneumothorax children admitted to our hospital from January 2017 to December 2020 were systematically reviewed and analyzed. **Results:** Among the 30 cases of pneumothorax, pathological pneumothorax was 16 (53.3%), iatrogenic pneumothorax was 12 (40.0%), spontaneous pneumothorax was 2 (6.7%). Of the 12 cases with lung compression ratio $\leq 30\%$, 8 cases received conservative treatment, and 4 cases received conservative gas absorption after thoracic ventilation. 18 patients with lung compression ratio of $>30\%$, 10 patients (55.6%) did not receive pleural aspiration and closed drainage under HFOV assisted breathing, and 8 patients (44.4%) received closed thoracic drainage. After treatment, 29 cases (96.7%) were cured and 1 case (3.3%) gave up treatment. **Conclusion:** asphyxia recovery \ mechanical ventilation, meconium inhaled syndrome, neonatal pulmonary hyaline membrane disease is the high risk factors of neonatal pneumothorax occurred, the principal means of treatment for mechanical ventilation (HFOV), pleural puncture extraction and chest closed drainage; Strengthening the understanding and early diagnosis of neonatal pneumothorax and taking the correct treatment means can effectively improve the success rate of treatment.

Keywords: *Pneumothorax Neonatal Etiology Treatment*

Neonatal pneumothorax is a common acute critical condition in neonatal NICU, accounting for between 1% and 2% of live births [1]. In recent years, the incidence of neonatal pneumothorax has been increasing due to the use of endotracheal intubation, ventilator and continuous positive pressure ventilation in asphyxia resuscitation. In order to reduce the incidence of pneumothorax, the clinical data of 30 neonatal pneumothorax children admitted to our hospital from January 2017 to December 2020 were retrospectively analyzed and summarized as follows.

1.1 Data and methods: Pneumothorax was diagnosed according to ICD-10 disease code. 30 cases of neonatal pneumothorax were treated from January 2017 to December 2020, including 20 males and 10 females. Gestational age ranged from 32 weeks to 41+2 weeks, including 6 cases of gestational age from 32 weeks to 35+6 weeks, 3 cases of gestational age from 36 weeks to ≤ 37

weeks, and 21 cases of gestational age $>$ at 37 weeks. The birth weight ranged from 1700g to 4400g, including 4 cases with birth weight $<$ 2500g and 26 cases with birth weight ≥ 2500 g. 16 cases of normal delivery, 14 cases of cesarean delivery; Apgar score $<$ 7 in 22 cases, Apgar score ≥ 7 in 8 cases; There were 9 cases of III degree amniotic fluid contamination and 21 cases of clear amniotic fluid. There were 5 cases of premature rupture of membranes and 25 cases without premature rupture. There were 7 cases of asphyxia resuscitation, 5 cases of mechanical ventilation, 5 cases of neonatal hyaline membrane disease, 9 cases of meconium inhalation syndrome, 2 cases of neonatal pneumonia and 2 cases of spontaneous pneumothorax. Eighteen cases received endotracheal intubation and mechanical ventilation (HFOV), 8 cases received continuous positive pressure ventilation, and 4 cases received oxygen inhalation by headhood. Time of pneumothorax: 22

cases $<$ 3 hours, 5 cases 3-6 hours, 3 cases $>$ 6 hours after admission.

1.2 Clinical manifestations: the children with mild symptoms were only mild shortness of breath, moaning, and no obvious pulmonary signs; Sever patients show varying degrees of dyspnea, decreased percutaneous oxygen saturation, cyanosis, moaning, and restlessness. During the course of non-invasive and invasive assisted ventilation, the patient's condition improved and then suddenly experienced instability of oxygen saturation, moaning, worsening of dyspnea, and changes in skin color (livid or pale). Physical examination: in severe cases, bilateral thoracic asymmetry and respiratory movement asymmetry were observed. Percussion on the raised side of the chest presented drum sound, and respiratory sound on the affected side was weakened on auscultation. Blood gas analysis showed that PO₂ decreased less than 50mmHg in 23 cases (77%), PCO₂ increased more than 45mmHg in 15 cases (50%), SO₂ decreased less than 90% in 21 cases (70%). Chest radiograph showed reduced lung volume, loss of lung texture and pneumothorax line outside compressed lung. Severe heart, mediastinum to the healthy side displacement, low diaphragm; Partial display of uneven lung transmittance. For chest radiographs showing uneven transmittance and considering air leakage, chest CT examination was performed.

1.3 Auxiliary examination

(1) All children received emergency bedside chest X-ray examination. Chest X-ray findings: some showed reduced lung volume on the affected side, loss of lung texture outside the compressed lung, and presence of pneumothorax line. In severe cases, the heart was displaced from the mediastinum to the healthy side, and the diaphragm was low. Partial display of uneven lung

transmittance. There were 6 cases of left pneumothorax, 14 cases of right pneumothorax, and 10 cases of bilateral pneumothorax. Lung compression was less than 30% in 12 cases, and $\geq 30\%$ in 18 cases. Some chest X-rays and CT scans are shown in Figure 1.

(2) Chest CT examination: in order to further confirm the location, range and degree of air leakage, 20 cases were examined by chest CT examination. Among them, 10 cases were bilateral pneumothorax and 4 cases were combined with small volume of gas in mediastinum. There were 10 cases of unilateral pneumothorax combined with small volume of mediastinal gas in 1 case and medium volume of mediastinal gas in 1 case. CT showed severe exudation of both lungs in 18 cases.

(3) Blood gas analysis is shown in Table 1. Although blood gas analysis is nonspecific in the diagnosis of pneumothorax, pneumothorax is often characterized by decreased blood oxygen partial pressure, increased carbon dioxide partial pressure, acidosis, and increased lactic acid.

1.4 Treatment and outcome: All the children were treated with anti-infection, sedation and support for the primary pulmonary disease after admission. The clinical symptoms and signs of 8 patients with pneumothorax were relatively light. X-ray indicated that lung compression was about 10%, and oxygen chest was absorbed by headwear. X-ray and CT showed lung compression of 10%~30% in 4 cases, and pneumothorax absorption was followed by chest puncture and ventilation with nasal obstruction and continuous positive airway pressure. The remaining 18 cases showed lung compression > 30% by X-ray and CT, and all of them were treated with high frequency oscillatory bypass (HFOV). All the 18 children in this group received HFOV ventilation after pneumothorax. ① The HFOV machine is Draeger and Swiss

Blood gas analysis of 30 children

Table 1

PH	PO2 (mmHg)	PCO2 (mmHg)	LAC (Mmol/L)	SO2 (%)
7.23	48.0	51.0	3.8	88
6.94	49.4	42.5	3.5	72.8
7.10	56.2	68.3	5.2	97
7.11	42.6	67.8	5.1	74.7
7.36	54.3	40.5	3.3	94.3
7.44	63.6	27	3.1	96.4
7.35	39.2	42.1	5.1	84.1
7.14	49.8	52.6	5.2	84.0
7.33	42.3	39.7	3.1	88.5
7.28	48.8	45.8	4.6	87.9
7.34	97.5	34.9	3.3	99.0
7.34	40.3	38.2	3.7	83.8
7.22	37.9	53.5	5.3	77.0
7.42	43.6	31.4	2.3	90.6
7.20	36.7	52.1	2.8	73.6
7.32	49.8	39.3	1.4	90.9
7.25	72.5	44.5	4.1	95.0
7.33	35.6	38.8	2.1	81.0
7.30	40.4	40.0	2.5	82.9
7.37	43.9	27.1	3.5	90.5
7.28	41.2	47.5	2.6	82.3
7.23	20.4	47.8	6.2	36.7
7.28	36.5	47.7	2.5	80.0
7.23	41.8	51.2	3.1	79.5
7.21	81.4	50.4	1.6	97.3
7.28	31.9	49.1	3.5	68.6
7.34	42.8	42.3	2.1	85.4
7.16	51.5	52.4	5.3	85.9
7.34	49.5	38.5	5.0	87.4
7.39	45.2	39.9	2.0	88.9

Fuping high-frequency ventilator. The principle of selecting initial parameters is to improve the oxygenation and ventilation status of children with as low average airway pressure as possible. The permissible partial pressure of oxygen is low, while the partial pressure of carbon dioxide is high. Initial parameters: the average airway pressure was 12 ~ 14cmH₂O, the oscillation frequency was 10 ~ 12Hz, the amplitude was 25 ~

35cmH₂O, and the oscillation amplitude was appropriate to the umbilical cord. Initial parameters were selected according to child weight, gestational age and transcutaneous oxygen saturation. ② Parameter adjustment: All children were monitored by a multifunctional monitor to maintain normal heart rate, blood pressure, body temperature and percutaneous oxygen saturation between 90% and 95%. Regularly review the blood gas analysis and adjust the parameters according to the results; ③ Removal method: the child's vital signs were stable, the transdermal oxygen saturation was between 90% and 95%, the blood gas analysis was normal, and the bedside X-ray chest film showed that basic pneumothorax absorption and lung ventilation were significantly improved. The children with closed thoracic drainage were free of gas for 24h. According to the condition of the original disease, it was maintained for 1 to 4 days, then the ventilator was changed to non-invasive ventilator, and the ventilator was removed. All the 17 cases recovered and

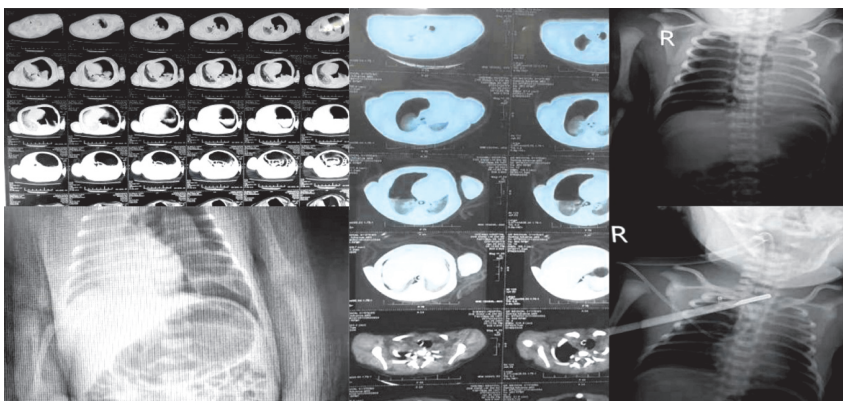


Fig1 Partial chest radiograph and chest CT

were discharged from hospital. One patient gave up treatment. Of the 18 cases, 10 did not receive thoracic ventilation and closed drainage, and 8 cases were combined with closed thoracic drainage.

1.5 the results

Among the 30 patients with pneumothorax, 16 cases (53.3%) were pathologic pneumothorax, including 9 cases (56.3%) of meconium inhalation syndrome, 5 cases (31.2%) of neonatal hyaluronic membrane disease, and 2 cases (12.5%) of neonatal pneumonia. There were 12 cases of iatrogenic pneumothorax (40.0%), 7 cases of parturient asphyxia resuscitation (58.3%), 5 cases of mechanical ventilation (41.7%), 2 cases of spontaneous pneumothorax (6.7%). Lung compression ratio $\leq 30\%$ in 12 cases, 8 cases of pneumothorax clinical symptoms and signs were light, X-ray indicated that lung compression was about 10%, and oxygen was given to the head mask and pneumothorax absorption. X-ray and CT showed lung compression of 10%~30% in 4 cases, and pneumothorax absorption was followed by chest puncture and ventilation with nasal obstruction and continuous positive airway pressure. In 18 cases, lung compression ratio was 30% >, 10 cases (55.5%) did not receive pleural ventilation and closed drainage after HFOV, and 8 cases received closed thoracic drainage (44.4%). After treatment, 29 cases were cured (96.7%), 1 case gave up treatment (3.3%).

2 DISCUSS

2.1 Common causes of pneumothorax

The incidence of pulmonary air leakage in live births is 1% ~ 2% [2], and the incidence of air leakage in inpatients in our hospital is 5.9%. Alveolar pressure increase, alveolar hyperinflation and expansion caused by any factor can cause alveolar rupture and air leakage, and more than half of them are pneumothorax. According to the causes and mechanisms of neonatal pneumothorax, the common types are pathologic, iatrogenic and spontaneous. Among the 30 patients with pneumothorax, 16 were pathologic pneumothorax, 12 were iatrogenic pneumothorax and 2 were spontaneous pneumothorax.

2.1.1 Common causes of pathological pneumothorax

2.1.1.1 Meconium Inhalation Syndrome: In meconium Inhalation Syndrome, meconium inhaled into the airway can cause flap embolism, stimulate bronchial tubes, lead to bronchospasm and aggravate inflammation, airway resistance is increased and lung compliance is inconsistent, gas is easy to en-

ter and not easy to exit, and alveolar rupture is easy to cause pneumothorax. In this group, there were 9 cases of meconium inhalation syndrome in pneumothorax, accounting for 56.3%, which was consistent with the reports in literature [3,4]. All of them suddenly developed dyspnea and cyanosis within 6 hours after birth, chest X-ray and CT showed that the lung tissue was compressed by 30% >, and improved after thoracic closed drainage and mechanical ventilation (HFOV).

2.1.1.2 Neonatal hyaline membrane disease There were 5 cases of neonatal hyaline membrane disease, accounting for 31.2%, all of which were premature infants. The lack of surfactant in the lungs of premature infants leads to extensive alveolar atrophy, decreased alveolar stability, uneven alveolar pressure and different alveolar sizes, which are prone to pneumothorax. In addition, the use of CPAP and two-level assisted ventilation in premature infants can also cause pneumothorax.

2.1.1.3 Neonatal pneumonia In this group, there were 2 cases of neonatal pneumonia, accounting for 12.5%. Both cases were caused by intrauterine infection, which caused severe pneumonia, resulting in decreased pulmonary compliance and uneven lungs. Pneumothorax was easy to occur in the process of respiratory adjuvant therapy.

2.1.2 Common causes of iatrogenic pneumothorax

2.1.2.1 Neonatal asphyxia resuscitation In this group, there were 7 cases of neonatal asphyxia resuscitation, accounting for 23.3%. As reported by Cui Yutao (5) et al., the incidence of neonatal asphyxia complicated with pneumothorax was as high as 26.1%. Medical personnel on the implementation of resuscitation of neonatal asphyxia when the air bag pressure to give oxygen when the pressure is too large or tracheal intubation action is rough, the catheter is too deep, also easy to cause pneumothorax.

2.1.2.2 Mechanical Ventilation Mechanical ventilation and other diseases are considered risk factors for the development of pneumothorax and may affect the prognosis of pneumothorax. Studies [6] have shown that during mechanical ventilation, high positive end-inspiratory pressure (PIP) and positive end-expiratory pressure (PEEP) can cause the occurrence of pneumothorax. In this group of cases, mechanical ventilation complicated with pneumothorax in 5 cases, accounting for 41.7%. In newborns, especially premature infants, lung immature, poor lung compliance, large airway resist-

ance, if the intubation position is too deep, mechanical ventilation parameters are not reasonable, such as high pressure, inhalation time is too long, sputum suction is not standard caused by airway injury. In the case of improved condition, alveolar rupture caused by unregulated pressure can also cause iatrogenic pneumothorax [7]. In the course of treatment, the symptoms include relief of dyspnea and sudden aggravation of shortness of breath, persistent blueness, pale complexion, obvious trichoeva of aspiration, thoracic asymmetry, thoracic eminence on the affected side, asymmetry of breathing sounds on auscultation, decreased percussive oxygen saturation, urgent chest radiograph or chest CT examination, and urgent treatment of pneumothorax.

2.2 Treatment of pneumothorax

2.2.1 Conservative treatment: the lung compression ratio of 12 cases in this group was less than 30%, among which 8 cases had mild clinical symptoms and signs of pneumothorax. X-ray and CT indicated that lung compression was about 10%, and lung lesions were mild. Therefore, oxygen was given to the head mask and pneumothorax absorption was given.

2.2.2 Auxiliary ventilation after thoracic puncture and ventilation: X-ray and CT showed lung compression of 10%~30% in 4 cases. Due to the presence of pulmonary inflammation and poor pulmonary dilatation, patients were treated with pneumothorax absorption after nasal obstruction CPAP after thoracic puncture and ventilation.

2.2.3 High frequency vibration ventilation or combined with closed thoracic drainage: lung compression ratio of >30% in 18 cases, 9 cases (50%), although lung compression ratio of BBB>% but less than 50%, did not perform thoracic ventilation and closed drainage pneumothorax absorption after HFOV, and clinical dyspnea improved quickly. High frequency concussion ventilation combined with closed thoracic drainage: 9 cases (50%). High frequency oscillation ventilation (High Frequency Oscillatory Ventilation, HFOV) in our hospital NICU utilization rate is higher than Chang Pin breathing machine, use effect is better Yulan Lin 's study showed that PaCO₂ decreased significantly after the application of HFOV, while PaO₂ increased stably, both of which were statistically significant compared with before treatment [8]. HFOV has a tidal volume less than or equal to the anatomical dead space, a high frequency close to lung resonance, and a low mean airway pres-

sure. The alveolar pressure is always constant in the process of ventilation, and the high-speed flow of gas increases the diffusion and convection effect. Therefore, effective gas exchange can be carried out under the condition of low inhaled oxygen concentration and airway pressure, and lung baroinjury caused by high airway pressure can be avoided [9]. It has a very good effect in the treatment of air leakage. In addition to HFOV, 9 cases of pathological pneumothorax were treated with closed thoracic drainage. One patient gave up treatment. The existing problems of HFOV are as follows: (1) The severe effects of simultaneous pulmonary lesions in newborns with large body weight may be worse than that of regular mechanical ventilation. (2) The use of preterm infants with gestational age less than 32 weeks is limited due to immature brain development. In this study, a total of 18 cases of neonatal pneumothorax caused by various reasons were treated with HFOV. Results: 17 cases were cured, 1 case gave up, and no intracranial hemorrhage and other complications were found. The application of HFOV in the treatment of neonatal pneumothorax has good efficacy, and it is worthy of promotion in the treatment of neonatal air leakage.

To sum up, pneumothorax sometimes symptoms are atypical, some dyspnea is not obvious, but the color of the skin is pale, or pale gray, some of the performance of the heart rate increased, so neonates within 24 hours after birth should pay attention to the observation of vital signs at the same time, pay attention to the abnormal color of the skin, the performance of dyspnea timely conduct chest X-ray examination. Chest CT examination should be performed in time when air leakage is not confirmed by chest X-ray examination. However, for children with basic pulmonary lesions, asphyxia resuscitation, CPAP, dual-level auxiliary ventilation and mechanical ventilation, attention should be paid to the changes of pulmonary signs and early bedside chest X-ray examination can detect pneumothorax in time when the condition is not relieved or the condition suddenly deteriorates after comprehensive treatment. In addition, children at high risk need continuous monitoring of vital signs, and should be alert to pneumothorax when there are unexplained changes in vital signs. Correct endotracheal suction and the use of respiratory balloon, skilled endotracheal intubation, the application of lung protective ventilation strategy in mechanical ventilation, and the use of

alveolar surfactant in children with RDS can reduce the incidence of pneumothorax [10]. For children with less than 30% lung compression area and mild clinical symptoms, only conservative treatment with oxygen inhalation is required, or even no oxygen inhalation is required. In children with spontaneous breathing, non-tension pneumothorax with lung compression greater than 30% May be cured by a single thorax aspiration. For children requiring CPAP and mechanical ventilation, airway pressure should be as low as possible after ventilation. For patients with persistent gas discharge after thorax puncture, closed thoracic drainage should be performed in time to reduce the adverse effects on respiratory and circulatory systems, and high frequency oscillatory ventilation (HFO) should be given. HFO can effectively improve oxygenation and increase gas exchange without increasing ventilation pressure, and avoid recurrence of air leakage and related lesions caused by prolonged and high oxygen concentration. In recent years, pneumothorax, as one of the routine applications of high-frequency oscillatory ventilation, has been promoted clinically [11]. When there was no gas discharge in the drainage tube for 24 hours, the respiratory sounds were normal and symmetrical on auscultation of both lungs, and the chest X-ray suggested pneumothorax absorption, the drainage tube could be pulled out after the withdrawal of the machine and the clamping tube were reexamined for 2 days without pneumothorax. Pathological pneumothorax frequently occurs in newborns. With the improvement of medical technology and the promotion of ventilator, more and more severely ill children have been treated, and the incidence of iatrogenic pneumothorax has also been increased [12]. Therefore, lower ventilation pressure should be used as far as possible in the treatment of pulmonary substantial lesions. The incidence of pneumothorax can be reduced by the combined treatment of low tidal volume, permalable hypercapnia and alveolar surfactant, correct airway management and rational use of resuscitated airbag. For children with dyspnea whose comprehensive treatment effect is poor and their condition suddenly deteriorates, attention should be paid to the pulmonary signs, and chest X-ray examination should be conducted in time to detect pneumothorax as soon as possible. Reasonable treatment after the occurrence of pneumothorax can save the life of most children.

Thorax puncture and ventilation can reduce the mortality rate when the respiration and circulation are seriously affected. Closed thoracic drainage combined with high frequency oscillation ventilation is effective in the treatment of pneumothorax.

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KALEIDOSCOPE OF INTERESTING WORKS

MIMICRY IN HUMANS

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SUMMARY

After reading this paper, you may get the impression that the experiments conducted by David Eagleman were more about empathy than mimicry, but there are so many genetic and epigenetic programs working in our body at the same time that sometimes it is very difficult to say where mimicry begins and ends. And in general, is it mimicry?!

Key words: *genetic, epigenetic, mimicry, senior parents, Grandparents, genes expression.*

It is well known that in the 21st century, modern medical-biological science is evolving so rapidly that some scientific terms and concepts are becoming obsolete, losing their original content and in need of renewal. Moreover, in parallel with new discoveries, more and more new scientific terms are emerging, and these processes, in turn, contribute to the development of science too.

In one of our papers we tried to introduce a new scientific term in the Georgian scientific literature (1) and this term was Uprosi Mshoblebi (უფროსი მშობლები), which due to the specificity of the Georgian language corresponds to the word - senior parents and not Grandparents, however, carry the same load in their meaning. In general, it should be noted that the Georgian language is rich in many scientific terms that exist in our native language (for example, the English term - Siblings -fits perfectly with the Georgian Dedmami-shvili) and it can be said that in this regard we are not so bad, but any language is a living organism by nature looks like and requires particularly careful handling.

The same applies to our Georgian language. At the same time in the name of scientists and linguists, it must be said that recently due to the rapid development of biology and in particular molecular biology and genetics and on the other hand the spread of new diseases (e.g. COVID-19 widespread worldwide) occurred and many important scientific terms have been established in the world scientific literature. But lately our attention has been drawn to the term molecular mimicry and the amazing ability of parasites to use molecular mimicry to significantly inhibit the action of our immune system even in the brain itself. It also seemed interesting so-called **Müllerian mimicry** - is a natural phenomenon in which two or more well-defended species, often foul-tasting and that share common predators, have come to mimic each other's honest warning signals, to their mutual benefit.

At the same time mimicry - phenomenon characterized by the superficial resemblance of two or more organisms that are not closely related taxonomically. This resemblance confers an advan-

tage - such as protection from predation - upon one or both organisms by which the organisms deceive the animate agent of natural selection.

Mimicry is widespread particularly among butterflies and moths. It is also found in various birds and some mammals. But what about humans?

In ordinary life, people quite often imitate famous actors, singers, politicians, dancers, athletes, scientists and even gangsters. Moreover, it can be said that they almost live their lives, dress like them, talk like them, dance like them, sometimes play football like them and try and, if nothing else, at least look like their idols with their hairstyles. However, apart from this, there are pairs of people who carry completely different genes and yet bear such a strong resemblance to other humans that sometimes it is so difficult to distinguish them from each other as identical twins.

To prove that humans also have the ability to mimic, we decided to include in this paper an excerpt from a book by the famous American scientist David Eagleman;

THE BRAIN

The story of you

Every moment of our lives, our brain circuitry decodes the emotions of others based on extremely subtle facial cues. To better understand how we read faces so rapidly and automatically. American scientist David Eagleman invited a group of people to his lab. Scientists placed two electrodes on their faces- one on the forehead and one of the cheek- to measure small changes in their expressions. Then they had them look at photographs of faces.

When participants looked at a photo that showed, say, a smile, or a frown, scientists were able to measure short periods of electrical activity that indicated participant's own facial muscles were moving, often very subtly. This is because of something called mirroring: they were au-



(a) Cuckoo bee

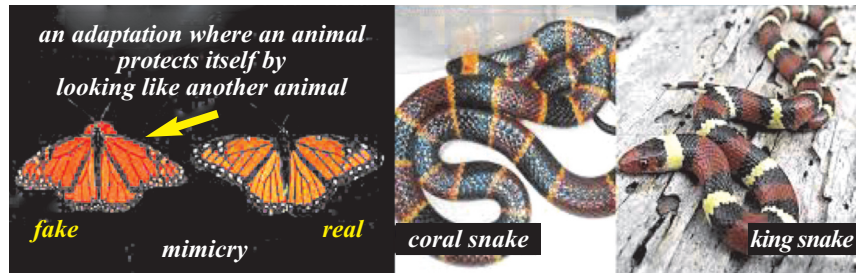
(b) Yellow jacket

tomatically using their own facial muscles to copy the expressions they were seeing. A smile was reflected by a smile, even if the movement of their muscles was too slight to be visually obvious. Without meaning to people ape one another.

At the same time this mirroring sheds light on a strange fact: couples who are married for a long time begin to resemble each other, and the longer they have been married, the stronger the effect. Researchers suggests this is not simply because they adopt the same clothes or hairstyles, but because they've been mirroring each other's faces for so many years that their patterns of wrinkles start to look the same.

Why do we mirror? Does it serve a purpose? To find out, David Eagleman invited a second group of people to the Lab-similar to the first group, except for one: this new group of people had been exposed to the most lethal toxin on the planet-this is the Botulinum toxin, derived from a bacterium, and it's commonly marketed under the brand name Botox. When injected into facial muscles, it paralyzes them and thereby reduces wrinkling.

However, beyond the cosmetic benefit, there's a less known side effect of



Botox. Scientists showed Botox users the same set of photos. Their facial muscles showed less mirroring on our electromyogram. No surprise there-their muscles have been purposely weakened. The surprise was something else, originally reported in 2011 by David Neal and Tanya Chartrand. Similar to their originally experiment, David Eagleman asked participants from both groups (Botox and non-Botox, to look at expressive faces and

to choose which of four words best described the emotion shown.

On average, those with Botox were worse at identifying the emotions in the pictures correctly. Why? One hypothesis suggests that the lack of feedback from their facial muscles their ability to read other, we all know that the less mobile faces of Botox users can make it hard to tell what they are feeling; the surprise is that those same frozen muscles can make it hard for them to read others.

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SUMMARY

The aim of our study was to determine how the difference in the health of twins was affected by a seemingly insignificant factor such as fear of animals, particularly dogs. For this we interviewed the twins among which the attitude to the dogs was different, one of the twins had a fear of dogs and the other had some pleasure in interacting with animals. Specific questionnaire was used for this. It was revealed that each twin who had a sense of fear for dogs was more allergic comparing with its twin. It's noteworthy that parasite invasion cases were rare among them. The immunity of animal-loving twins was still found to be more resistant to infectious diseases. It is obvious that relationship with animals act as an environmental factor that may influences on various genetic programs both in monozygotic and dizygotic twins.

Early observations on make-up twins showed that their birth was quite rare and unique, although the percentage of birth rates for both monozygotic and dizygotic twins has increased significantly around the world recently (1). This is due to several factors, including the fact that a large proportion of women in the

world become pregnant between the ages of 30 and 40. In addition to excessive consumption of new means of fertilization, which can fertilize several egg (2). It is no coincidence that the birth of twins is called an "experiment in nature" and allows us to study the influence of genetic, epigenetics and environmental

factors on an individual (3). Moreover, the twin research method helps scientists to determine the role of genes and environmental factors in the development of the disease and to establish real symptoms for example for COVID-19 (4).

The aim of our study was to determine how the difference in the health of twins



was affected by a seemingly insignificant factor such as fear of animals, particularly dogs. For this we selected only cases of those twins where one of the twins had a fear of dogs and the other had some pleasure in interacting with dogs. We distributed them questionnaires in which we asked the following questions:

1. Which twin was born first and which was born second?
2. At what time intervals did they differ at the time of birth?
3. What was the difference between them in terms of weight and height at the time of birth and now?
4. Which twin was the leader among them?
5. Which was right-handed and which was left-handed and if they differed from each other in this sign?
6. Were their fingerprints identical or not?
7. Did they have a different calligraphy and signature?
8. Whether they had their own spoken language?
9. Did they have moles or any different marks on the body?
10. Which twin was most bothered by dental problems?
11. Which foods did they prefer and what was their favorite dish?
12. Did they like to dress alike and which twin was the leader in this regard?
13. Did they always live in the same environment or for some time they had to separate for different reasons?
14. Did their parents, relatives and friends choose them from each other (question was only for monozygotic twins)?

15. Do strangers realize that they are a dizygotic twins (question was only for non-identical twins)?

16. Which twin was more susceptible to infectious diseases and which was more severe?

17. Whether any of the twins had contracted an infectious or invasive disease that did not affect any of them?

18. How did they react to the mosquito bite and how often did the insect bite them?

19. Which twin was afraid of dogs and which was not?

20. Were they bothered by allergies in general and allergies to dog fur in particular?

21. What is their hobby?

Based on the answers to the questionnaires, we came to the conclusion that a survey of only 4 twins did not allow us to get comprehensive answers to some of the questions related to the study of twins. However, on the other hand, we found that each twin who had a sense of fear for dogs was more allergic comparing with the second. To our surprise, sisters which were monozygotic twins and had the same fingerprints revealed different attitudes towards dogs, i.e. fear of an animal was a common occurrence for one of the twins, the other dreamed of having an animal in the family. As for infectious diseases, the ad-

vantages of animal-loving twin are not so obvious here. In only one case both twins suffered similarly from the same infectious disease. Also, the case of infestation has been reported only once, and here the "scared" twin of dogs was more easily cured of parasitic diseases. As for the rest of the cases, the immunity of animal-loving twins was still found to be more resistant not only to infectious but also to other diseases.

In our opinion, the method of twins is a very important method in the study of the development of various diseases. Of particular interest in this regard is the different "tolerance" of each twin in both parasitic and infectious diseases. At the same time of interest are allergic diseases with different currents in both monozygotic and dizygotic twins and the role of the environment in the dynamics of the development of this disease. It is no coincidence that interactions with animals play a role in boosting immunity, although it should be noted that the number of animal-borne parasitic diseases has risen sharply around the world recently, and adherence to rules such as "hand hygiene" and other approaching of hygiene would help people to feel protected from these kinds of diseases and to "make friends" with animals better.

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COVID-19 SITUATION IN GHANA-BRIEF ANALYSIS

SUMMARY

The Government and MOH have taken serious measures since the first reported cases of COVID-19 in Ghana. Despite a large number of recoveries and low death rates the cumulative cases of COVID-19 would continue to rise since new infections are occurring. Most of the deaths were linked to existing health problems or chronic cardiovascular and respiratory conditions, diabetes and malignant diseases.

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OVERVIEW OF GHANA

Ghana is a Sub-Saharan African country in the West Africa and shares a border with Togo to the East, Cote d'Ivoire to the West, Burkina Faso to the North and the Atlantic Ocean at its southern coast. Ghana has the largest economy in West

THE SITUATION OF COVID-19 IN GHANA

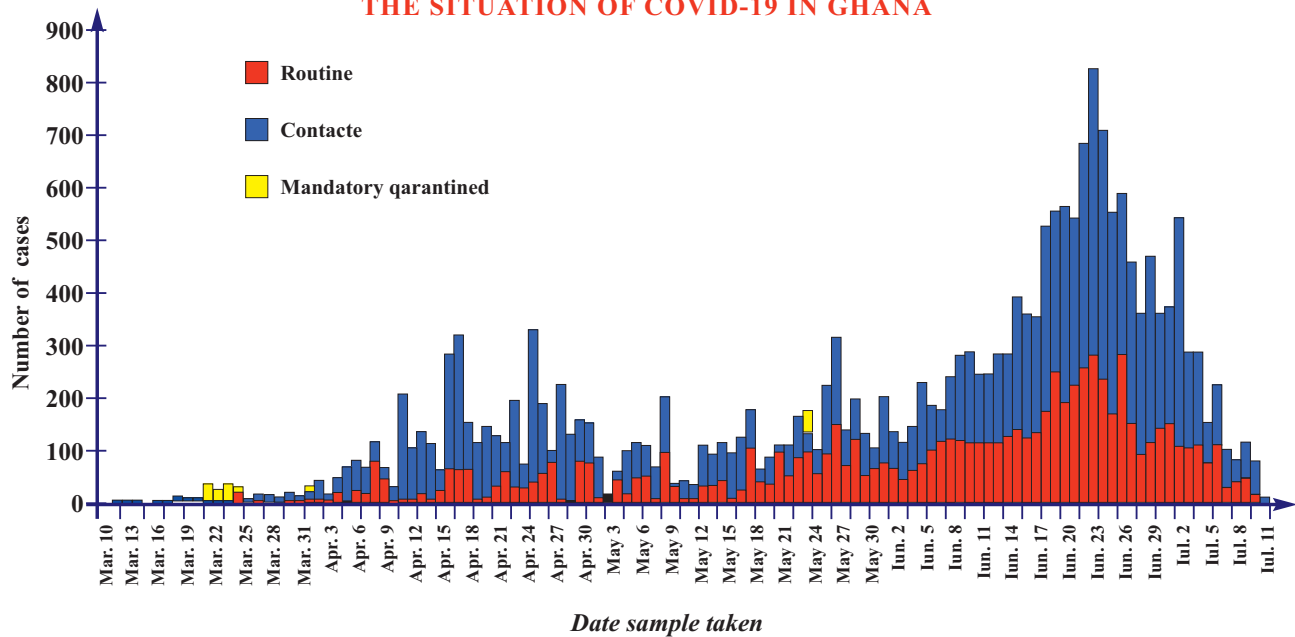


Fig. 1. Regional Distribution of Confirmed, Recovery, and Active cases of COVID-19 (16/7/2020)

Africa and currently has 16 administrative regions. The estimated population is 31,070,940 people as of the year 2020

Ghana recorded its first two cases of COVID-19 on the 12th of March 2020 as imported cases one each from Turkey and Norway. The laboratory test confirming the two cases was performed at the Nogushi Memorial Institute for Medical Research in the capital city Accra. The cumulative case count as at 16th July is over 26,000 confirmed cases with over 22,000 recoveries/discharges, 139 deaths and 3716 active cases. In Late May 2020, the Ghana Health services reported that over 91% of cases were asymptomatic. Also, preliminary data released by the Ghana Health Service showed about 80% of deaths were attributable to co-morbidities.

The current trend in cases reported shows community infections are prevalent at about 6% in samples tested. The rate of increase in the cumulative cases does not appear to have an exponential trend but the absence of a sustained flattened curve means more needs to be done to minimize COVID-19 infections. Currently, the borders of Ghana are still closed to the international community; however entry of the country through unapproved routes posing serious challenges to the fight against COVID. There is also the lack of adherence to preventive measures such as social and physical distancing, wearing face mask and hand washing which the government has been advocating since the partial lockdown was lifted in mid April 2020. The figures 1-3 below shows some details.

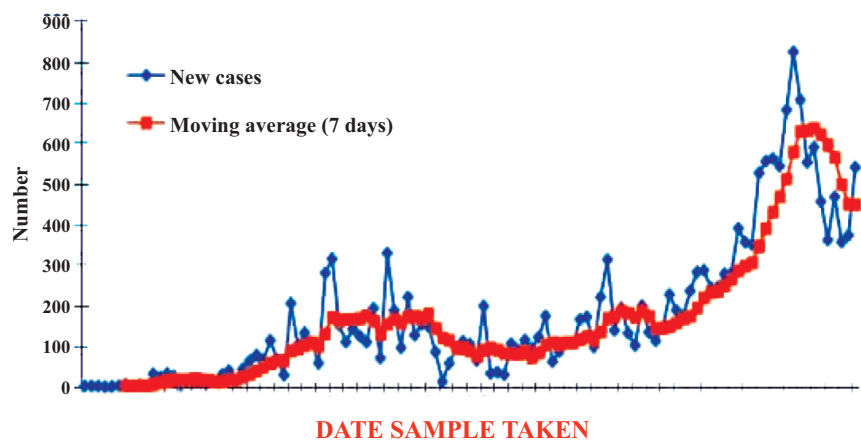


Fig. 2. Distribution of COVID-19 cases and 7 days moving average in Ghana by date sample taken. March - July 2020

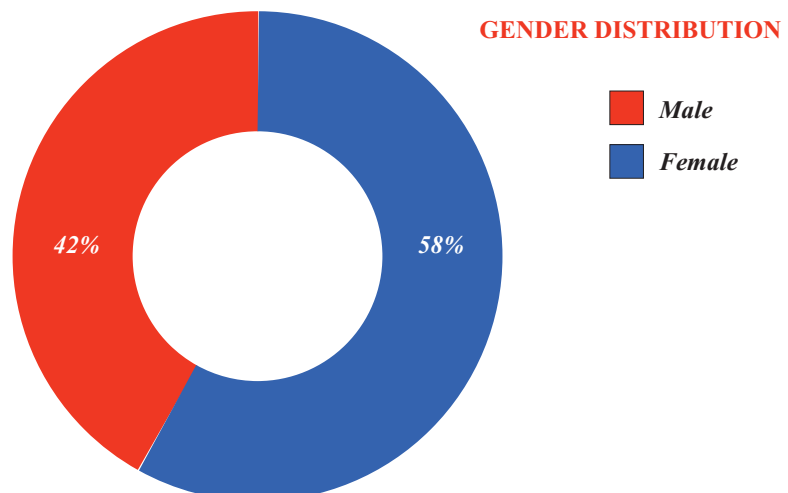


Fig. 3.

Region	Cases	Recovered/ Discharged	% Recovered/ Discharged	Active Cases
Ahafo	98	11	11.22	87
Ashanti	5259	4,786	91.01	424
Bono	107	96	89.72	11
Bono East	205	198	96.59	7
Eastern	948	830	87.55	114
Central	1110	866	78.02	234
Greater Accra	13690	11093	81.03	2536
Northern	267	170	63.67	90
North East	9	7	77.78	1
Oti	128	102	79.69	25
Savannah	57	48	84.21	9
Upper East	282	275	97.52	4
Upper West	70	70	100.00	0
Volta	418	350	83.73	67
Western	2140	2025	94.63	113
Western North	200	140	70.00	60
Total	24988	21067	84.31	3782

Government Preventive strategies for the General Public

Since the day of the confirmation of the first cases (12th March) of the COVID-19 in Ghana, the Government and the Ministry of Health together with the Ghana Health Service have instituted various strategies to prevent the spread of the infection. Some of the strategies include;

1. Intensive General public education

on COVID-19 on symptoms and preventives measures.

2. On the 15th of March public gathering including conference, schools workshops were suspended.

3. On March 28, 2020, the government of Ghana imposed lockdown restrictions in two regions (Greater Accra and Ashanti regions) but it was lifted after three weeks.

4. Travel restrictions were issued on the same date.

5. Transport operators were advised to observe social distancing,

6. Stay at home, observe social distancing, and avoid handshaking.

7. Wash your hands often with soap and water for at least 20 seconds.

8. Cover your cough or sneeze with a tissue, dispose of the tissue in a closed bin, and then wash your hands.

9. Always wear a mask, particularly when leaving home.

10. Avoid touching your eyes, nose, and mouth

11. Avoid contact with people who have fever, cough, or difficulty in breathing.

12. Call the designated emergency line(s) 112 and 311 for COVID-19 or the national ambulance service.

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PROGRESS IN THE EPIGENETICS OF KAWASAKI DISEASE

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ABSTRACT

Kawasaki disease (KD) is an autoimmune disease with acute vasculitis, mainly involving the coronary artery, and is currently the main cause of acquired heart disease in children. As the incidence of Kawasaki disease increases year by year, its etiology and pathogenesis have attracted more and more attention and attention from scientific research and clinical personnel. Epidemiological studies have shown that Kawasaki disease is closely associated with innate inheritance and the acquired environment, and that infection is the main predisposing factor. Epigenetic, affected by the gene interaction with the environment, is caused by not changing the gene sequence. Inheritable alterations in cellular phenotypes and altered gene expres-

sion can reasonably explain the interconnection of genetic genes with acquired factors in KD. The analysis of epigenetic factors can provide the diagnosis of KD and predict the biomarkers of KD, and can contribute to the development of pharmacogenomics and targeted therapies for KD. This paper analyzes the existing literature on the epigenetics of DNA methylation, microRNA, and long-chain non-coding RNA, summarizes its recent research advances, and discusses how these mechanisms are involved in the pathogenesis and development of KD and contribute to the study of biomarkers associated with KD.

Key words: *Kawasaki disease; Epigenetics; DNA methylation; Noncoding RNA*

Kawasaki disease (KD), also known as mucocutaneous lymph node syndrome, was first reported by Japanese doctor Dr. Tomisaku Kawasaki in 1967. The main clinical manifestation is persistent fever for more than 5 days, lip and oral mucosal changes, pleomorphic skin rash, non-suppurative lymphadenopathy in the neck, conjunctival hyperemia in both eyes, rigid edema of hands and feet, and peeling of the fingertips [1]. KD mainly affects children under 5 years of age. The incidence of Asian children is higher than that in European and North American countries, and there are obvious gender differences, more men than women [1]. According to the results of the national epidemiological survey of Kawasaki disease in Japan, the incidence of Kawasaki disease in children under 5 years of age from 2015 to 2016 was (309.0~330.2) per 100,000 [2]. The results of the epidemiological survey of Kawasaki disease in South Korea showed that the incidence of Kawasaki disease in children under 5 years of age in 2014 was 194.7 per 100,000 [3]. The results of the regional epidemiological survey in my country showed that the incidence of Kawasaki disease in children under 5 years old was (40.9~55.1) per 100,000 in Beijing from 2000 to 2004 [4]; (30.3~71.9)per 100,000 in Shanghai from 2008 to 2012 [5]. The main pathological changes of KD are inflammatory lesions of small and medium blood vessels throughout the body, especially coronary arteries [6]. The standard treatment for KD is intravenous gamma globulin combined with high-dose aspirin. Although it can significantly reduce the incidence of coronary aneurysms, there are still coronary arteries abnormalities (CAAs) [7].

In recent years, studies at home and abroad have found that the incidence of KD is significantly related to environmental infections, genetic susceptibility and immune response. Epidemiological and clinical reports indicate that KD can be triggered by streptococcus, staphylococcus aureus, mycoplasma, chlamydia, boca virus, rhinovirus, rotavirus, measles virus, adenovirus, parvovirus B19, fungi, etc.[8-12]. The susceptibility to KD is closely related to genetic factors. The role of epigenetics

in diseases where genetic inheritance and environmental factors influence each other has been extensively explored [13-14]. The concept of epigenetics was first proposed by Waddington in 1942. It is a process of studying how genotypes produce phenotypes. Through various mechanisms such as DNA and histone chemical modification, RNA interference, chromatin remodeling, etc., it affects and regulates the function and characteristics of genes, determines the way of gene expression, and can be passed on to offspring through cell division and proliferation cycles [15]. At present, the research on epigenetics at home and abroad mainly focuses on the regulation mechanism of gene expression changes. Some scholars have shown that epigenetic regulation and dysfunction are increasingly important in human physiology and disease, and they play an important role in the pathogenesis of rheumatic immune diseases, tumors, cardiovascular diseases and other diseases [16-20]. Related studies have shown that epigenetics is more sensitive to environmental stimuli and plays an important role in the occurrence and development of environmental-related diseases. In recent years, some scholars have conducted related research on the epigenetic regulation of genes involved in the pathogenesis of KD. Epigenetic modification can occur in several ways, including covalent modification of cytosine (such as DNA methyltransferase methylation), post-transcriptional modification of histones (such as acetylation, phosphorylation, phosphorylation, methylation, citrullination, citrullination, ubiquitination, ribosylation and subunitization) and the regulation of RNA-based transcription mechanisms [21]. This article focuses on the epigenetics research related to KD, and then provides new ideas for the pathogenesis of KD, early recognition, biomarkers, and new treatments.

1. THE ROLE OF DNA METHYLATION IN KD

DNA methylation is an important part of epigenetics. It is the earliest discovered and most typical epigenetic modification. It plays an important role in maintaining cell structure, function, genetic factors and disease occurrence

and is the most widely studied epigenetic modification in KD. The mechanism of DNA methylation is regulated by a set of DNA methyltransferases (DNMTs) and other accessory proteins. Under the action of DNMTs, S-adenosylmethionine (SAM) is used as a methyl donor, it combines with the C5 position of cytosine to form a chemical modification process of 5-methylcytosine (5mC) [22]. This modification reaction mainly occurs at the cytosine-guanine (G) dinucleotide (CpG) site [23]. The promoter region, some exons, and intron-rich regions of CpG dinucleotides of housekeeping genes are called CpG islands. In the entire genome, CpG islands are usually located in the promoter region of genes [24]. The covalent binding of methyl groups to the CpG islands of the genome can regulate gene expression without changing the gene sequence, thereby affecting protein expression. DNMTs family including DNMT1, DNMT3A, DNMT3B, DNMT3L, DNMT3L-AS1. DNMT1 not only maintains DNA methylation level, but also plays an important role in the expression of T lymphocyte differentiation stage. The main function of DNMT3A and DNMT3B is to initiate methylation[25-26], its epigenetic changes play a very important role in immune pathogenesis. In the human genome, methylated genes are usually related to actively transcribed genes. Hypermethylation of CpG islands in the promoter region can lead to long-term stable gene suppression by recruiting transcription repressors or masking the binding of transcription activators [27]. At the overall or individual gene level, the dynamic changes of DNA methylation are essential for normal development and cell differentiation in diseases [28].

Huang et al. conducted genomic DNA methylation and gene expression analysis on KD and found that the expression levels of DNMT1 and DNMT3A in KD patients were significantly lower than those in the normal control group, and the transient DNA methylation process occurred in the acute stage of KD [29]. Li et al. studied the changes in DNA methylation before and after IVIg administration in KD patients, and proved that IVIg treatment

mainly changes DNA methylation by reducing methylated CpG markers, and that genes that change DNA methylation are also clearly related to inflammation [30]. Chen et al. studied the difference in methylation between KD patients and normal controls and found that the methylation of the CpG region of the two is significantly different [31]. Different methylated regions contain genes involved in inflammatory response, innate immunity and chemokine signaling pathways [31]. KD-related epigenetic changes can be observed in FCGR2A, matrix metalloproteinases (MMPs), toll-like receptors (TLRs), NOD-like receptors, HAMP and other genes, providing a new basis for the pathophysiology of KD.

TLRs are one of the initial responders involved in the activation of the inflammatory response by the immune system, and they are mainly involved in non-specific immune and inflammatory responses. TLRs widely recognize the characteristic pattern molecules present on bacteria (lipopolysaccharide) and viruses (dsDNA/RNA, ssDNA/RNA), and mediate inflammation and cytokine by activating protein kinases (such as IRAK1/4, TBK and IKKi, etc.) biosynthesis. Except TLR3 and TLR7 in the acute phase of KD, the mRNA expression of TLRs in KD patients has increased. However, compared with the normal control group, the expression levels of methylation pattern molecules on TLR1, 2, 4, 6, 8, and 9 in the acute phase of KD patients were lower. After IVIg treatment, this difference is more significant [32]. Studies have shown that stimulating TLR2 and TLR4 with LPS can regulate the expression of IL-2, IL-6, IL-10, MCP-1, TNF- α and INF- β in the KD mouse model. This observation provides evidence that KD is triggered by bacterial infection [33-34].

In the acute phase of KD, the activation of macrophages from M1 to M2 has been studied. In recent years, gene chip arrays have been used to analyze the transcriptome of patients with acute KD. In addition to the markers associated with M2 macrophages, the expression of TLR2 and IL2RA (M1 macrophages) has increased (such as MS4A4A, MS4A6A, TLR1, TLR8,

TLR5, CD36, CCR2 and ARG1). The promoter regions of these genes are in a state of hypomethylation. IVIg treatment for KD patients further enhances the expression pattern of these genes by enriching the hypomethylation state. Abnormal neutrophil activation is also related to KD. Increased expression of CD177, a neutrophil activation marker with abnormal methylation patterns, was observed in KD patients. The level of CD177 in the VIg(IVIg)-sensitive KD patient group decreased, but the level of the IVIg resistant KD patient group increased [35].

Fc receptors in immune cells [immunoreceptor tyrosine-based activation motif (ITAM) related receptor family] can bind to antibodies or antigen-antibody complexes to help regulate phagocytosis, degranulation and cytokine biosynthesis [36, 37]. In recent years, studies have found that changes in the expression level and function of Fc receptors are related to the occurrence of rheumatic immune diseases [38-40]. The genome-wide study (GWAS) has confirmed that the FCGR2A gene is a susceptibility gene for KD. FCGR2A mainly encodes the immunoglobulin IgG (Fc region receptor II-a) receptor which is widely expressed in activated immune cells. Studies have shown that the methylation level of this gene affects the binding of IgG2 to its receptor [41]. A latest GWAS study found that, compared with the control group, the FCGR2A gene of KD patients has 15.54% epigenetic regulation of hypomethylation mode. Compared with IVIg-sensitive KD patients, IVIg-insensitive patients also have significantly higher levels of hypomethylation [42].

2. THE ROLE OF MICRORNAS IN KAWASAKI DISEASE

MicroRNAs (miRNAs) are endogenous, single-stranded non-coding small RNAs (18-25 nucleotides long), which play an important role in controlling mRNA translation. Non-coding RNA is transcribed but not converted into protein, but as an epigenetic mechanism to regulate gene expression. They regulate post-transcriptional gene expression by combining the translation part, and

have the function of inhibiting the transcription and translation of target mRNA or being able to cut target mRNA and promote its degradation [43, 44]. Most miRNAs are highly conservative, sequential and tissue specific. The expression of miRNA is controlled by the epigenetic mechanism, which itself also controls the epigenetic mechanism, forming an "epigenetics-miRNA regulatory loop", and the abnormality of its regulation link is related to many diseases [45].

miRNA has a unique expression pattern, so it is used as a new non-invasive biomarker for disease diagnosis [46]. It has been reported that miRNAs can be released in peripheral blood, and these miRNAs are related to certain specific pathophysiological conditions [47]. Therefore, peripheral serum miRNAs are widely used as diagnostic and therapeutic biomarkers for various diseases. According to reports, the expression of abnormal miRNAs is closely related to immune diseases, cardiovascular diseases, inflammation and tumors [48-51]. Many studies at home and abroad have shown that miRNAs play an important role in the pathogenesis of KD [52]. Studies have shown that there are differences in the expression of miRNA in KD patients. In the acute phase of KD, the expression of miR-143, miR-199b-5p, miR-618, miR-223 and miR-145 is significantly higher [53-56]. Another study showed that in KD patients, serum miR-200c and miR-371-5p levels were significantly higher than healthy controls. These miRNAs may play an important role in the pathogenesis of KD and can serve as potential biomarkers of KD [57]. Scholars have studied the role of serum miRNA, such as miR-1246, miR-4436b-5p, miR-197-3p and miR-671-5p, as biomarkers in KD [57-60]. Zhang et al. conducted a study on 102 patients with KD. And found that the serum levels of miR-200c and miR-371-5p were significantly increased in the acute phase of KD; in patients with IVIG-resistant KD, their levels were also higher; the study also showed that after treatment, its level decreased from before [61]. In another study by Zhang et al., plasma miR-328, miR-575, miR-134, and miR-671-5p have been shown to be potential organ-

isms for diagnosing KD and potential biomarkers for predicting the outcome of IVIg treatment by affecting the expression of inflammatory genes [62]. Wang et al. showed that in KD, hsa-let-7b-5p and hsa-miR-223-3p were slightly down-regulated, while miR-200c, miR-197-3p and miR-671-5p levels were up-regulated [63]. Research by Li et al. showed that, compared with healthy controls, the expression of 18 miRNAs in the plasma of KD patients is different. miR-125a-5p is significantly increased in the plasma of KD patients. It induces vascular endothelial cell apoptosis by regulating the target gene MKK7, and plays a role in the pathogenesis of KD [64].

3. THE ROLE OF LONG NON-CODING RNAs IN KAWASAKI DISEASE

Long non-coding RNAs (lncRNAs) are non-coding RNAs with a length greater than 200 nucleotides, which participate in the regulation of various processes in cells by regulating gene transcription. More than 27,000 lncRNAs have been found in the human genome, and new studies have shown that their functions are closely related to the development of human diseases [65-68]. Ko et al. studied the changes in the expression of lncRNA in 37 KD patients, and the results showed that the transcription of XLOC_006277 in IVIg-sensitive KD patients was too high in the acute phase and decreased after IVIg treatment; Higher levels of XLOC_006277 transcription were also found in KD patients who later developed CAAs [69].

Studies have found that lncRNA can enhance the inflammatory response by increasing the transcription of pro-inflammatory cytokines and other inflammatory target genes or enhancing inflammatory signals. THRIL (TNF- and hnRNPL related immunomodulatory lncRNA) is one of many lncRNAs induced by TLR2 activation [70]. CXCL10 is one of the genes regulated by THRIL that has been discovered so far. It is up-regulated at the acute stage of KD patients and has been confirmed as a biomarker of KD [71]. In a study of 17 patients with KD, it was found that in the acute phase of KD, when the level

of TNF α increases, the expression of linc1992/thril is low, so linc1992/thril is considered to be a new biomarker for immune activation of KD.

lncRNAs are induced to express during inflammatory response and regulate gene transcription during the inflammatory response. At present, there are few studies on KD and lncRNAs, but studies have shown that KD is closely related to changes in the expression of lncRNAs. In order to understand the biological functions and roles of lncRNAs in KD, more research is still needed to discover new treatment strategies and evaluate as biomarkers.

In summary, KD, as a relatively common immunoinflammatory disease in children, is often accompanied by coronary artery damage, and even severe complications such as coronary aneurysm rupture, myocardial infarction, and sudden death, which affect the growth and development of children, and it brings a heavy psychological and financial burden to the family. KD is controlled by both heredity and environment. Changes in the external environment closely affect the occurrence and development of KD, so further research on this disease is needed in terms of epigenetics.

The current understanding of epigenetics in KD is still preliminary. This article describes several new biomarkers for KD diagnosis and disease prediction. Most of the studies are based on single-center studies with a limited number of patients, and a larger sample size is needed for verification. As the switch of gene regulation, epigenetics can provide new ideas for the pathogenesis of KD, early identification, biomarkers, new treatments and other aspects of related research on epigenetic regulation mechanisms.

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CLINICAL ANALYSIS OF 5 CASES OF CHILDREN WITH SARS-COV-2 INFECTION IN FAMILY CLUSTER OUTBREAK

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SUMMARY

Objective To explore the clinical, laboratory, imaging features and main points of diagnosis and treatment of 5 children with novel coronavirus infections caused by family clusters. **Methods** A retrospective analysis of clinical data of five cases of children infected with SARS-CoV-2 in family cluster outbreak at Henan Children's Hospital (Children's Hospital Affiliated to Zhengzhou University) from January to February 2020. **Results** Five children from four families were included, involving 20 family members infected with the novel coronavirus. **Patients:** 2 males and 3 females. Age from 5 days to 8 years and 6 months. Four of the five patients showed low to moderate fever. Fever lasted 2 to 18 days. Example 3 had no other clinical manifestations such as fever. **Type:** One case of asymptomatic infection, three cases of mild, and one case of critical illness. Peripheral blood lymphocytes decreased in four exceptions. The hemoglobin and erythrocytes in patient 1 were reduced, and the D2 polymer in patient 1 was 22 times higher than the other four patients. C-reactive protein and calcitonin were normal in 5 patients. Patient 1 had a blood cell sedimentation rate of 40, and the other four patients were normal. Influenza A and B virus of five patients were normal. The novel coronavirus nucleic acid by throat swabs and blood tests were positive. All five patients underwent chest radiographs and CT examinations. Three of the chest radiographs showed rough lung texture, but CT case 1 showed small patchy shadows in multiple sites, cases 2 and 3 showed patchy shadows of the right lung, and cases 4 and 5 were all normal. Five children were treated with interferon nebulization and oral Chinese medicine, and four patients were treated with ribavirin. Two patients took oral lopinavir / ritonavir orally (1.5ml, 2 times / d×5d) antiviral treatment. Five patients except the ICU were treated in the remaining 4 cases only supported symptomatic treatment, all cured and discharged and followed up were normal.

CONCLUSIONS: In children with novel coronavirus infection, there are mostly mild common types, which can also be asymptomatic and less critical. Patients' peripheral blood lymphocytes decreased. In critically patients, D2 polymer increased significantly, C-reactive protein and procalcitonin were not necessarily abnormal. Except heavy and critically, other light general types are mainly supported by symptomatic treatment, and the prognosis is mostly good. Attention should be paid to avoid transmission among family members, and timely monitoring and evaluation of the pediatric status of infected families in order to detect and diagnose early.

Key words: children; novel coronavirus; family cluster infection; diagnosis and treatment

The new coronavirus (SARS-CoV-2) has caused huge losses to human life and economy [1-2]. 334,981 confirmed COVID-19 cases and 14,652 deaths were reported in 190 countries and territories, but data on the epidemiological and clinical characteristics of pediatric patients are limited. Children have become susceptible to 2019-nCoV infection due to immature immune function. As of 24:00 on February 7, 2020, 285 children with new-type coronavirus pneumonia were reported nationwide, including 10 newborns. Epidemiological investigations suggest that the population is generally susceptible to the new coronavirus, and some children have a clear family gathering history [3-4]. On March 3, the National Health Commission stated in the updated "Pneumonitis Diagnosis and Treatment Program for New Coronavirus Infection (Trial Version 7)" that children, infants, and young children were also affected. Some children and neonatal cases may have atypical symptoms, manifested as gastrointestinal symptoms such as vomiting and diarrhea, or only manifested as poor spirit and shortness of breath. Mild children showed only low fever, mild fatigue, and no clinical manifestations of pneumonia.

OBJECTIVES AND METHODS

Subject Retrospective case summary.

Five children who were diagnosed with SARS-CoV-2 new coronavirus infection through nucleic acid testing

Table 1

General information and clinical manifestations of 5 children with novel coronavirus infection

№	gender	age	Date to hospital	Epidemiology			Main clinical manifestations				Days Of fever	Days Of Being hospitalized
				Number of household infections	Wuhan related	Days between exposure and diagnosis	Fever (°C)	sneeze	cough	vomiting And diarrhea		
1	M	5D	2/2	5	Y	5	38	N	Y	N	18	29
2	F	6M	30/1	3	Y	4	38.1	N	Y	N	5	16
3	M	7Y6M	19/2	2	Y	20	Normal	N	N	N	N	16
4	F	6Y7M	2/2	5	Y	8	38.6	N	N	N	2	15
5	F	8Y6M	2/2	5	Y	9	37.4	N	N	N	2	15

and other treatment in Henan Provincial Children's Hospital (Children's Hospital Affiliated to Zhengzhou University) from January to February 2020 were enrolled as research subjects. This study was approved by the Ethics Committee of Zhengzhou Children's Hospital and informed consent was obtained from the children's families.

METHOD

1. Diagnostic criteria. (1) Both throat swabs and blood nucleic acid tests were positive. (2) The diagnostic criteria were conducted in accordance with the first edition of the Chinese Journal of Pediatrics "Children's 2019 New Coronavirus Infection Diagnosis and Prevention Suggestions" on a trial basis.

2. According to the ICD-10 number, query and retrieve clinical data through electronic medical records.

The gender, age, epidemiology, laboratory examination and imaging data (chest X-ray and CT MRI) of the children were collected and analyzed.

3. Clinical types According to the infection status of children and the clinical characteristics of confirmed diagnosis, they are divided into five types [6-

7]. Asymptomatic infection, mild, common, severe, critical.

STATISTICAL METHODS

Descriptive analysis, measurement data are expressed as M (range).

RESULT

I. General Information

Five children were from four families, and epidemiological suggestion was caused by cluster infection among family members, which involved 20 family members, including family members including grandparents, parents, and sisters.

Gender: 3 girls and 2 boys. Age range: 5 days-8 years and 6 months). There was 1 neonate at 5 days, 1 case at June, 1 case at 7 years old, 1 case at 6 years old, and 1 case at 8 years old in June.

Case 1 The child's parents lived in Wuhan until birth. Department G1P1, born 38 + 5 weeks after cesarean section, A's score and other unknown. On January 22, the child returned to Xinyang, Henan with his parents from Wuhan. In the afternoon of the same day, the mother of the child felt cold and lethargic, but she was not diagnosed and treated. She had a cesarean section on

January 31, and a positive nucleic acid test on February 1, confirmed a new type of coronavirus infection. This suggests that the mother had a new coronavirus infection before cesarean section. Although the new coronavirus infection occurred only 5 days after birth, it was not caused by vertical mother-to-child infection, because the mother was infected with the new coronavirus before cesarean section.

Clinical manifestations and laboratory tests

Fever is the main symptom of most children. Except for Case 3, fever is low to moderate, with a maximum body temperature of 38.6°C. Case 3 No fever, no runny nose, cough, diarrhea and other symptoms.

The total number of neonatal leukocytes in case 1 was 12.41, and the other 4 cases ranged from 4.79 to 9.02. The number of lymphocytes was 6.88 except Case 1. One of them was 3.52 and the other three were between 2.28 and 2.71. Before the second crossover of children's white blood cells, lymphocytes should be predominant, but the lymphocytes in this group were lower, suggesting that it is related to viral infection.

Table 2

Laboratory and imaging (chest X-ray, chest CT) examination of 5 children with novel coronavirus infection

№	Blood routine						CRP (mg/L)	PCT (ng/dL)	ESR (mm/h)	flu virus A/B	ALT (U/L)	AST (U/L)	LDH (U/L)	CK-MB (U/L)	D-2 polymer	Chest radiograph	Chest CT
	WBC ($\times 10^9/L$)	N(%)	L(%)	RBC ($\times 10^{12}/L$)	HGB (g/L)	PLT ($\times 10^9/L$)											
1	12.95	0.505%	0.495	3.07	101 g/L	356	<0.5	0.092	40	NA	46.7	37.8	NA	48.3	22.48	Rough lung texture	Multiple small patches
2	4.79	0.175%	0.772	5.05	127 g/L	451	0.5	0.11	11	-	21.8	55.3	NA	NA	0.4	Rough lung texture	Multiple small patches
3	9.02	0.613%	0.319	5.23	148 g/L	447	<0.5	0.039	12	-	48.4	32.8	261.3	14.7	0.2	Rough lung texture	Patchy shadow of right lung
4	4.82	0.427%	0.247	4.52	126 g/L	283	NA	NA	NA	NA	NA	NA	NA	NA	NA	Normal	Normal
5	5.02	0.388%	0.271	4.60	135 g/L	261	NA	NA	NA	NA	NA	NA	NA	NA	NA	Normal	Normal

Table 3

Treatment of 5 children with novel coronavirus infection

No	Heart failure	ICU	mechanical ventilation	Supportive oxygen therapy	Nebulized inhaled interferon alpha-2b	Rib-avirin	Lopinavir /ritonavir	Oselta-mivir	Cefop-erazone	Gluco-corticoid	Immunoglo-bulin (IVIG)	Chinese her-bal medicine
1	N	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y
2	N	N	N	N	Y	N	Y	N	N	N	Y	Y
3	N	N	N	N	Y	Y	N	N	N	N	N	Y
4	N	N	N	N	Y	Y	N	N	N	N	N	Y
5	N	N	N	N	Y	Y	N	N	N	N	N	Y

Case 1 Hemoglobin and red blood cells were reduced, hemoglobin 101g, red blood cells 3.12 suggested anemia. Two patients had platelets > 470.

Five patients with alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, and creatine kinase isoenzymes were normal.

Case 1 newborn D-dimer 22.48, significantly higher than other children.

Third, imaging examination All 5 patients underwent chest radiograph and CT. Three of the chest radiographs showed rough lung texture, but CT case 1 showed multiple small patchy shadows in both lungs, cases 2 and 3 CT showed right lung patchy shadows, and cases 4 and 5 (siblings) showed no abnormalities in CT.

TREATMENT

All 5 cases were treated with α -2b interferon nebulization and oral Chinese medicine. All but ribavirin was used except for Example 2. Except for the neonate of Example 1, the remaining 4 cases were all mild, without IC λ , mechanical ventilation, gamma globulin, and other treatments. Only symptomatic treatment was supported. All patients were cured and discharged. Follow-up was normal. Examples 1 and 2 received oral antiviral therapy with lopinavir / ritonavir (1.5ml, 2 times / d \times 5d). No oseltamivir phosphate was used in 5 cases [6-9].

The total length of hospital stay was 91 days, with an average of 18.2 days. Case 1 was hospitalized for 29 days. Cases 2 and 3 are 16 days, and Cases 4 and 5 are 15 days. Fever days were 28 days, with an average of 5.6 days.

DISCUSS

Familial cluster infection 5 children from four family epidemiology suggest a family cluster infection, of which 20 family members were involved in the infection. Including grandparents, grand-

ma, father, mother and sister. Among them, the neonates were critically ill only 5 days after birth. Before birth, his parents were in Wuhan. After the mother became infected with the new coronavirus pneumonia, she had a fever and then had a cesarean section. A positive checkup confirmed the diagnosis.

Clinically, fever is the main manifestation. Four children (80%) had fever ranging from cough, asthma, vomiting and diarrhea. This shows that fever is the most common manifestation of neonatal coronavirus infection in children. It's also a signal and clue. It is the first performance that should be taken seriously. Italian studies report that fever is the most common manifestation of 83% - 98%, while cough and shortness of breath account for 31% - 55%. None of the 5 children had congenital, genetic and metabolic diseases [8-11].

According to its symptoms and clinical manifestations, it is divided into asymptomatic infection, mild, common, severe, and critical. Studies suggest that children with new type of coronavirus infection have five characteristics clinically. First, the number of infections is smaller than that of adults. Second, symptoms and clinical manifestations are lighter than those of adults. Third, there are fewer complications than adults. Fourth, recovery is faster than that of adults, and fifth has a better prognosis. This may be related to less exposure of children than adults, pediatric immune function is not yet fully developed, and pediatric infections are mild and inaccurate, and the diagnosis cannot be found in time and is easily missed.

The minimum age is 5 days after birth. The parents lived in Wuhan until the child was born. Department G1P1, born 38 + 5 weeks after cesarean section, A's score and other unknown. Before admission, the parents of the child returned to Xinyang, Henan from

Wuhan on January 22, and the mother of the child felt cold and lethargic in the afternoon. A cesarean section was performed on January 31, and a new coronavirus infection was confirmed on February 1 with a positive nucleic acid test, indicating that the mother had a new coronavirus infection during childbirth.

Although the new coronavirus infection occurred only five days after birth, it suggested that it was not caused by vertical infection of mothers and infants. Because the mother was infected with the new coronavirus before cesarean section.

Five cases had family members with a history of infection. Fever is the main symptom of most children. Except for Example 3, fever is low to moderate, with a maximum body temperature of 38.6. Example 3 had no fever, no runny cough or vomiting.

The clinical and immunological characteristics of children need attention, and further research and discussion are needed. One patient in this group had no clinical manifestations despite a nucleic acid test and a family member who was diagnosed with a new coronavirus infection. It should be noted that children with asymptomatic infection should be vigilant, because those with no symptoms or mild symptoms are likely to become a hidden source of infection should be paid attention to. It has been reported that most of the early lymphocytes were reduced in adults and lower in 4 cases. Leukocytes in children under 5 years of age have two crosses. Lymphocytes are normally higher than neutrophils. So if the lymphocytes decrease, it may be related to viral infection.

Increased D-dimer is an indicator of serious infection. The D-dimer in this group of cases was as high as 22.248. It is 22 times higher than other cases, but there is no significant difference between CRP, PCT mild and critical illness. In

adult patients, AST, ALT, lactate dehydrogenase, isoenzymes, etc. increased, but no significant increase in children in this group. Positive nucleic acid test is an important basis for the diagnosis of new crown infection. In this group of 5 children, throat swabs, blood nucleic acid tests were positive twice, and no negative children. The patient was discharged from hospital with a negative secondary test, and continued to be separated and observed at home for two weeks after discharge. [3-7]

It has been reported that the nucleic acid test may be negative in the early stage, so the chest radiograph and CT of epidemiological history and symptoms suggest that children with new crowns should be repeatedly tested for nucleic acid to avoid missed diagnosis. Negative throat swabs but positive anal swabs have been reported to indicate a long period of exclusion of the virus from the intestinal tract. Chest radiographs of 3 patients in this group showed rough lung texture, but CT examination showed patchy consolidation shadows in multiple parts of both lungs or right lung.

It shows that chest CT is earlier and more diagnostic value than chest radiograph. In view of the low sensitivity of nucleic acid detection, in order to prevent missed diagnosis, epidemiological and clinical manifestations should be combined, and combined diagnosis of nucleic acid examination and chest CT should be used to reduce missed diagnosis [7-8].

In terms of treatment. In view of the fact that children with neo-crown infection are less ill and have a better prognosis, they are mainly family-gathered. For ordinary, asymptomatic, mild cases, special medication is not emphasized. Except for case 1 who was treated in the ICU in the group, the remaining 4 cases were closely observed after hospitalization, and they were cured after being supported by symptomatic treatment. No special changes were observed after two weeks of follow-up. Example 1 The patient recovered and was discharged from hospital despite the onset of disease on 5 days after birth and treatment with mechanical ventilation. The application of antiviral drugs such as ribavirin in children with new crown infection suggests that further studies on efficacy, safety, and toxic side

effects are needed. Patients 1, 2 orally took lopinavir / ritonavir orally (1.5ml, 2 times / dX5d antiviral treatment. None of the 5 patients received oseltamivir phosphate [6-10].

Except for neonates in this group, the remaining four cases were not treated with antibiotics, and emphasis was placed on avoiding blind or incorrect use of antibacterial drugs. Reasonable selection of antibiotics should be based on bacterial infection and bacterial culture and drug sensitivity tests. For critically ill patients, a short course of small doses of gamma ball and glucocorticoid can be given. The application of traditional Chinese medicine should be treated with individualized syndromes according to the age, physique, and condition of the child. It is recommended to take traditional Chinese medicine instead of injecting traditional Chinese medicine preparations.

A2b interferon nebulization, as a medication for respiratory diseases, is currently widely used, but the clinical efficacy of novel coronavirus infection is still lacking theoretical and clinical evidence of rigorous scientific research such as randomized double-blind placebo control. Therefore, further clinical rigorous scientific research is needed to provide scientific theoretical and experimental evidence for clinical applications. Moreover, atomization may increase the risk of aerosol infection, which deserves further discussion and discussion.

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NEW PROGRESS IN NURSING RESEARCH OF KAWASAKI DISEASE

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ABSTRACT

Kawasaki disease is one of the main causes of acquired heart disease in children. The damage degree of the heart coronary artery determines the main therapeutic methods and follow-up time of children. The main clinical manifestations of Kawasaki disease are acute or persistent fever, oral cavity mucous membrane inflammation, eye conjunctival congestion, swollen lymph nodes, etc. In recent years, the diagnosis and treatment experience of Kawasaki disease has been popularized, among which clinical nursing is the key to ensure and improve the treatment effect. The nursing types are mainly divided into holistic nursing for Kawasaki disease, evidence-based nursing for Kawasaki disease, clinical pathway nursing for Kawasaki disease and internet-based continuous nursing, including: diet, skin mucosa, medication methods and other issues. In order to explore the effective nursing methods of Kawasaki disease, this paper comprehensively describes the current research status and intervention methods of Kawasaki disease nursing at home and abroad, so as to provide theoretical reference for the nursing work of Kawasaki disease in the later stage.

Key words: *Kawasaki disease; Systemic vasculitis; Nursing; New progress*

Kawasaki disease is also called the mucocutaneous lymph node syndrome, common in 6 months to 6 years old children, its' main clinical manifestation is acute or persistent fever, oral cavity mucous membrane inflammation, eye conjunctival congestion, swollen lymph nodes, etc. The main pathological change is a systemic inflammatory lesions of small and medium-sized blood vessels, especially the coronary arteries. In the long term, it may cause coronary artery thrombosis and ischemic heart disease in children, which seriously threatens to children's normal growth and development and physical health [1,14]. In addition, in the acute phase of Kawasaki disease in children, pericarditis, myocarditis and other symptoms may also occur, which further induces serious complications including heart failure [19], directly threatening the life and health of children [12]. Kawasaki disease is a global disease, and the incidence varies by race and country, but

the incidence of Kawasaki disease is relatively high in Asian populations. It is relatively common in pediatric clinic, and the incidence has been increasing in recent years [2,16]. In recent years, there has been a further understanding and development of kawasaki disease nursing measures and methods. In order to promote the quality of medical nursing for Kawasaki disease, this paper is summarized as follows.

I. HOLISTIC CARE FOR KAWASAKI DISEASE

1.1 Diet nursing: For suckled children, pay attention to the supplementation of relevant nutrients, for weaned children, to maintain a balanced nutrition. Due to fever and high energy consumption, children should be given high nutritious and digestible diet, mainly of semi-liquid food, such as egg cake and soybean milk, etc. Spicy and stimulating food should be banned. Eat small, frequent meals at a controlled speed to avoid stim-

ulating oral mucosa, and fatty acids and amino acids should be properly supplemented to ensure daily nutrient intake [4].

1.2 Skin and mucous membrane nursing: Keep the skin dry and clean, scrub daily, and clean the sweat in time after sweating; Wear soft clothing, often cut nails, avoid scratching the skin; Bed sheet neat and soft; Clean buttocks and surrounding skin after use. Finger and toe stiffness and swelling are common complications of such children, which generally do not need intervention and can disappear spontaneously in about 7 days, but the infectious rash that may occur during this period should be avoided. Calamine lotion should be applied externally for early scarlet fever-like rash with obvious itching; If children have acra and perianal peeling, they should regularly clean their skin and limit their hand and foot movement to prevent skin damage, local infection and other complications caused by scratching skin; Children with Kawasaki disease can have lip flushing, dryness, bleeding and other conditions, use normal saline to clean the children's mouth daily, more than twice a day, to avoid the occurrence of oral ulcer; Lip balm for lip dry and peeling; Oral ulcer powder is used to give oral care to children with ulcer; For obvious eye conjunctival hyperemia, avoid light stimulation and rinse with normal saline [4].

1.3 Complications nursing: Fever is the main symptom of Kawasaki disease in children. Clinical temperature monitoring was strengthened after admission, and the temperature was measured once 2 hours. After the high temperature drop, take the temperature again in half an hour. Drink more water to prevent febrile convulsion. For patients with body temperature > 39°C, physical cooling can be adopted on the basis of routine aspirin

treatment. Note to monitor the body temperature once every 4 hours, adjust the indoor temperature and humidity appropriately, and encourage children to drink more water; Physical cooling through alcohol bath, ice pillow, antipyretic patch, and appropriate medication; Monitor vital signs, complexion, pupils and consciousness, and pay attention to possible abnormalities. During hospitalization should limited movement, rest in bed, and careful observation of disease development. For children with pre-existing coronary artery dilatation or coronary aneurysm, carefully observe of blood pressure, heart rate, breathing, complexion, consciousness, and observe whether had tachycardia, arrhythmia and so on, when it is necessary to give continuous eeg monitoring, close observation of the patient's eeg, alert to early changes of cardiovascular, always ask whether chest distress and shortness of breath, and malaise of the precordial area.

1.4 Psychological nursing: Communicate with children and their families with friendly tone and relaxed language, comfort and encourage children. Educate parents about the disease and the effects of treatment to reduce tension and help build confidence in treatment. Before using drug, explain the nature of the drug, the mechanism of action, the possible symptoms, the causes of the adverse reactions and in what case need to inform the staff to the family members in detail to remove the unnecessary tension and explain even if children appear symptoms also need not nervous, just inform medical staff, who will deal with the situation and monitor the entire infusion process to avoid anxiety, fear and suspicion among family members. In terms of psychological intervention, due to the repeated illness of the children, the fever lasts for a long time, and the high cost of hospitalization, the family members of the children will inevitably have anxiety. The nursing staff should introduce the child's condition, the doctor's treatment plan and the outcome of the disease to the family in detail, patiently listen to the child's family's appeals, and assist them to solve.

1.5 Out-of-hospital nursing: pay attention to discharge guidance, remind the return visit after discharge, guide children to take medicine on time and in quantity, can not stop or reduce at will. Details to be filled in the discharge guidance card include: the usage and dosage of oral drugs; time of review: 1, 3, 6, 9 months after each review; pay attention to diet nutrition, prevent colds; do not carry out strenuous ac-

tivities within 1 year to avoid recurrence or aggravation of the disease; vaccination is not allowed within 9 months [5,17].

1.6 Medication nursing: make clear the dosage, way of administration and time of medication, explain the matters needing attention and possible adverse reactions, closely observe whether there are abnormal conditions such as drug eruption, and immediately stop the drug for treatment after discovery. At present, the commonly used drugs for pediatric kawasaki disease include gamma globulin, aspirin, etc. [2,18]. The transfusion of gamma globulin should be carried out according to the operation standard of blood products, and parents should be informed of the pre-transfusion examination. Input strictly aseptic operation, before using other drugs to wash pipe with normal saline, and out of the box. Infusion speed should be slow, generally under 3 years old 10 ~ 20 drops /min, over 3 years old 20 ~ 30 drops /min. Pay attention to observation, once nausea, vomiting, palpitation, chest tightness, sweating and other symptoms, can slow down infusion speed or stop infusion; If symptoms worsen, such as shortness of breath, cyanosis, urticaria, etc, immediately stop medication, give oxygen, keep warm, and cooperate with the physician to give anti-allergy treatment. When using aspirin, it is necessary to emphasize the accuracy of dosage, give it on time, and do not increase or decrease or stop taking it at will. Communicate the effects of medications and possible reactions to parents to get their cooperation. Generally choose enteric-soluble aspirin, should be taken in 15 minutes after meals, infants after grinding and dissolution, when necessary, with aluminum hydroxide, while drinking more water. During medication, children should be closely observed for drug eruption, skin, mucous membrane, gum bleeding and stool color, and regular reexamination of blood routine, coagulation function and liver function, etc [15].

II. EVIDENCE-BASED NURSING FOR KAWASAKI DISEASE

Evidence-based nursing is an important branch of evidence-based medicine, meaning "to follow the evidence of nursing", may be defined as carefully, accurately and wisely apply the best available research evidence. Combine perfectly years of clinical experience, nursing skills and patient's values and principles at the same time, to develop nursing measures. Its core is to carry out nursing work based on the best evidence [6]. Kawasaki disease evidence-based nursing as an

ideal practical activity, can maximum limit satisfy the needs of children and parents, on the basis of clinical practice of nursing problems, look for evidence in the relevant research literature, then make a critical evaluation on the validity, reliability, clinical application and universality of the evidence, and pick out the best evidence, to solve the actual problem of children. In order to improve the quality of nursing, then sublimation of nursing theory and practice on an evidence-based basis. By looking for scientific evidence of Kawasaki disease and consulting a large number of professional related materials, nurses also promoted the update of professional knowledge.

The specific methods of implementing evidence-based nursing intervention are as follows [6]: (1) Look for evidence-based evidence: combined with the literature report, comprehensive clinical nursing actual need, put forward the following evidence-based nursing basis: ① Evidence 1: In the process of the treatment for children with injection of gamma globulin, can cause adverse reactions such as rash, fever, headache, impact on diagnosis and treatment; ② Evidence 2: After the onset of children, gastrointestinal dysfunction, need to be focused; ③ Evidence 3: The families of children with insufficient knowledge of the disease, can not accurately participate in the care of children. (2) Put forward nursing countermeasures: combined with the above evidence-based nursing evidence, put forward the necessary nursing rectification measures. ① Evidence 1: Nursing countermeasures: According to the high fever, rash and other symptoms caused by the treatment process, the causes of adverse reactions were analyzed, and the possible safety risks in the process of drug use were deeply explored. Necessary measures were taken for scientific intervention. At the same time, nurses continue to improve their own nursing skills, have a clear understanding of the adverse reactions of gamma globulin, and timely convey to the children's families. Be aware of risks and sign the informed consent for medication, to avoid causing family members do not understand, resulting in poor communication between nurses and patients related disputes. ② Evidence 2: Nursing countermeasures: Timely observation of the children's skin and body temperature, combined with the change of indicators to judge the condition. For children with abnormal defecation, nursing staff to the children during the treatment of gastrointestinal function of the correct judg-

ment, in order to avoid damage to the intestinal mucosa, enteric preparations can be appropriately given, fully protect the gastrointestinal function. The frequency of stool movement and stool character of children were observed, in order to detect potential risks in time, such as toxic reaction. The vital signs of the children were closely monitored, and the drugs were stopped in time when abnormalities were found, and the corresponding treatment was carried out. (3) Evidence 3: Nursing countermeasures: Communicate closely with family members, inform them of their important role in the treatment of children, and give full play to their initiative. Inform family members of Kawasaki disease related knowledge, demonstrate nursing operation points. Family members' emotions should be channelled so that they can participate in the child care. Prior to discharge, do a good job of guidance, and agree on the time of return to the hospital.

III. CLINICAL PATHWAY NURSING FOR KAWASAKI DISEASE

The clinical treatment of Kawasaki disease in children is mainly drug therapy, clinical nursing plays a prominent role in the treatment, and combined with the clinical path, the nursing effect will effectively improve.

Clinical pathway nursing is implemented in the following process [7]: ① Establish a clinical pathway group: Head nurse as the leader, Nurse-in-charge as the deputy leader, 4 responsible nurses as the team members, assign tasks according to individual work area and nursing expertise; (2) Evaluation before nursing: Assess the condition and nursing first, then to understand the basic condition of children, the past medical history, medication history, analysis of possible nursing problems, to screen the nursing risks; (3) Evidence-based support: According to the problems found, through the search of literature and integration of previous nursing records, seek for targeted nursing methods; (4) Nursing implementation and records: Group discussion of nursing plan and make nursing process table, in strict accordance with the nursing process table implementation of nursing. After complete the corresponding nursing measures, marking and observing the effect of implementation record. Last, check the process table whether there are nursing errors; (5) Nursing evaluation: According to the nursing records and children's family feedback, evaluate the nursing effect, and continuously improve the nursing plan.

The clinical path was applied to the nursing of the research group, the implementation of nursing measures is more organized, nursing division of labor is clear. The use of nursing process table, to avoid the absence of nursing measures, continuous improvement of the nursing plan, quality control effect is more ideal, and nursing quality is significantly improved. Clinical pathway can improve the efficiency and scientificity of nursing.

IV. INTERNET-BASED CONTINUOUS NURSING

In recent years, with the development of mobile network tools, Internet-based continuing nursing services have been gradually applied in out-of-hospital nursing health education for patients with chronic diseases [13]. The level of caregivers' disease knowledge can affect their care ability, and providing caregivers with disease knowledge will help them to provide professional and scientific home care services for patients with chronic diseases. In order to improve the medication compliance of children with Kawasaki disease coronary artery injury after discharge and reduce the family care burden of the children, continuity of care and health guidance can be provided for them, to improve the treatment compliance of the children [8]. In recent years, with the emergence of the Internet, internet-based continuous nursing intervention can effectively save medical materials and is not affected by time and space, so that continuous nursing services can be better carried out [9].

First, set up a network platform management team [10]: the team members included 1 head nurse, 1 Senior title cardiovascular specialist doctor, 3 specialist nurses in charge, 1 psychological consultant and 2 network engineers. The head nurse and cardiovascular specialist are responsible for developing home health education programs for the children, and the nurses and psychological consultants answer related questions for the children and their caregivers through wechat every Tuesday and Thursday. Vascular specialists are responsible for providing treatment, examination, dietary guidance, daily life guidance, medication guidance and other post-discharge issues for children and caregivers through mobile APP or wechat group. The network engineers shall be responsible for the operation training and maintenance guidance of wechat group, wechat official account and mobile APP for the team members.

Then, build a network communication platform [10]: (1) WeChat group: estab-

lish WeChat group called "health communication group of Kawasaki disease", through weekly rotation, the supervisor nurses communicate with the children on the wechat network platform, patiently answer questions raised by children and caregivers, and encourage caregivers to exchange Kawasaki disease nursing experience in wechat group. ② Wechat official account: establish Kawasaki disease wechat official account, children and caregivers when they are admitted to hospital, let them follow the public account, which includes disease knowledge, question answering, classic case sharing, online booking and other functions. The health education content uploaded on the official account should be verified by the head nurse and cardiovascular specialist.

Specific contents of continuous nursing [10]: (1) Hospitalization: establish health education archives of children with Kawasaki disease, including gender, age, course of the disease, cardiovascular damage, medication (including the preparation methods, types, adverse drug reactions), caregivers' education degree, contact information, healthy condition, etc. To confirm that caregivers can skilled use of smart phones and WeChat public, and invite specialist doctor to join WeChat group APP. (2) 1 ~ 3 months after discharge: children with kawasaki disease coronary artery injury need to take anticoagulants such as warfarin and aspirin after discharge. Anticoagulants are easy to cause bleeding, When taking them the dosages should be controlled well and medication should be strictly followed as prescribed by the doctor. Some children may develop rashes and other adverse reactions after taking aspirin, and their performance should be closely monitored during taking aspirin. During the medication period, caregivers can send the medication situation and medication reaction of the child to the wechat group in the form of photos or videos. Specialist doctors can make a preliminary diagnosis of the child through the pictures or videos, and determine whether the child needs to go to the hospital according to the diagnosis results. Medical staff conducted remote online video health education for children and caregivers once a week to improve their awareness of disease. (3) 3 months after discharge: inform children and caregivers of daily Kawasaki disease health care, prevention of adverse behavior events and other knowledge through wechat platform or mobile APP. Due to the prolonged discharge, the coordination degree and medication compliance of chil-

dren and their families for regular follow-up visit will decrease. The medical staff conducts online videos for the children and their caregivers through Wechat groups every 4 weeks, so as to know the medication status and the outcome condition of the children. 1 ~ 2d before the follow-up, the children and caregivers were reminded to make online registration and appointment for various examinations through Wechat group. According to the cardiovascular conditions of the children, the diet plan, exercise plan and the time to return to school were determined, and the caregivers were instructed to learn to observe the symptoms of angina pectoris or myocardial infarction. For the elderly children, we should pay attention to the clinical symptoms, whether there is chest pain, chest tightness and other discomfort. For the young children, we should pay attention to whether there is dysphoria, loss of appetite, depression and other manifestations. For children with heavy family burden, psychological counselors should be arranged to conduct psychological intervention on children and caregivers through online platforms, so as to reduce their bad emotions and promote their physical and mental health.

V. SUMMARY

Kawasaki disease in children, also known as cutaneous mucosal lymph node syndrome, can lead to small and medium-sized vascular lesions throughout the body, which is a vasculitis syndrome. It can cause serious damage to the coronary arteries in children, and is one of the important causes of coronary artery disease in children. It is also a potential threat to the onset of coronary heart disease in children as adults. Clinical mainly adopts drug therapy, clinical nursing is the key to ensure and improve the effect of drug therapy. Holistic nursing is a comprehensive and meticulous nursing mode, which can meet the nursing needs of patients from more dimensions, effectively improve the physical and mental conditions of children, and has a high clinical application rate. Compared with traditional nursing methods, Kawasaki disease evidence-based nursing model has more obvious effect. It can meet the needs of children's medical treatment, further strengthen the correct cognition of family members, and achieve satisfactory clinical nursing effect. The clinical pathway can improve the efficiency and scientificity of nursing. Internet-based continuous nursing through Wechat, mobile App and other channels,

regularly push Kawasaki disease basic knowledge, updating drugs knowledge, and regularly use pictures and video to make disease knowledge become more image, vivid, make caregivers can better understand the disease knowledge, can provide a more comprehensive, targeted nursing service for children and caregivers, thus improve the caregivers disease awareness, So that it can better urge children to take medication, so as to improve their medication compliance [20].

In short, in recent years, with the in-depth research on the pathogenesis of Kawasaki disease and the accumulation of therapeutic experience, as well as the background of mobile networking era, various nursing techniques and methods for Kawasaki disease change and development, timely application, Kawasaki disease nursing quality effectively improved, children benefit significantly, it is worth promoting.

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DIFFERENT

PHYSICAL GROWTH AND PUBERTAL DEVELOPMENT OF SCHOOL-AGED CHILDREN IN ULAANBAATAR

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(ABSTRACT)

Key words: *physical development, puberty, anthropometric measurement, secular trend*

Background: Growth patterns and anthropometric measurements of school-aged children in Mongolia are well-known from previous several nationwide studies. Secular trends in height and weight were observed in each study, but changes in the timing of puberty are still unknown.

The objective of the study: To perform a physical development assessment of school-age children, establish the median age pubertal stages both in girls and boys. And determine relationships of pubertal stages and anthropometric measurements.

Methods: A cross-sectional study of the growth and pubertal stages of healthy 385 school-aged children (aged 7-17 years) who live in the suburban area of Ulaanbaatar. Pubertal stages were determined by Tanner and Marshal's method. Height and weight were also recorded, and BMI was calculated. Mean age at pubertal stages were estimated using probit analysis. Mean age at menarche was calculated by status quo method.

Results: The prevalence of obesity and overweight were 6.5%, 12.0% respectively. And 4.9% of total students were underweight, 11.7% were stunted. The median age of onset of Tanner stages 2 for breast development was 9.58, and pubic hair stage 2 was 10.94 in girls. The median age at menarche was 12.26. The median age of testicular enlargement (Tanner 2 stage) and pubic hair Tanner 2 stage were at 10.96 and 13.30 years, respectively. BMI, waist circumference, and hip circumference had a medium to strong correlation with pubertal stages and menarche in girls. Height was strongly correlated with pubertal stages in boys.

Conclusions: The prevalence of obesity and overweight (24.1%) are highest among elementary school students, and stunting (13.3-14.5%) is twice higher in middle and high school students. Breast and pubic hair development start at 9.58 and 10.95 in girls, the median age at menarche is 12.26, and testicular and pubic hair development starts at 10.29 and 13.30 in boys, respectively. Hip circumference in girls ($r=0.809$, $p<0.05$), height in boys ($r=0.843$, $p<0.05$) had strongly correlated with pubertal stages.

INTRODUCTION

Puberty is a transitional period for the child to become a young adult. Disorders of puberty can impact physical and psychosocial well-being and also risk factors of various diseases later in adult life. The most visible changes during puberty are increased growth velocity and the development of secondary sexual

characteristics. The first sign of pubertal initiation is breast development in girls and testicular enlargement in boys. The landmark studies of Marshal and Tanner¹, which classified puberty into five stages in girls and boys, have been widely used to assess pubertal development. Precocious puberty is the onset of one or more pubertal signs at an age of

2-2.5 standard deviations (SD) earlier than population reference data. In the majority of studies, increased body mass index (BMI) is related to precocious puberty in girls. Delayed puberty is considered as the absence of sexual maturation signs by an age of more than 2-2.5 standard deviation values above the mean of the population. Constitutional delay of growth and puberty is the most common cause of delayed puberty in boys. In clinical practice, assessment of pubertal stages for each child is extremely useful, but should all times be related to updated and reliable reference data from the same population². The growth and pubertal development of an individual child is a dynamic statement of his or her general condition or health. Puberty is a transitional period for a child to become a young adult. Disorders of puberty can impact physical and psychosocial well-being and also risk factors of various diseases later in adult life. The most visible changes during puberty are increased growth velocity and the development of secondary sexual characteristics.

The sequence of pubertal events is remarkably consistent across countries and ethnic groups, although the timing varies by country. The timing of puberty is influenced partly by genetics, but largely by nutrition and economic development³.

Growth patterns and anthropometric measurements of school-aged children in Mongolia are well-known from previous several nationwide studies. Secular trends in height and weight were observed in each study, but changes in the timing of puberty are still unknown. Therefore, we need to study the timing

and tempo of puberty in healthy Mongolian children and look for any possible downward secular trends in pubertal development.

OBJECTIVE

- To perform physical development assessment of school-age children, establish the mean age of pubertal stages both in girls and boys.
- To determine relationships of pubertal stages and anthropometric measurements.

METHODS

A cross-sectional study of the growth and pubertal stages of healthy 385 school-aged children (aged 7-17 years) living in the suburban area of Ulaanbaatar. The school is located 15km from the center of Ulaanbaatar.

Pubertal stages were determined according to Tanner and Marshal’s method by visual inspection and palpation. Testicular size was measured by Prader’s orchidometer. Height was measured using a mobile stadiometer to the nearest 1 mm and weight was measured by electronic scale to the nearest 100 gram. And body mass index (BMI) was calculated.

Mean age at pubertal stages were estimated using probit analysis. Mean age at menarche was calculated by status quo method.

RESULTS

The prevalence of obesity and overweight were 6.5% and 12.0%. And 4.9% of total students were underweight, 11.7% were stunted.

The prevalence of obesity and overweight (24.1%) are highest among elementary school students, and stunting (13.3-14.5%) is twice higher in middle and high school students.

The median age of onset of Tanner stages 2 for breast development was 9.58, and pubic hair stage 2 was 10.94 in girls. The median age at menarche was 12.26.

The median age of testicular enlargement (Tanner 2 stage) and pubic hair Tanner 2 stage were at 10.96 and 13.30 years, respectively.

Hip circumference in girls (r=0.809, p<0.05), height in boys (r=0.843, p<0.05) had strongly correlated with pubertal stages.

Table 1

Mean height and weight of students.

		Class			p value
		Elementary	Middle	High	
Gender					
Male	Height	134.0	148.0	170.8	0.01
	Weight	34.7	42.5	61.0	0.01
	BMI	19.3	19.3	20.7	0.215
Female	Height	133.6	151.1	159.9	0.01
	Weight	30.4	44.0	55.1	0.01
	BMI	17.0	19.1	21.7	0.01

Table 2

Nutritional status of students.

		Class						p value
		Elementary		Middle		High		
		N	%	N	%	N	%	
BMI								0.015
Normal	97	70.8%	132	76.3%	66	88.0%		
Overweight	17	12.4%	23	13.3%	6	8.0%		
Obesity	16	11.7%	7	4.0%	2	2.7%		
Underweight	7	5.1%	11	6.4%	1	1.3%		
Height								0.134
Normal	127	92.7%	148	85.5%	65	86.7%		
Stunting	10	7.3%	25	14.5%	10	13.3%		

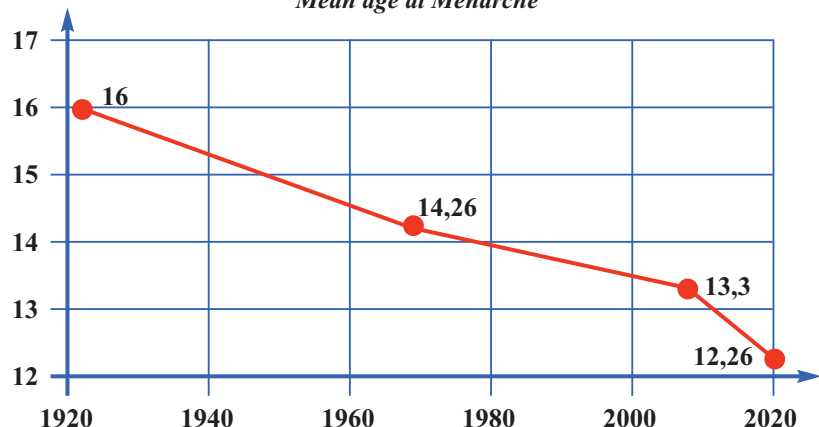
DISCUSSION

According to the fifth national nutritional survey, the prevalence of overweight was 22.2% and the prevalence of obesity was 6.4% among primary school children in Mongolia. Overweight prevalence was higher in boys (26.6%) compared to girls (17.8%)4. In our survey, the prevalence of overweight was lower in the suburban area of Ulaanbaatar, the capital city of Mongolia.

We compared the anthropometric measurements of school-aged children with previous several studies. To compare the study conducted from 50 years ago with our current result, mean height increased by 9.2 cm in boys, 8.9 cm in girls. And mean weight increased by 8.9 kg in boys, 5.7 kg in girls, respectively 5, 6. And the age at peak height velocity occurred 1-2 years earlier in our survey. A previous study in Ulaan-

Graphic 1

Mean age at Menarche



Pubertal development.

	Age				
	5 th percentile	25 th percentile	50 th percentile	75 th percentile	95 th percentile
Breast stage					
2	8.09	8.97	9.58	10.19	11.06
3	9.15	10.21	10.95	11.68	12.74
4	10.62	11.78	12.59	13.39	14.55
5	12.16	13.34	14.17	14.99	16.17
Pubic hair stage (Girls)					
2	9.21	10.23	10.94	11.65	12.67
3	10.06	11.26	12.10	12.93	14.13
4	11.72	12.69	13.37	14.04	15.01
5	12.95	13.97	14.67	15.37	16.38
Menarche					
	10.05	11.35	12.26	13.17	14.47
Genital stage (Boys)					
2	8.02	9.36	10.29	11.21	12.55
3	10.53	11.90	12.86	13.81	15.19
4	12.70	13.90	14.74	15.58	16.78
5	12.81	14.28	15.29	16.31	17.78
Pubic hair stage (Boys)					
2	10.37	12.10	13.30	14.50	16.23
3	12.26	13.34	14.09	14.84	15.92
4	12.87	14.49	15.62	16.75	18.37
5	15.17	16.84	18.00	19.16	20.83
Voice change					
	9.78	11.30	12.36	13.416	14.93

baatar shows that 69.5% of boys, 71.7% of girls' anthropometric measurements were in the normal range⁷. But in the current study, 70.6% of boys, 82.0% of girls were normal to their age.

The mean age at menarche is a very sensitive indicator of an individ-

ual's general health and socioeconomic status. The first survey of the growth and pubertal development in Mongolia was conducted in 1920 by a Russian researcher⁸. The mean age at menarche was 16 years old in girls. A century later, in our study, a girl's

Table 3

mean age of menarche decreased to 12.2 years old.

CONCLUSIONS

● The prevalence of obesity and overweight are highest among elementary school students, and stunting is twice higher in middle and high school students.

● Downward secular trend of growth and pubertal development is still observed in Mongolia. The mean age at menarche is decreased by four years in the last 100 years. Age of pubertal stage milestones are decreasing, and median height and weight are increasing.

● BMI, waist circumference and hip circumference had a medium to strong correlation with pubertal stages and menarche in girls. Height was strongly correlated with pubertal stages in boys.

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Table 4
Correlation between growth measurements and pubertal stage.

	Pearson's correlation			
	BMI	Hip circumference	Waist circumference	Height
Gender				
Female				
Breast stage	.592**	.809**	.639**	.791**
Menarche	.501**	.698**	.548**	.678**
Pubic hair stage	.574**	.774**	.616**	.743**
Male				
Genital stage	.151*		.339**	.843**
Pubic hair stage	0.143		.290**	.774**

** p <0.01

* p <0.05

A CASE REPORT OF FAMILY CLUSTER CARBON MONOXIDE POISONING WITH DELAYED ENCEPHALOPATHY AND LITERATURE REVIEW

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ABSTRACT

Objective To investigate the course, symptoms and advantages of early comprehensive treatment of carbon monoxide (CO) poisoning in a child with delayed encephalopathy due to family carbon monoxide poisoning. **Methods** The medical history, physical examination, imaging examination and later recovery of the child in our hospital during rehabilitation treatment. **To summarize the benefits of early comprehensive treatment for delayed encephalopathy due to carbon monoxide poisoning in children.** **Results** The local hyperbaric oxygen treatment of CO poisoning in the child was not good, and there were coma, convulsion, paralysis and other delayed encephalopathy. **After being transferred to our hospital for comprehensive treatment, the condition gradually recovered.** **Conclusion** It is important to strengthen the clinical observation of CO poisoning patients, especially children, to find the damage of delayed encephalopathy and various organs in time, and to timely comprehensive treatment.

Key words: Carbon monoxide poisoning; Delayed encephalopathy; Hyperbaric oxygen.

AN OVERVIEW,

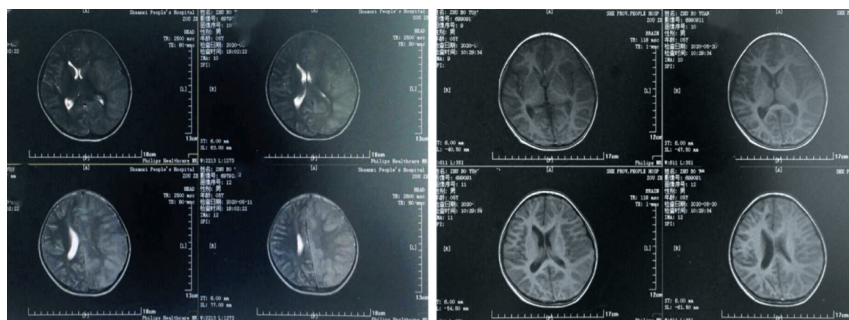
Acute carbon monoxide poisoning (ACMP) is a common disease in winter in northern China, mainly occurring in rural areas with underdeveloped economic conditions, and its mortality and disability rate are high. More than 2.5 million people die of carbon monoxide poisoning every year in the world. According to national statistics, the number of people who die of gas poisoning every year in China is about 1,500 people. Because of the cold winter, and the doors and Windows are also very tight, especially the substandard coal or not burning, people die of chronic poisoning in their sleep at night. http://www.so.com/s?q=%E5%9C%A8%E4%B8%AD%E5%9B%BD&ie=utf-8&src=internal_wenda_recommend_textnhttp://www.so.com/s?q=%E7%85%A4%E6%B0%94%E4%B8%AD%E6%AF%92&ie=utf-8&src=internal_wenda_recommend_textnhttp://www.so.com/s?q=%E4%BA%BA%E6%95%B0&ie=utf-8&src=internal_wenda_recommend_textnhttp://www.so.com/s?q=%E5%86%AC%E5%AD%A3&ie=utf-8&src=internal_wenda_recommend_textnhttp://www.so.com/s?q=%E9%97%A8%E7%AA%97&ie=utf-8&src=internal_wenda_recommend_textnhttp://www.so.com/s?q=%E5%9C%A8%E5%A4%9C%E9%87%8C&ie=utf-8&src=internal_wenda_recommend_textnhttp://www.so.com/s?q=%E6%85%A2%E6%80%A7%E4%B8%AD%E6%AF%92&ie=utf-8&src=internal_wenda_recommend_textn CO poisoning is still one of the highest acute poisoning cases in incidence, disability and mortality so far, and the incidence of Delayed encephalopathy after acute carbon monoxide poisoning (DEACMP) has been reported in China by 10% to 30% [1], 13% to 50% abroad [2]. The causes of poisoning are mostly coal burning for heating, including coal burning for heating, improper use of gas water heater, gas leakage and so on. Hemoglobin (Carboxy-hemoglobin (COHb) forms when the body inhales CO, which affects the retention, transport, and use of oxygen in the body. All tissues and cells in the body

are impaired, especially those organs with high oxygen demand, such as the brain and heart. By clinical comprehensive treatment, most patients can recover, but the more "fake" period of severe CO poisoning patients after 60 days (2 -) easy to appear with dementia, mental symptoms and extrapyramidal abnormal brain dysfunction, known as delayed encephalopathy in acute carbon monoxide poisoning (DEACMP), reported incidence of 10% to 30%, and domestic foreign reported 13% to 50% [3]. Patients often have cognitive and memory disorders and other sequelae, severe cases can die. Clinical manifestations include cognitive impairment, dysmorrhea, forced crying, forced laughter, Chorea and Parkinson's disease [4,5]. The pathogenesis of DEACMP is still unclear, which may be related to vascular damage caused by ischemia and hypoxia, oxygen free radical damage, cell apoptosis, cytotoxicity and other possible mechanisms [4]. The treatment of CO poisoning is based on reducing the damage by eliminating CO and reversing cellular metabolic disorders. The occurrence of this disease will lead to the decrease or loss of the working ability of patients, which will greatly affect the quality of life of patients, and also bring a heavy burden to patients, families and society.

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II. CASE REPORT

Gas poisoning is northern winter, especially northern rural heating, a kind of accident that often occurs, gas poisoning is to point to carbon monoxide in gas and hemoglobin binding inside human body, and bring about hemoglobin inside human body, cannot be in contact with oxygen and make the organization hypoxia, place produces the critical situation that endangers life seriously.



MRI at 1 week after poisoning (1) Treatment in the later half moon (2)

There has been a lot of rain this year. In a certain area of northern Shaanxi, the weather suddenly turned cold in May, and the cave dwelling was even colder. My parents were living in the county town, so I was left behind by a family of four children (grandpa is 54, grandma is 52, boy is 5, girl is 3) to make a charcoal fire for warmth that night. Dad called home nobody answer the next day, around two o'clock in the afternoon go home only to find that the four gas poisoning, emergency hospital, when grandpa, girls, and poisoning the heaviest unfortunately died in the process of hospital, the lightest grandma symptoms, hyperbaric oxygen therapy better soon after 1 week, life care, I have a headache, the grandson of fever, vomiting, three days after hyperbaric oxygen therapy with limbs twitch, coma, local poor treatment effect to our hospital. After more than 20 days of mental stimulation, grandma showed a slow reaction, was reluctant to speak, suffered from memory loss and incontinence. Considering carbon monoxide poisoning, tardy encephalopathy was hospitalized in the rehabilitation department of our hospital.

III. (1) GENERAL INFORMATION (CASE INTRODUCTION OF CHILDREN)

Male child, 5 years old, chief complaint: carbon monoxide poisoning for 6 days, accompanied by fever and vomiting for 2 days. History of present illness: Six days ago, four children in a family were found to have carbon monoxide poisoning and were in coma. They were immediately hospitalized in Suide District, Yulin First Hospital for "hyperbaric oxygen and supportive treatment" (the specific treatment process and examination were not

known, but the family members spoke about it). Local head CT: basically normal. 2 days ago with fever, vomiting, the highest temperature of 38.5°C, vomiting for gastric contents, the jet shape, about 5-6 times (unknown), accompanied by intermittent right and involuntary shaking head, no obvious cough, head CT: no exception (families of oral, did not see the result), chest CT: double lung exudation and inflammation, because of the treatment the effect not beautiful. Children with irregular breathing, limb involuntary shaking, the condition is critical. Since the onset of the disease, no cough, no rash, no dyspnea, nasal feeding, poor mental, large, normal urine.

Physical examination: T: 36.3°C, P: 100 times/min, R: 22 times/min, Wt: 20kg, SO₂: 95%, BP: 90/60mmHg. Normal development, moderate nutrition, shallow coma, strong stimulation response, occasionally can wake up, simple response "ah, ah", the whole body skin and mucosa no yellow, rash, bleeding points, no edema. No enlargement was observed in superficial lymph nodes of the body. The skull is normal in size and has no deformity. The eye moves freely, the pupil is as big as the circle, about 3mm, and the response to light reflection and regulation exists. Normal hearing in both ears, no abnormal secretion in external auditory canal, no tenderness in mastoid process. Nasal septum unbiased, lip ruddy, pharyngeal hyperemia, tonsil II degree is big, neck soft, no resistance, tracheal middle and carotid pulse without exception, thoracic symmetry without exception, percussion sound clear, double lung auscultation breath sounds clear, audible and sputum song, heart rate 100 / cent, law of qi, each valve auscultation area did not smell and pathologic murmur. The abdomen is flat, the

abdominal wall is soft, no tenderness or rebound pain, the liver, spleen and ribs are not touched, the whole abdominal percussion is drum sound, no percussive pain in the liver and kidney area, and the bowel sounds are normal. No obvious abnormality was found in anus and external genitalia. The spine was physiologically curved, the muscle tension of the lower limbs was low, muscle strength could not be judged in the sedative state, physiological reflex existed, and pathological reflex was not elicited. Outpatient auxiliary examination: Blood routine examination: WBC: $10.1 \times 10^9/L$, N: 0.85, L: 0.07, M: 0.08, PLT: $116 \times 10^9/L$, RBC: $3.86 \times 10^{12}/L$, HGB: 109g/L, CRP: normal, procalcitonin: 5.42ng/ml, coagulation series: FDP 7.48mg/L, D-dimer: 1.41 mg/L, arterial blood gas: PH: 7.4 PCO₂: 43.7mmHg PO₂: 23.5mmHg BE: 2mmol/L SO₂: 99.8%, chest CT: double lung texture weight gain blur.

(2) Admission diagnosis: 1. Delayed encephalopathy due to carbon monoxide poisoning; 2. Bronchopneumonia; 3. Sepsis.

Assisted in-hospital examination: re-examination of blood gas analysis: Potassium 2.2mmol/L sodium 144mmol/L lactic acid 1mmol/L PH 7.51 PCO₂ 21.3mmHg PO₂ 120mmHg BE-4.8mmol/L electrocardiogram: no obvious abnormalities; reexamination of electrolyte ion analysis: Potassium 3.3mmol/L sodium 134mmol/L liver function and myocardial enzyme: ALT 334U/L AST 156U/L CK 2596U/L CK-MB 55U/L LD 899U/L, coagulation test: normal, PCT 3.9ng/ml, no abnormal glucose. After admission, cranial MRI was urgently checked (Figure 1): left cerebral hemisphere swelling, abnormal signal shadow of left cerebral hemisphere, right frontotemporal parietal lobe and corpus callosum, which were considered as hypoxic-ischemic encephalopathy. Severe cerebral hemisphere swelling, brain line extrusion to the right. 10 days later, head MRI was rechecked (Figure 2): abnormal changes in left cerebral hemisphere, bilateral basal ganglia region, thalamus, right frontal lobe and lateral ventricular posterior horn were consistent with the manifestations of carbon monoxide toxic encephalopathy. Cerebral hemisphere swelling was basically restored. Electroencephalogram: abnormal electroencephalogram (eeg) (background eeg rhythm slowed down significantly in the

whole brain region and bilateral cerebral hemispheres were significantly asymmetric, and no abnormalities were observed in the rest). 1 week review of prolactin: normal; liver function review at discharge: ALT 51U/L AST 121U/L; myocardial enzyme spectrum: CK 108U/L CK-MB 51U/L.

(3) Treatment: "ceftriaxone sodium (T)" anti-infection for 1 week, midazolam sedation and support treatment for 2 days. At the same time, HBO, dexamethasone, citicoline, physiotherapy and acupuncture were used to improve brain function, protect liver, nourish myocardium, maintain internal environment balance, hyperbaric oxygen and rehabilitation treatment.

(4) Results: After three days of comprehensive treatment, the child was conscious and unable to speak, with complete paralysis of the right upper and lower limbs. After continuous hyperbaric oxygen rehabilitation, the physical strength of the child gradually recovered. After one month of hospitalization, the child was discharged with normal speech and intelligence, and was able to communicate with others at a relatively slow speed. Right upper and lower limbs can be lifted, support can stand for a short time, can not walk.

IV. DISCUSSION

Acute carbon monoxide poisoning is an emergency, early effective treatment is very important, the most serious is the occurrence of delayed encephalopathy, and then severe death. The incidence of carbon monoxide poisoning in children is small, but the disability rate is high. After admission, the child was in coma and paralysis, with obvious mri brain edema on imaging, midline shift, severe brain damage, accompanied by myocardial and liver damage, which were very rare. After effective comprehensive treatment such as HBO, dexamethasone, citicoline, physiotherapy and acupuncture, the children recovered gradually for one month. They could stand on their hands and could not walk. They could talk to each other and communicate with others at a relatively slow speed. Compared with her grandma, she showed the importance of early intervention. Her early symptoms were mild, delayed encephalopathy appeared half a month later, which was manifested as unclear consciousness, quadruplegia, incontinence and other

manifestations. Meanwhile, she was considered to be related to the recovery of viscera functions and basic diseases of the old. Because children are smaller and ventilate faster, they absorb carbon dioxide faster than adults, but for the same reason, they remove it faster. [7-8]. The mechanism of hyperbaric oxygen therapy: (1) hyperbaric oxygen can accelerate the dissociation of carbon oxygen hemoglobin and promote the elimination of CO. (2) Hyperbaric oxygen can rapidly increase the blood oxygen content of the body, improve blood oxygen partial pressure, and quickly correct the hypoxia state of the body tissues. (3) Hyperbaric oxygen can quickly correct tissue hypoxia, improve aerobic oxidation, reduce organic acid, and fundamentally improve acidosis. (4) Hyperbaric oxygen can reduce intracranial pressure to prevent cerebral edema after hypoxia. (5) Hyperbaric oxygen can rapidly control cerebral edema, which is of positive significance to the recovery of CO poisoning caused by shock, brain, kidney, liver and other important organ function damage. (6) Hyperbaric oxygen has obvious prevention and treatment effect on late onset encephalopathy caused by CO poisoning. Since the pathogenesis of DEACMP is still unclear, treatment is also based on its possible pathogenesis. Currently, nutritive nerve, improved circulation, hormone immunosuppression combined with HBO and rehabilitation therapy are widely used clinically. The main pathological basis of DEACMP is diffuse demyelination of the white matter of the brain, proliferation of capillary endothelial cells in brain tissue and abnormal neurotransmitter metabolism in the brain [9]. Most scholars believe that the brain is the most vulnerable to damage due to the lack of tissue hypoxia after ACMP and the vigorous metabolism due to the lack of vascular anastomosis. Adenosine triphosphate is rapidly depleted in the absence of oxygen, the sodium pump does not work properly, and sodium ions accumulate in cells, causing edema in brain cells. The microvascular wall endothelial cells swell and denature, and the accumulation of acid metabolites in the brain increases the vascular permeability, resulting in the interstitial edema of brain cells. Blood oozes from the walls of blood vessels or extravasates in veins, occlusive endarteritis and microthrombogenesis, which in turn leads to necrosis of brain

cells and demyelinating changes in the white matter [10]. HBO is widely used in the treatment of delayed encephalopathy due to carbon monoxide poisoning in China. A number of clinical studies have shown that HBO is effective in improving clinical symptoms and signs, and improving the cure rate and recovery rate. However, due to ethical problems, a prospective non-HBO treatment group cannot be designed as a control group [11]. Et al. conducted a retrospective cohort study on 56 and 23 DEACMP patients who received different times of HBO treatment, and found that early and long course of HBO treatment could improve the prognosis of patients. Foreign scholars from Taiwan in 2010 [12] HBO treatment five times a week during hospitalization was applied to 9 DNS patients, and HBO treatment was found to improve the prognosis of DEACMP. Japanese scholars in 2014 [13] Three men over the age of 50 who developed DNS 25 days after CO poisoning were treated with HBO for 30 times, and the improvement in nerve damage was significantly improved. There are studies [14][15][16] The mechanism of glucocorticoid therapy for DEACMP is as follows: it can stabilize biofilm, increase vascular densification, reduce endothelial cell edema and endovascular inflammation, and produce immunosuppressive effect, so as to effectively prevent demyelination lesions. At the same time, can also expand spasmodic contraction of blood vessels, improve the blood circulation in the brain and prevent the degeneration and necrosis of brain cells. Additionally, glucocorticoid still can improve the excitability of nerve center, reduce carbon monoxide to the damage of central nerve cell, improve central nerve symptom thereby. Therefore, glucocorticoid has a practical and effective effect on brain protection.

In summary, both hyperbaric oxygen and glucocorticoid have certain curative effects on ACMP and DEACMP, but a small amount of adverse reactions are inevitable. As a vulnerable group, children with delayed encephalopathy accompanied by serious imaging damage will have high mortality rate, high possibility of sequelae and high expectation of parents, which should be paid enough attention to by doctors. Therefore, adverse reactions should be closely monitored and symptomatic treatment should be con-

ducted in the clinical treatment of ACMP and DEACMP children. In addition, treatment should be carried out in strict accordance with the formulated treatment plan. Meanwhile, changes in the condition should be closely observed and the treatment plan should be timely adjusted in order to get the best effect of treatment. At present, the pathogenesis of DEACMP is not very clear, and the research on this disease is still in the early stage of exploration. It is hoped that there will be a specific treatment for this disease in the near future.

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RESEARCH PROGRESS OF BREASTFEEDING IN CHINA

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Breastfeeding is the best source of nutrition for infants and young children and is one of the most effective measures to ensure the healthy growth

and development of children. The abundant anti-infective substances in breast milk can prevent the infection of digestive tract and respiratory

tract, and effectively reduce the infant mortality rate. Breastfeeding promotes early cognitive and non-cognitive development in infants.

China has cooperated with the World Health Organization and other organizations to promote a series of international standards and policies on breast-feeding, and advocates and promotes effective measures to protect, promote and support breast-feeding. Therefore, the pure breast-feeding rate of 0-6 months babies in China has been significantly improved along with the development of social and economic level, and it is higher in rural areas than in cities.

The World Health Organization (WHO), the United Nations Children's Fund (UNICEF) and other international organizations have formulated a series of international standards and policies on breastfeeding, including the International Code of Marketing of Breast Milk Substitutes and the Baby-Friendly Hospital Initiative, to advocate and promote effective measures to protect, promote and support breastfeeding in all countries around the world. The World Health Organization (WHO) to the global initiative: encourage mothers to exclusively breastfeed for six months, and then gradually add complementary food breastfeeding to 2 years old or more. By 2020, 50 per cent of babies should be exclusively breastfed up to the age of six months, according to the Guidelines for the Development of Chinese Children. The benefits of breastfeeding to the growth and development of infants are self-evident, this paper through the study of the current situation and progress of breastfeeding, improve mothers' awareness of breastfeeding, improve the rate of breastfeeding in China.

I. ADVANTAGES OF BREASTFEEDING

① The various nutrients contained in breast milk are most suitable for the digestion and absorption of infants, and have the highest bioavailability. It can meet the physiological needs of infants at different stages, and can not be replaced by any other food.

② Breast milk can reduce the incidence of neonatal diseases. Breast milk is an essential nutrient for in-

fants. Breast milk, especially colostrum, contains immune substances, which can meet the growth and development needs of infants 4 to 6 months after birth. Infants and infants are prone to various diseases due to lack of breastfeeding.

③ Breastfeeding is associated with the incidence of breast cancer. Studies have shown that less or no breastfeeding mothers have an increased risk of breast cancer. When breastfeeding, the mother's physical contact with the baby enhances the communication between the mother and the baby, enhances the baby's sense of security, and promotes the healthy development of the baby's physical and social adaptability.

2. THE CURRENT SITUATION OF BREASTFEEDING

① The current situation of breastfeeding

According to data on breastfeeding rates in China, breastfeeding levels vary from place to place, with 41 per cent of babies exclusively breastfed within six months, 71 per cent continuing to breastfeed at the age of one and 45 per cent breastfeeding at the age of two.

482/5000

② The current situation of breastfeeding in China

According to a report by the United Nations Children's Fund (UNICEF), from 2012 to 2014, the rate of exclusive breastfeeding for babies under 6 months of age in China was low. According to a survey report (2019) released by the China Development Research Foundation, the rate of exclusive breastfeeding within six months in China is generally low.

In 1998, when the World Bank surveyed China, breastfeeding rates stood at 67 percent.

In February 2019, the China Development Research Foundation released the Investigation Report on Factors Influencing Breastfeeding in China, which focused on infants under 1 year of age, and examined exclusive breastfeeding of infants aged 0-5

months (i.e., within 6 months), continued breastfeeding of infants aged 6-11 months, and early exposure to early opening of milk within 1 hour after birth. The survey data showed that the rate of exclusive breastfeeding within six months was highest in big cities, followed by rural areas and small and medium-sized cities. According to a report on the influencing factors of breastfeeding in China released by the China Development Research Foundation in February 2019, the exclusive breastfeeding rate of infants within six months in China is low. The exclusive breastfeeding rate was the highest in big cities, reaching 36 percent. The lowest rate for small and medium-sized cities was just 23 percent. According to the 2018 Investigation Report on the Publicity and Sales of Breast-milk Substitutes released by the China Consumers Association, the proportion of exclusive breastfeeding has decreased compared with a decade ago. In 2018, 49.05 percent of babies were exclusively breastfed by mothers, compared with 52.4 percent in 2007.

In recent years, the data of breastfeeding rate in different regions of China show that the situation of breastfeeding is different in different regions, provinces and cities. In 2010, a survey was conducted in some secondary and tertiary hospitals in Shanghai, among which 24.8% of women were exclusively breastfed. In 2012, the rate of exclusive breastfeeding among 260 newborns in Feicheng City People's Hospital of Shandong was 76.2%. In the same year, a survey of Longhua Community in Shanghai found that the rate of exclusive breastfeeding was 41.9%. Li Yunfang et al. investigated the feeding methods of four baby-friendly hospitals in Weinan City, and found that the rate of exclusive breastfeeding was 48.7%. In 2012, a study selected five regions in North China, East China, Northwest China, Southwest China and Northeast China, including Tongliao City of Inner Mongolia, Changzhou City of Jiangsu Province, Ningxia City of Gansu

Province, Bijie District of Guizhou Province and Harbin City of Heilongjiang Province. The results showed that the average rate of exclusive breastfeeding in the five cities was 62.56%

A 2012 survey of breastfeeding in urban, urban and rural areas in Guangdong province found that 75.6 percent and 65.8 percent of babies aged 4 months and 6 months were breastfed, respectively

According to a 2012 survey of breastfeeding in Hong Kong, a 2013 survey of nine counties and cities in Zhejiang province found that the rate of exclusive breastfeeding was 30.3%. In 2014, a survey was conducted on the feeding patterns of women in Nanhu Community of Changchun City, and the rate of exclusive breastfeeding in the area was 50.8%.

A 2016 survey in Shenzhen found that the exclusive breastfeeding rate within six months was 61.2%.

A 2015 survey of breastfeeding in Beijing found that 51.6% of infants within four months were exclusively breastfed. A 2017 survey in Shenzhen found that 61.2 percent of babies within six months were exclusively breastfed. Breastfeeding varies, though. The Program for the Development of Children in China (2011-2020) set the goal of "50 percent or more exclusive breastfeeding for infants aged 0-6 months" in 2011.

3. THE INFLUENCING FACTORS OF BREASTFEEDING

At present, China's exclusive breastfeeding rate is very low, 28.1% of the people think it is the maternal own reasons, such as the lack of milk, etc. 22.9% of the people, choose breastfeeding knowledge popularization is not enough; 20.4 percent attributed it to poor feeding conditions.

Many people have misconceptions about breastfeeding, thinking that as long as you give your baby breast milk is breastfeeding, in fact, this is not comprehensive. The World Health Organization recommends optimal breastfeeding: all babies should be breastfed within one hour of birth and

exclusively breastfed for six months without water or any other liquid or solid food. Nutritionally adequate and safe complementary foods are started after six months, while breastfeeding continues until two years of age or beyond., of course, this is the most ideal way of feeding, and in fact in addition to some social factors, many mothers breastfeeding is a lack of enough knowledge of science, including breast milk secretion regularity, neonatal physical characteristics and methods of promoting lactation, and insufficient understanding of the benefits and the importance of breastfeeding, this also is they don't stick to breastfeeding. This, coupled with the influence of older or traditional child-rearing attitudes, creates more barriers for mothers to breastfeed. Many mothers think it's good to give formula to their children. If there is a temporary shortage of milk, do not give up easily. Mixed feeding can be carried out first, and then by increasing the number of sucking, breastfeeding mothers can reasonably replenish water (6-8 glasses of water a day) to promote milk secretion, so as to ensure a good supply of milk and achieve the ultimate exclusive breastfeeding.

IV. PROGRESS IN BREASTFEEDING IN CHINA

4, New progress has been made in breastfeeding in China. In recent years, with the development of the economy and the overall improvement of the national education level, the country has paid more and more attention to breastfeeding. With the establishment of the China Breastfeeding Action Alliance, China has set May 20 as the National Breastfeeding Publicity Day every year. In 2013, the first breast milk bank in the mainland of China was established in Guangzhou. In January 2017, Yili Group and 10 major domestic hospitals including Peking Union Medical College Hospital jointly promoted the establishment of a standardized and standardized Chinese breast milk bank. In August 2017, the National

Breastfeeding New Progress Training Course was successfully held in Jinan Women. In April 2019, the "International Conference on Breastfeeding New Progress and Cases in China" was successfully held. In August 2020, the Chinese Nutrition Society issued the "Standards for the Establishment and Management of Human Milk Banks in Medical Institutions". Although there is a long way to go to improve breastfeeding rates, national and social efforts are being made to improve breastfeeding. From the perspective of policy, both the Outline of China's Child Development (2011-2020), the National Nutrition Plan (2017-2030) and the Action Plan for Healthy Children (2018-2020) have clearly stated that the breastfeeding rate of 0-6 months babies in China should reach more than 50% by 2020. Actively, China has created more than 7,300 baby-friendly hospitals to better publicize the benefits of breast-feeding, teach breastfeeding skills, and help women build their confidence in breast-feeding. In addition, maternal and child facilities are also actively supporting. Taking Beijing as an example, by August 2018, more than 4,000 maternal and child facilities had been established in public places such as airports and large railway stations, as well as in enterprises and institutions.

5. THE SUMMARY

It is not difficult to see from the data and reports of various studies on breast milk at home and abroad that breastfeeding in China still needs to continue efforts, which should rely on the joint efforts of the whole society, such as constantly improving public breastfeeding facilities, giving scientific guidance and more psychological care to breastfeeding mothers, and popularizing more breastfeeding knowledge. It is believed that through a series of corresponding measures, we will continue to promote the improvement of the current situation of breastfeeding in China, improve the breastfeeding rate, and lay a solid foundation for the healthy growth of the next generation.

PRACTICING PHYSICIANS

„COVID-19 PNEUMONIA: THE FIRST CASE OF SUCCESSFUL TREATMENT OF A CRITICAL ILL NEWBORN AFTER CESAREAN SECTION“

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ABSTRACT:

In the XXI century a great attention should be devoted to the problems of global heating, resulting in natural calamities and spread of different diseases. Therefore, measures against expected epidemic should be taken.

Science and security must be determined together with social-economic and ecological environment. Together with each of these two factors science may have both positive and negative sides. Thus, in my opinion, science of the XXI century should serve the mankind at high level of urbanization, safety of each citizen of this country and carry on preventive measurements against possible negative influence. Introduction of high technologies in investigations, existence of precise medical statistical database, creation of modern computer programs and their usage (prognosis of disease course, establishment of risk factors and groups, etc) – that is all on the basis of which it will be possible to solve many problems existing in the XXI century.

Keyword: *Pediatrics, Security, Disease, Preventive measurements Children's rights.*

CORRESPONDENCE

We report about a 5 day old newborn with critically pneumonia SARS-CoV-2 after cesarean section infect-

ed by a family cluster infection. A male newborn was admitted 22 days after delivery due to "intermittent fever for 17 days". That means that on

the fifth day after delivery, due to Cesarean section, the newborn began to fever. In short, history of pregnancy and delivery modus was G1P1, 22 days ago (31 jan 2020). The newborn was delivered in 38 + 5 weeks gestation by c-section. Amniotic fluid, umbilical cord and placenta was normal, APGAR score at 1,5 and 10 minutes normal. 18 days ago (04 feb 2020) the child developed fever with a peak of 38.0°C. The child showed choking cough, had no running nose, no vomiting, no diarrhoea, any convulsions or skin rashes.

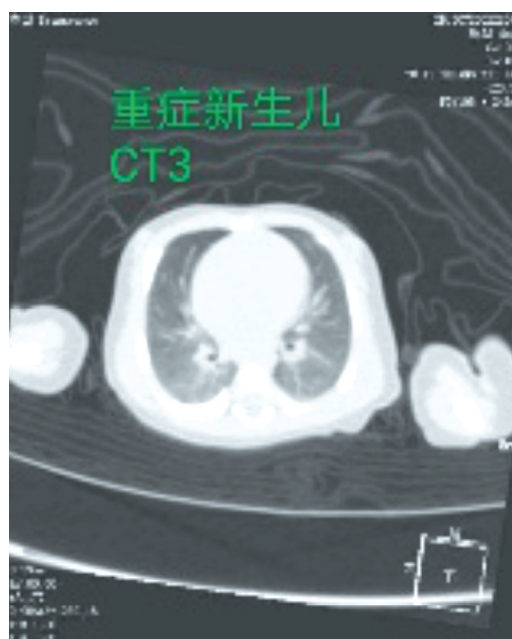
17 days ago, on 02 of February 2020, the fever in outpatient clinic in Xinyang Center Hospital processed. A swab test for SARS-CoV-2 virus nucleic acid testing was positive. 15 days ago, on 6th of february 2020, fever was present once up to 37.7°C. 17 days before the child see a doctor in the center of the Xinyang Hospital. The medical treatment was based on

ribavirin, cephalosporin, immunoglobulin (2.5 g, application 5 days), albumin (3 g, application of 3 days), atomization interferon, Lopinavir/Ritonavir (0.5 ml /per time, all 12h). Under these medication the child had temperature fluctuations with highest temperature of 37.5°C, discontinuous, when administering oxygen inhalation through nasal catheter oxygen intolerance. The child had no failure to thrive, but had choking cough. For further treatment, with a diagnosis of "COVID-19" the newborn was admitted to our hospital from emergency ambulance. In this moment of admittance, the child's mental reaction was poor, but sleep was normal, the newborn showed normal stool and normal urine.

The parents had been living in Wuhan City, before the baby was born. On January 22, the parents of the baby returned to Xinyang City from Wuhan. In the afternoon of that day, the mother felt cold and drowsy. The father and grandfather of the child were diagnosed with COVID-19 on April 4th. The baby's grandmother was diagnosed on February 25. Physical examination showed full month appearance, weight of 3600g, body temperature was 36.5°C, pulse rate 172 times/min, respiration rate of 40 times/min. The blood pressure was initially measured by 74/36mm Hg, height was 51cm. There was no malformation in the skull, the anterior fontanelle was 2.5cm × 2.5cm, the posterior fontanelle was closed, flat and soft, and the tension was normal. Bilateral pupil showed isocorie, the reflex to light existed. The breath was smooth under oxygen inhalation by nasal catheter was performed. No expiratory dyspnoea was found. The three concave signs were negative.

The breath sounds in both lungs were rough. Heart rhythm was uniform, heart sounds were strong, no murmur was heard, abdomen was soft, umbilical cord did not fall off,

liver reached 1.5cm below right costal, soft, spleen was not reached, bowel sounds were normal. The extremities were warm at the end, with free movement, normal muscle tone, and primitive reflexes. Laboratory blood routine examination showed leukocyte $12.95 \times 10^9/L$, erythrocyte $3.07 \times 10^{12}/L$, hemoglobin 101 g/L, platelet $356 \times 10^9/L$, lymphocyte percentage 49.5 %, c-reactive protein



Ground glass opacity in a newborn infected with COVID-19

quantitative determination <0.5 mg/L. Liver and kidney function, myocardial enzymes, electrolytes: total bilirubin 13.7 umol/L, conjugated bilirubin 2.7 umol/L, unconjugated bilirubin 11.0 umol/L, alanine transaminase 46.7 U/L, glutamate transaminase 37.8 U/L, creatine kinase isoenzyme 48.3 U/L, potassium 6.75 mmol/L.

Computertomography showed local thickening of double lung texture, small patch density increased shadows. A fuzzy edge was found. Chest CT reviewed on March 1 showed, that the lung film was more clearly absorbed than before. After admission, the child was placed in the isolation ward for treatment and have been given a warm box insulation. The newborn had nasal catheter application of oxygen, interferon injection by oral cavity and amproxole at the same time. The heart rate

was closely monitored. Respiration, blood pressure, electrolyte were also closely monitored. Furosemide was given as diuretic, cefoperazone was given. Sedation, heart strengthening, diuretic, fluid limitation, circulation improvements were initiated. IN the next days, the child's body temperature was normal, no cough, no dyspnea, good nursing, normal defecation and urination. Further two time nucleic acid tests were negative and the condition of the newborn was significantly improved. They were followed up for two weeks after discharge. Finally, the baby recovered normal, and the spirit and aspect was finally very good. No rise of temperature of fever was found in course.

In conclusion, because of the family gathering, the clinical diagnosis and treatment characteristics of a new coronary pneumonia combined with psychological exhaustion caused by non-mother-to-child transmission after cesarean section were analyzed. It is a description of a case of neonatal severe coronavirus pneumonia 5 days after cesarean section in Children's Hospital affiliated to Zhengzhou University. As a result the neonate lived for 5 days with febrile COVID-19 infection. However, the children turned into micro-severe, coronavirus pneumonia, combined with psychological failure, after rescue treatment, accounting and testing twice negative at discharge. Cesarean section and family members infection easy caused neonatal critical pneumonia, and this should strengthen the diagnosis and treatment. This case shows impressingly the course of a COVID-19 infected neonate due to cluster infection of the whole family.

Picture 1: Computertomography of the lungs in newborn with COVID-19 infection

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MULTICENTER CLINICAL STUDY OF 156 CHILDREN WITH KAWASAKI DISEASE DURING COVID-19

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ABSTRACT

Objective: To explore the differences and connections between 156 children with Kawasaki disease (KD) from 6 sub-centers during the outbreak and the 48 patients with KD reported during the epidemic period in relevant countries. **Methods:** Retrospectively analyzed the relationship between the clinical manifestations and laboratory examinations of children with KD who were hospitalized after the outbreak and children with KD reported in other countries during the outbreak. **Results:** There are many cases of KD in children in China, of which 83.6% are complete and 16.4% are incomplete, but they are not SARS-CoV-2 infections. This is different from the KD children recently discovered in European and American countries, but the clinical manifestations are similar. The inflammatory index of patients with KD-like symptoms reported in the literature is much higher than that of normal KD patients. Among them, the proportion of patients with CRP>200mg/L is as high as 46%; secondly, combined with diagnostic criteria, we found that typical KD patients have PLT is higher than normal, but the PLT levels of patients with KD-like symptoms that we have counted in the literature are mostly within the normal range.

Conclusion: the etiology of Kawasaki disease is unclear, but the relationship between the new crown and Kawasaki needs further study. Due to the characteristics of immunity, children are prone to infection and develop multisystem inflammatory syndrome in children (MIS-C) and KD-like manifestations. Therefore, timely diagnosis and correct treatment should be made to reduce the damage of coronary artery.

Key word: *Kawasaki disease; COVID-19; MIS-C;*

1. BACKGROUND:

A novel coronavirus pneumonia (COVID-19) outbreak in Wuhan in mid December 2019, which caused by the infection of a new coronavirus—severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2). The WHO announced that COVID-19 was a public health emergencies of international concern in January 30, 2020. Then, it quickly spread around the world and was accepted as a pandemic on March 11, 2020 [1]. As of June 11, 2020, more than 7.3 million people worldwide have been diagnosed with COVID-19. COVID-19 epidemiology shows that the population is generally susceptible, but the proportion of children affected seems to be much smaller than that of adults, and only 2% of cases are described as patients under 20 years old [2]. The epidemiology report describes novel coronavirus pneumonia cases diagnosed in children, and more than 90%

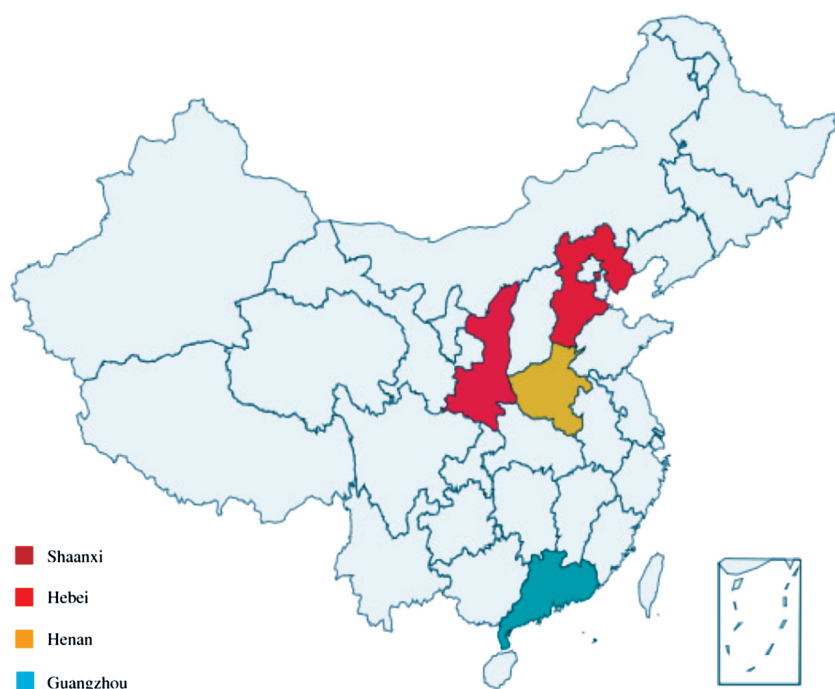


Table 1

than three years [8]. The French health minister reported that about 15 children had KD symptoms in hospitals in Paris [8]., The New York City Department of Health issued a health alert on May 4, 2020, describing 15 cases of multisystem inflammatory syndrome characterized of KD or toxic shock syndrome (TSS) [9]. New York said it was investigating 85 cases of "multisystem inflammatory syndrome in children associated with COVID-19" [10]. Shelley rifagan said they noticed that eight children had unprecedented high inflammatory shock, similar to atypical Kawasaki disease, Kawasaki shock syndrome or toxic shock syndrome in 10 days from mid April 2020. Among them, two children tested positive for SARS-CoV-2. And they support that such children should receive early attention from the community and be given priority early recognition of the disease [7]. The US Centers for Disease Control and Prevention published an official name on May 14, 2020, calling the disease " multisystem inflammatory syndrome in children (MIS-C)" [11].

2. MATERIALS AND RESEARCH METHODS:

2.1 Methods:

Since the outbreak of novel coronavirus pneumonia in Wuhan in mid December 2019, we have jointly conducted 4 centers to investigate the diagnosis and treatment of KD children, including Shaanxi, Henan, Hebei and Guangzhou. 156 cases of KD were diagnosed and treated, including 95 boys and 61 girls, with a male to female ratio about 1.6: 1. Among them, children aged 1-5 years were the main, followed by infants ≤ 1 year old, and children aged 11-18 years were the least.

Inclusion criteria: Fever persisting ≥ 5 days, plus at least four out of five of the following principal features

Bilateral bulbar conjunctival congestion;

② Hyperemia of oral cavity and pharyngeal mucosa (lip redness, lip chapped, bayberry tongue);

③ Pleomorphic rash;

of them are asymptomatic, mild or moderate [3].

In the past few weeks, there have been significant clusters of KD-like symptoms in children in the United Kingdom, the United States and Italy, with similar test results reported, and some of these children have confirmed SARS-CoV2 infection by RT-PCR. Kawasaki disease (KD), also known as mucocutaneous lymph node syndrome, is an acute febrile disease in children with systemic vasculitis as the main pathological change. It is commonly seen in children under 5 years old, and usually manifested as fever, rash, diffuse mucosal inflammation, non exudative conjunctivitis, cervical lymph node lesions and limb changes [4]. The disease causes inflammatory changes in the walls of small and medium-sized arteries in any part of the body. However, coronary artery is mainly involved. In untreated KD children, up to 25% may have coronary artery disease, which leads to serious complications, such as coronary artery dilatation, coronary aneurysm and acute myocardial infarction [5].

KD is a disease with unclear etiology. At present, it has been reported that KD is related to infection and immune-mediated, which mainly in-

vades coronary artery, and is related to susceptible genes. A study in 2014 showed that HCoV-229E may be a possible pathogen of Kawasaki disease [6]. Epidemiology shows that the incidence of typical KD is higher in Asian children. However, more than 50% of children with KD-like syndrome reported during the outbreak were African Caribbean [7]. It is stipulated that all hospitalized children should undergo nucleic acid test. Therefore, all hospitalized KD children have been tested for COVID-19. 156 of our KD children are not infected with COVID-19. All the nucleic acid tests are negative. KD or KD-like symptoms have not been observed in pediatric patients since the outbreak of new crown pneumonia in China, which has increased the possibility of racial background and genetic susceptibility.

In an article published in the Lancet on May 7, 2020, eight critically ill children characterized of severe inflammation were described in detail. However, not all children have confirmed the infection or exposure to COVID-19 [7]. In Bergamo, Italy, 20 children were diagnosed with KD, roughly equivalent to the total number of cases in the region for more

Table 2

		Initial diagnosis	return visit
Gender	male	38 (23.4%)	57 (36.5%)
	female	28 (17.9%)	33 (22.2%)
Age	≤1 year	26 (16.7%)	35 (22.4%)
	1-5 years	27 (17.3%)	47 (30.1%)
	6-10 years	9 (5.7%)	7 (4.5%)
	11-18 years	4 (2.6%)	1 (0.7%)
Extent of coronary artery damage	normal	32 (20.5%)	57 (36.5%)
	Coronary artery dilatation	32 (20.5%)	20 (12.8%)
	aneurysm	2 (1.3%)	3 (8.4%)
Hemoglobin (HGB) /g/L	<60	8 (5.1%)	6 (3.8%)
	60~90	12 (7.7%)	16 (10.3%)
	90~120	31 (19.9%)	50 (32.1%)
	>120	15 (9.6%)	18 (11.5%)
Platelet (PLT) × 10 ⁹ /L	≤100	2 (1.3%)	3 (3.8%)
	100~300	20 (12.8%)	31 (19.9%)
	≥300	44 (28.2%)	53 (34.0%)
		Within 3cases≥800 2cases≥1100	
C-reactive protein (CRP) /mg/L	normal	24 (15.4%)	57 (36.6%)
	>30	8 (5.1%)	17 (10.9%)
	>60	18 (11.5%)	8 (5.1%)
	>100	5 (3.2%)	2 (1.3%)
	>120	11 (7.1%)	6 (3.8%)
	One of them was up to 297		
Erythrocyte sedimentation rate (ESR)/mm/h	normal	4 (2.6%)	54 (34.6%)
	>30	12 (7.7%)	9 (5.8%)
	>60	24 (15.4%)	13 (8.3%)
	>100	19 (12.2%)	8 (5.1%)
	>120	7 (4.5%)	6 (3.8%)
Follow up months	≥1 month	-	39 (43.3%)
	≥3 months	-	24 (26.7%)
	≥6 months	-	15 (16.7%)
	≥1year	-	13 (13.3%)
			One of them was followed up for 7 years
Treatment effect	recovery	22 (14.1%)	54 (35.3%)
	better	42 (26.9%)	36 (23.1%)
	death	0 (0%)	1 (0.6%)
			The child died after strenuous exercise and was not infected with SARS-CoV-2

④ Changes in extremities, including erythema and edema in palmoplantar and finger-end (toe-end) in acute stage and membranous desquamation of the transitional area of the nail bed of the finger(toe) in the convalescent stage;

⑤ Acute non suppurative lymphadenopathy of neck.

Exclusion criteria:

① Congenital heart disease

② Viral myocarditis

③ Rheumatic carditis and other connective tissue diseases

④ Hematological diseases (leukemia, etc.)

⑤ Incomplete data and incorrect diagnosis

Patients with Kawasaki like symptoms were defined according to the American Heart Association's 2017 criteria, including classic (≥ 5 days of fever plus 4 or more clinical criteria, including bilateral bulbar non exudative conjunctivitis, lip or oral changes, non suppurative cervical lymph node lesions, pleomorphic rash, erythema on the palms and soles of the feet, hand foot induration, or both) and incomplete types. For the incomplete type (≥ 5 days of fever plus the above two or three clinical criteria), the value of erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), or both, can be used as an indicator, also including anemia, thrombocytosis after 7 days of fever, hypoproteinemia, hypertransaminaemia, leukocytosis, aseptic pyuria, or showing coronary hemangioma or cardiac insufficiency by echocardiography (left ventricular dysfunction, mitosis) related additional diagnostic criteria [12].

According to the following criteria [13]: Dilation: diameter ≥ 2.5SD; small aneurysms: localized dilation with internal diameter ≤ 4 mm (5-year-old children: the inner diameter of one segment is 1.5 times of the adjacent segment) Z score ≥ 2.5 to < 5; medium aneurysm: aneurysm diameter > 4 mm and < 8 mm (children ≥ 5 years: segment diameter is 1.5-4 times of adjacent segment) Z score ≥ 5< 10; giant aneurysm: display inner diameter of 8 The Z-score of aneurysms

(children ≥ 5 years old: the inner diameter of one segment is more than 4 times that of adjacent segments) was ≥ 10 mm. According to the results of echocardiography, KD children were divided into three groups: normal group, coronary artery dilation group and coronary artery aneurysm group.

2.2.Research methods:

Retrospectively analyzed the relationship between the clinical manifestations

and laboratory examinations of children with KD who were hospitalized after the outbreak and children with KD reported in other countries during the outbreak.

We summarized the information of KD patients during the epidemic period and drew a table.

In the three groups of coronary artery damage, the initial diagnosis and return visit were not the same, the difference was statistically significant. After further comparison, it was found

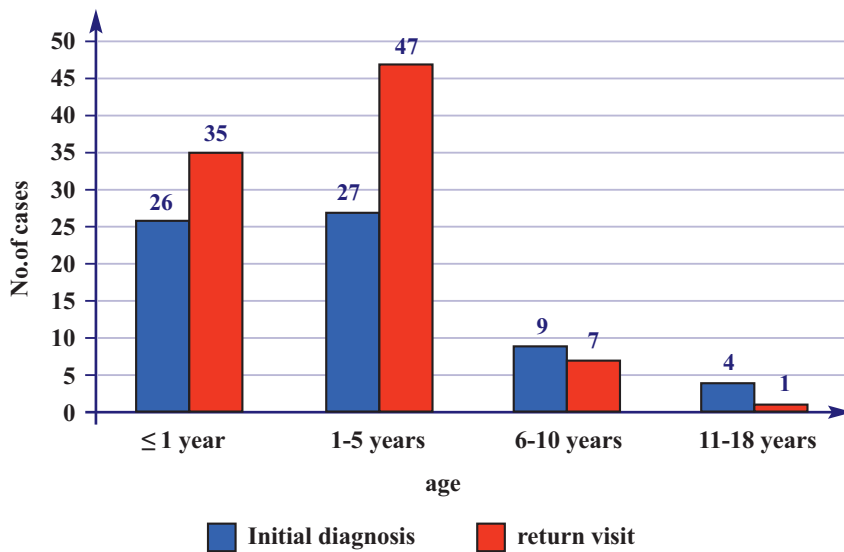


Table 3

posterior wall of the nasopharynx cavity. It will stay for a moment and then slowly rotate to exit. Take another polypropylene fiber swab and collect the other nostril in the same way. The two swabs were immersed in the same tube containing 3ml virus preservation solution, the tail was discarded, and the tube cover was tightened

The diagnosis and treatment of children with fever in China is divided into the following steps:

(1) Sub examination: all the children need to be examined by professional nurses, which can be divided into two categories: those without fever can go to the general outpatient department; those with fever should go to the fever clinic;

(2) Follow up patients: because KD children need regular review of cardiac ultrasound, but the hospital takes prevention and control measures during the epidemic, so these patients who need to be reexamined need to use:

- ① Online booking;
- ② The patients were treated in the local hospital nearby;
- ③ Video remote consultation;
- ④ Online outpatient appointment;
- ⑤ Hospitalized in non designated hospitals.

According to the above triage method, KD patients were diagnosed and treated in time, and the cure rate was greatly improved. There was no delay in the treatment of KD children because of the epidemic situation. Therefore, during the epidemic period, we should also develop a reasonable program for the treatment of non covid-19 children, so as not to delay the best treatment time.

1. There was no significant difference in gender of KD children between China and other countries.

2. There was significant difference in age groups between China and other countries. After further comparison, it was found that the number of KD children under 5 years old in China was the most, while that of other countries was over 6 years old, and the difference was statistically significant.

3. There was significant difference in CRP count between Chinese and other countries. After further comparison,

that the difference was statistically significant ($P = 0.003$) between the children of normal and coronary artery dilatation ($P = 0.003$), and the return visit of coronary artery dilatation was reduced; but there was no significant difference between the children of normal and aneurysm, coronary artery dilatation and aneurysm ($P > 0.0167$). It showed that most of the coronary arteries were normal in the initial diagnosis and return visit cases, and most of the cases were normal in the return visit, with significant difference, indicating that most of these children recovered after early treatment. It is suggested that the scheme of early treatment and the application of drugs are correct. The follow-up and treatment should be strengthened before return visit.

In this special case, children with fever need to go through layers of screening to exclude covid-19. In China, we have two kinds of nucleic acid test methods, real-time fluorescent RT-PCR and gene sequencing, but most of us use the former method. Real time fluorescent RT-PCR is real-time fluorescent reverse transcription polymerase chain reaction. It reverses the extracted viral genomic RNA into complementary DNA (cDNA) firstly. Then, the specific primers were used to amplify the nucleic acid sequence of the pathogen using cDNA as template. Because the fluorescent dye can be integrated into the product synchro-

nously during the amplification process, researchers can detect the intensity of the fluorescence signal in real time. The most widely used gene sequencing is called Next generation sequencing (NGS). We are more familiar with this technology is Non-invasive Prenatal Testing (NIPT). In the diagnosis of new coronavirus, NGS technology makes the viral RNA into a DNA library that can be recognized and analyzed by the sequencer, and then simultaneously tests millions of nucleic acid sequences on the sequencer. Real time fluorescent RT-PCR needs to be carried out in P2 level laboratory, and three-level protection should be implemented in operator area. The samples were mainly collected from respiratory tract because of its high positive rate. The sample types include throat swab, nasopharynx swab and sputum. It were collected according to the Laboratory Guidelines for Novel Coronavirus Pneumonia issued by National Health Commission. For pharyngeal swab collection, two plastic rod swabs with polypropylene fiber heads were used to wipe the posterior pharyngeal wall at the same time. The swab head was immersed into a tube containing 3ml virus preservation solution. The tail was discarded and the tube cover was tightened. For nasopharyngeal swab collection, a plastic rod swab with a polypropylene fiber head should be inserted into the

it was found that the number of CRP count of children with KD in China was significantly different between the two groups of ≤ 100 , >100 and ≥ 22 . It was most in the two groups of ≤ 100 in China, while that in other countries was most in the two groups of > 100 .

4. There was significant difference in platelet count between Chinese and other countries. Further comparison showed that the differences among the groups were statistically significant. The number of platelet count of KD children in China was the most in ≥ 300 group, while that in other countries was in 100-300 group.

3. RESULTS:

① KD in China is lighter than that in foreign countries

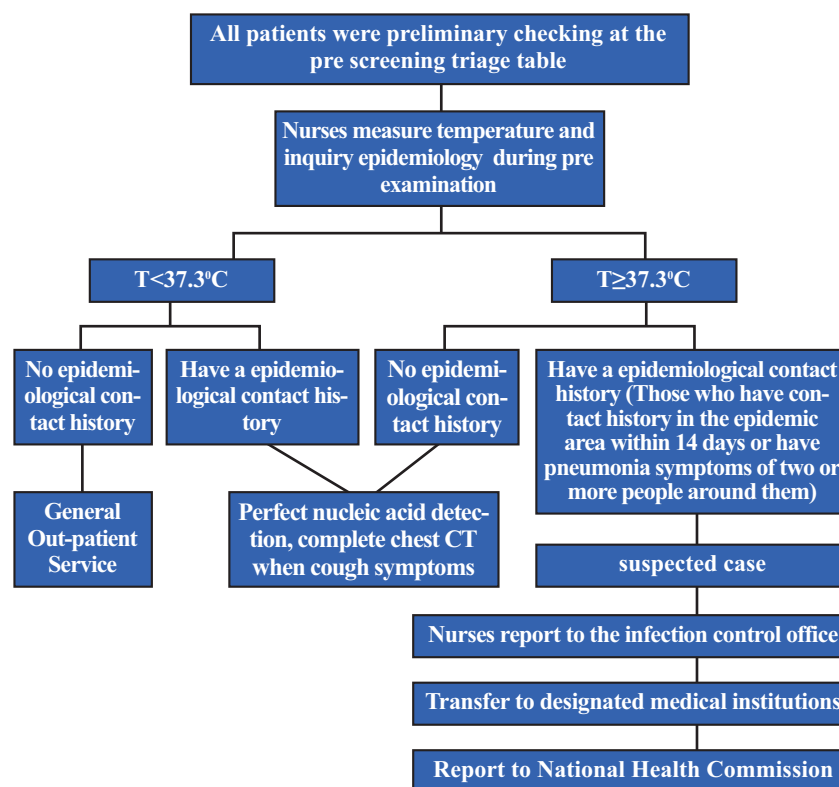
② Most of KD nucleic acids in China were negative

③ The PLT of KD in foreign countries did not increase or decrease, while that of KD in China increased

④ WBC and CRP increased in KD laboratories both in China and other countries.

⑤ The D-dimer of KD in foreign countries was significantly high, which can be up to 4000 in certain child

We compared the KD patients treated during the epidemic period with 48 KD patients reported by relevant countries during the epidemic period. The study found that the inflammatory indexes of patients with KD-like symptoms reported in the literature were much higher than those of normal KD patients, and the proportion of patients with CRP $> 200\text{mg/L}$ was as high as 46%. Secondly, combined with the diagnostic criteria, we found that the PLT of typical KD patients was higher than normal (The PLT of 2 cases were more than $1100 \times 10^9/\text{L}$; 44 were more than $300 \times 10^9/\text{L}$ accounting for 28.2%. The return visit patient were 53 cases (34%).), but most of the PLT levels of patients with KD-like symptoms in the literature were within the normal range. And the PLT of KD children in China is higher than normal level, which reported in Britain, France and Italy were mostly at or below the normal level. $P < 0.05$, comparing with KD children in China, there was significant



difference. Besides, there were significant differences among the three degrees of coronary artery damage. The cases of coronary artery dilatation and the normal accounted for 20.5% in the initial diagnosis group, while that of the aneurysm were only 1.3%. In the return visit group, 36.5% were normal, 12.8% were coronary dilation, and 8.4% were aneurysms. It is suggested that most of the children with coronary artery dilatation or aneurysms in the follow-up group were recovered after effective treatment.

4. DISCUSSION:

Since Mr. Tomisaku Kawasaki proposed KD, scholars have been committed to exploring the etiology of KD. However, the etiology of KD is still unclear. Many scholars believe that KD is related to infection. Therefore, early diagnosis and treatment should be given to children with KD during the epidemic period, so as to reduce the damage to the heart as much as possible. We should strengthen the follow-up and correct treatment. The coronary artery damage of most patients recovered after 6-18 months. However, the

giant aneurysm can just recover gradually after 2-3 years. In this study, a 12-year-old boy with a giant coronary aneurysm died suddenly after strenuous exercise two years later.

According to the severity of the disease, MIS-C is a multisystem inflammatory reaction, so the children were most with severe condition, multiple organs damage, and whose laboratory inflammatory index increased significantly. More and more children with MIS-C have been reported worldwide since late April 2020. Besides persistent fever, diarrhea and various degrees of rash, conjunctivitis and limb edema, there are also shock and myocardial dysfunction [7]. Both MIS-C and KD are characterized by fever, skin changes and coronary artery involvement. The similarity of the two diseases poses a new challenge to the diagnosis and treatment of KD children during the epidemic. None of the KD patients in our four centers during the outbreak were COVID-19 patients, which was different from the KD like symptoms of children infected with SARS-CoV-2 reported by other countries. A significant feature of KD is high and persist-

Table 5

		China	Other countries	%/ Fisher's exact test	p value
Gender	male	95 (60.9%)	30 (62.5%)	0.040	0.842
	female	61 (39.1%)	18 (37.5%)		
Age (y)	≤1	61 (39.1%)	6 (12.5%)	41.931	<0.05
	1-5	74 (47.4%)	13 (27.1%)		
	6-10	16 (10.3%)	17 (35.4%)		
	11-18	5 (3.2%)	12 (25%)		
C-reactive protein (CRP)/mg/L	normal	81 (51.9%)	6 (12.5%)	87.269	<0.05
	>30	51 (32.7%)	7 (14.6%)		
	>100	23 (14.7%)	13 (27.1%)		
	>200	1 (0.7%)	22 (45.8%)		
Platelet (PLT)×10 ⁹ /L	≤100	5 (3.2%)	13 (27.1%)	44.790	<0.05
	100-300	53 (34%)	28 (58.3%)		
	≥300	98 (62.8%)	7 (14.6%)		

ent fever, and poor response to antipyretic drugs. Most children recover completely after a few weeks, but early treatment is necessary to prevent possible complications. A serious complication is coronary artery aneurysm, whose rupture can lead to thrombosis and myocardial infarction [14]. Moreover, it has been found that the aggravation of endothelial inflammation and injury / function after SARS-CoV-2 infection may be realized through endothelial ACE2. Systemic inflammatory response to pneumonia may enhance the inflammatory response in coronary artery lesions, leading to endothelial dysfunction [15], so this may be an important reason for KD-like symptoms in COVID-19 patients. The results of this study found that the levels of inflammatory markers similar to those of KD patients reported by other countries were significantly higher than normal, and PLT levels were mostly within the normal range, which was different from the laboratory results of typical KD children. It may reflect the particularly strong immune response to SARS-CoV-2 [16].

The emergence of KD patients with positive SARS-CoV-2 test poses a new challenge to pediatricians and their parents. During the epidemic period, due to the inability to go out and fear of the hospital, KD patients were misdiagnosed, missed diagnosis and failed to get timely treatment. In addition, new requirements were put forward for the detection of SARS-CoV-2. In this case, the detection of SARS-

CoV-2 has more important meaning for KD patients. Therefore, we should early identify the presence of KD-like patients, give active treatment in order to reduce the incidence of coronary artery aneurysm, and improve the cure rate.

The sample size of this study is small, so more epidemiological and clinical data are needed to measure the prevalence of this condition, to assess the correlation between KD and SARS-CoV-2, and to determine whether KD-like syndrome in other countries is a unique clinical syndrome or a form of Kawasaki disease.

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CHINESE PEDIATRIC EXPERT CONSENSUS ON THE USE OF INTRAVENOUS IMMUNOGLOBULIN IN KAWASAKI DISEASE

ABSTRACT

Shaanxi Provincial Diagnosis and Treatment Center of Kawasaki Disease Clinical Research Center for Pediatric Medicine Diseases of Shaanxi Province The Children's Hospital of SPPH

Chinese Journal of Contemporary Pediatrics

Expert Committee of Advanced Training for Pediatrician, China Maternal and Children's Health Association

General Pediatrician Group, Society of Pediatrician, Chinese Doctor

ASSOCIATION ABSTRACT

Kawasaki disease is an acute, self-limited arteritis that mainly occurs in children under 5 years of age. Intravenous immunoglobulin (IVIG) has become an effective treatment regimen, which can effectively reduce the incidence of cardiovascular complications. However, the recent consensus or clinical guidelines for the application of IVIG in Kawasaki disease. This consensus was

formulated on the basis of domestic and international research progress on Kawasaki disease in children, and specific suggestions were provided on the clinical application strategy of IVIG in childhood Kawasaki disease as a first-line treatment drug and the prevention and treatment of adverse reactions.

Keyword: *Kawasaki disease (KD); Self-limited Vasculitis; Intravenous immunoglobulin*

**(IVIG); Expert consensus;
Children correspond author:
FUYONG JIAO**

INFORMATION

GEORGIAN PEDIATRICS IS 100 YEARS OLD

“THE ROLE OF THE SOCIAL PEDIATRICS PROTECTION FUND IN GEORGIAN PEDIATRICS - 1998-2021“

G. CHAKHUNASHVILI,
MD.PhD.D.Sc. Professor, Academician
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THE SOCIAL PEDIATRIC PROTECTION FUND

Date of Foundation: 30.09.1998

Date and Number Of Registration: #147 9.10. 1998w

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Job of Contact: Chairman of The Board

Branches of Fund: Mtskheta; Kutaisi; Gori.; Abasha.; Batumi.; Sagarejo; Gurjaani; Telavi; Tchiatura; Zugdidi; Territory of Operation: Georgia (eu)

Aim Social Pediatric Protection Fund is to execute programs of social pediatric development and maintain rights and healthcare of Children, Mothers and Adolescents. Fund has great organizational experience, technical equipment and skilled members. Most of the members are Professors at TSMU, who have clinical and educational experience of 15-20 years and were one of the first, Before the independence, to read lectures about congenital infections, sexually transmitted diseases and prevention of HIV. Fund is also coopera-

ting with physicians, psychologists, Lawyer (who operate in field of social assistance) and Public figures. By the joint forces of all the people above said SPPF is able to hold free medical examinations, juridical consultations, charity events, informational lectures about healthy way of life, congenital infection, HIV, Social subjects and etc.

Since 1997 more than 93.000 Children and Hundreds of older people have been medically for free in the framework of charity events.

Before Independence, The active members of SPPF and their consortium in 1980-1990 examined above 124 000 Children, all over Georgia.

ACTIVITIES

From 1992 to 1998 was periodically holding humanitarian examinations. From 1998 with the help of Social Pediatrics Protection Fund started charity activities, in

which Georgian pediatricists were participating. Activities included: Instrumental and laboratory research of patients in different regions of Georgia, Medical gifts, several funded emergency operations.

07.01.98 – 07.02.99 Tbilisi, - over 9200 children were examined.

23-24.01.99 East Georgia, - over 3500 children were examined.

12-13-14.02.99 Tbilisi, - over 100 children were examined and gifted medicines. Free consultations by professors were held by Mother and Child Diagnostic Centre and other hospitals once a week, consultations in leading pediatric clinics of the city once in a month. In these activities were also participating: 1. Institute of skin and vein 2. Scientific Institute of Parasitology and others.

12-13-14.03.99 expedition in Poti and Abasha (Qedisi, Marani and other), - 950 children were examined and gifted medicines.

29-30. 01-07.08.99 – 4400 children were examined and gifted medicines.

23-24-25.08.99 Khobi and Zugdidi, - Free instrumental and laboratory examinations were funded. Also medicines against louse and itch were given.

04.04.99 - Expedition in Pasaunauri – over 400 children were examined.

07.05.99 – Expedition in Lanchkhuti – Free instrumental and laboratory examinations were held and medicines were gifted.





18.05.99 Rustavi, - 250 children were examined and gifted medicines.

22.06.99 Sagarejo, - 250 children were examined and gifted medicines.

13-14.08.99 Chokhatauri, - over 1500 children were examined.

15.08.99 Bakhmaro, - over 2000 children were examined.

16.08.99 Adjara high-mountain regions, - over 750 children were examined.

17.08.99 Tbilisi, – Examinations in Homeless children house.

16.10.99 Dusheti region, - over 200 children were examined and gifted medicines.

2000.

26.02.2000 Gori, - over 500 children were examined. Different medicines were given out.

23.03.2000 Axalgori, - 30 children were examined.

01.04.2000 Marneuli region (Werakvi), - General blood analysis, instrumental examinations – echoscopy, encephalography were done. Over 1500 children were examined.

15.04.2000 Gurjaani, - 1200 children were examined, medicines were given out.

29.04.2000 Rustavi, - 300 children were examined.

05.06.2000 – Children from Avchala colony were examined.

20-28.07.2000 – Children in Tskhneti Orphanage were examined.

21-22-23.07.2000 – Examinations in Abasha and Samtredia region.

7-8.08. 2000, Bakhmaro-Beshumi – 1925 children were examined.

2001.

15.03.2001. Children of employees of Rustavi Nitrogen Factory were examined.

23.06.2001. Children of employees of Rustavi Nitrogen Factory were examined.

14-15-16.09.2001 Baghdati region (Sairme, Witelkhevi, Rokhi, Ochba, Xani, Zegani, Saqraula) – over 2500 children were examined.

2002.

10.03.2002 Axalgori, - 250 children were examined.

20-04.2002 Signaghi, - 450 children examined.

23-24-25-26.05.2002 Khulo, - 600 children and 100 adults were examined with the help of Patriarchy.

27-28-29.06.2002 Tbilisi, - 400 children were examined in different Hospitals.

16-17-18-19.07.2002 KodorisKheoba, - 250 children were treated.

3-4-5-6.08.2000 Tusheti (Dikolo, Omalo, Shenaqo) – 200 children were treated.

2003.

05.03.2003 Samtskhe-Javakheti, - 1250 children were examined.

17.04.2003 Werovani, - 450 children were examined.

20.05.2003 Borjomi, - 870 children were examined.

25.06.2003 Mta-Tusheti, - 320 children were examined.

30.07.2003 Bakhmaro, - 630 children were examined.

20.08.2003 Zestaponi, - 210 children were examined.

07.09.2003 Racha, - 170 children were examined.

18.10.2003 Dmanisi, - 180 children were examined.

2004.

March, April, May – Kaspi, Gurjaani, Telavi, Akhmeta, Lagodekhi, Signaghi, Bodbe, Aspindza, Axaltsikhe, Borjomi, Tbilisi, Zestaponi, Kharagauli, Chiatura – over 1728 children were examined. In different regions (Zugdidi, Khulo, Khelvacharui, Qeda, Lanchkhuti, OzurgetiIngiri), SPPF held charity activities with the help of Patriarchy – over 2400 children were examined and medicines were given out.

2005.

Marneuli region – 700 children and 80 adults were examined.

18th of July, Kaspi – 450 children were examined.

8th of October, Mtskheta – 300 children were examined.

14-15-16th of October, Lentekhi – 850 children and 250 adults were examined.

2006.

18th of February – 20 Painter Union families were examined.

March – over 100 refugee children were examined.

April – Charity activities were held by ambassadors in Guria.

31th of May – 450 children were examined in Rustavi.

1-2th of June - Open door day in TSMU, 400 children were examined. They were held free consultations and laboratory examinations.

9-10th of June, Kaspi - 300 children were examined.

1th of July, Ckhinvali region – 500 children of war participants were examined. In September-October – 120 children.



In November – over 200 of Journalist's families were examined.

2007.

Marneuli – Free consultations for 100 children. Childrens with Scoliosis were shown. They got espander gifts and were recommended how to treat scoliosis.

Dusheti – 250 children were examined.

Akhalsheni–85 children were held consultations.

9-10th of June, Kaspi – 300 children were examined.

1th of July, Ckhinvali region – 500 children of war participants were examined. In September-October – 120 children.

In November – over 200 of Journalist's families were examined.

2008.

1st of June – Open door day (200 children were examined).

2nd of June – Teddy bear (300 children examined).

14th of June, Akhmeta (QaQucoba) - 450 children were examined and gifted medicines. Also examinations like echoscopy of abdominal cavity and ECG were held.

27th of June – restoration of Georgian Section.

20th of August - STOP RUS-SIA (meeting at Igoeti)

1st of September, Tbilisi – STOP RUSSIA (meeting of chain)

4th of October – free consultations and examinations. Painters and artists master classes were held.

6th of December – 110 children were examined in Bergman Clinics with echoscopy of abdominal cavity, ECG and other.

2009.

13.06.2009, Khashuri – 750 children were examined.

26.12.2009, Barisakho – 80 children were examined.

2010.

4th of July – Open door day for family members of war victims (50 children were examined).

10th of July, Karaleti – 200 children were examined and medicines were given out.

4th of November – St. King Tamar orphanage children were examined.

3-4th of December, Tbilisi– 400 sportsmen children were examined.

2011.

1st of June, Tbilisi – 200 children were examined.

24th of December, Tbilisi – 200 children were examined.

2012.

1st of June, Tbilisi – 350 children were examined.

22th of December, Tbilisi – 250 children were examined.

Since 1997 more than 93.000 Children and Hundreds of older people have been medically for free in the framework of charity events.

2013.

1-4.06.2013. Tbilisi, Batumi, Gori, Telavi – 1250 children were examined.

17-21.12.2013. Tbilisi – 350 children were examined.

2014.

1st of June, Tbilisi – 150 children were examined.

28th of December, Tbilisi – 50 children were examined.

2015.

1st of June, Tbilisi – 350 children were examined.

11.12.2015. Chkorotscu – 1300 children were examined.



2016.

3035 children were examined.

2017.

1305 children were examined.

2018.

200 children were examined.

2019.

250 children were examined.

2020.

95 children were examined.

2021.

50 children were examined.

Since 1997-2012 more than 93.000 Children and Hundreds of older people have been medically for free in the framework of charity events.

Before Independence, The active members of SPPF and their consortium in 1980-1990 examined above 124 000 Children, all over Georgia.

Till today over 228 050 children were examined and thousands of old people. Charity activities continue.

17.12.1999. Mucoviszidose treatment and diagnostics.

01.06.2000. Young Pediatricists XVIII conference.

28.02.2001. Urgent questions of Therapy of respiratory diseases in pediatrics.

01.06.2001. "Child has right to be protected since embryo".

01.06.2001. "Child, adult and family violence".

13.02.2002. "Human genome project".



10.03.2002. Akhlagori, - Presentation of toner drink "Lomisi".

06.11.2002. National Conference: Medical and social problems of people who suffer from mucoviszidose and metabolism disorder.

07.11.2002. "Contemporary aspects of inborn diseases".

04.04.2003. "Urgent pediatric questions" (IX conference).

01.06.2003. Internet conference (X conference) – Social Pediatrics Protection Fund gave out journals and magazines called "Social Pediatrics" (In which is written about social, medical, pedagogic, psychological, religious and other urgent problems).

19.12.2003. Second Georgian Cardiology Congress.

22.10.2004. "Urgent Pediatric questions" dedicated to SPPF president, Victor Moroshkin.

01.06.2004. Second National Internet Conference.

01.06.2005. Urgent Pediatric questions.

09.09.2005. Tbilisi Marriot, - Second National Conference "Healthy child & Peaceful Caucasus".

1st of June, 2006. – SPPF conference. XXIII Congress of Young Pediatricists League.

31.05.2007. III congress of Pediatric Cardiology.

07.12.2007. SPDF XVII conference.

07.10.2008. Conference – "Section of child and adult".

20.12.2008. SPPF and ESMNS second conference.

12.06.2009. SPPF XX conference.

01.06.10. Second conference of Georgian surgeons and XXII conference of Tsalka.

03.12.2010. Conference dedicated to I. Kvachadze 85th anniversary.

01.06.2011. SPPF XXVI conference.

23-24.12.2011. SPPF XXVII conference.

01.06.2012. IV congress of Pediatric Cardiology. SPPF XXVIII conference.

21-22.12.2012. SPPF XXIX conference

1-4.06.2013. SPPF XXX conference

17-21.12.2013. SPPF XXXI conference

1-2.06.2014. SPPF XXXII conference

27-28.12.2014. SPPF XXXIII conference

1-2.06.2015. SPPF XXXIV conference

11.12.2015. SPPF XXXV conference

1.06.2016. SPPF XXXVI conference

9-10.12.2016. SPPF XXXVI conference

01.06.2017. SPPF XXXVIII conference

05.12.2017. SPPF XXXIX conference

01.06.2018. SPPF XL conference

07.12.2018. SPPF XLI conference

01.06.2019. SPPF XLII conference

14.12.2019. SPPF XLIII conference

31.05.2020. SPPF XLIV conference

20.12.20. SPPF XLV conference

01.06.2021. SPPF XLVI conference

18.12.21. SPPF XLVII conference

The most important in the work of the Foundation are the creative work

SIMPOSIUMS AND CONFERENCES HELD BY THE SOCIAL PEDIATRIC PROTECTION FUND:

1992. First pediatric cardiology conference – "believe the reality of better future".

01.06.1999. II conference – "Healthy child & peaceful Caucasus".

25.12.1999. III conference – "Today's economic directions in pediatric and its perspective". XXI century Pediatrics should be the start of invalid prophylaxis.

01.06.2000. IV conference – "Child must have right to be protected since embryo".

27.03.2001. Meeting in ombudsman's office – "Under aged criminals, their rights and reality".

01.06.2001. V conference dedicated to Children Protection National Day. 32.03.1999. 01.06.2000. 01.06.2001 "Child treatment in XXI century"

23.04.1999. 01.06.2000 "Child treatment in XXI century"

"Orthopedic school"



of Professor Irakli Tsitsishvili and Professor Avtandil Kvezereli-Kopadze (Pictures-1-2-3-4-5-6-8-), whose unstinting work to the last day of his life set a perfect example for the youth - first of all, And with all things how you must work in many ways for your land

to bring up worthy descendants. Again thank you to them and to the happiness that we have had in the relationship of such true persons. God enlighten their souls.

Newspapers and magazines have been published since 1998 at the direct

initiative of the Social Pediatrics Protection Fund.

At the same time, the Social Pediatrics Protection Fund continues the path of the Hospital Pediatrics Department of TSMU (both charitable and public), whose department was headed by Great Pediatrician, Doctor of Medical Sciences, Professor Ioseb Kvachadze. Georgian Pediatrics had its own professor, Mr. Ioseb Kvachadze, who informed us of the possibilities of our intellectual potential from the high tribunes of the world's congresses many times during that closed Soviet period (believe me, it was only the bumblebee). Figure N9 shows the members of the almost unchanged department from 1981-1991.

Thus, the Social Pediatrics Protection Fund continues its creative work, and most importantly, its priority for young people to be involved in its functioning remains unresolved.



First sit on the chairs from the left: Assistant Leila Komshiashvili, Assistant Nunu Shelia, Assistant Tamar Tsereteli, Professor Irakli Tsitsishvili, Head of the Department Professor Ioseb Kvachadze, Associate Professor Kristine Kutelia, Assistant Tamaz Marinashvili, Assistant Tina Beradze, Laboratory Assistant Nana Gvarjaladze.

In the second row stand from the left: (Third) Clinical Resident Nino Lapiashvili, Assistant Jana Sakvarelidze, Assis-

tant Nutsa Tatishvili, Assistant Marine Chikovani, Clinical Resident Tsisana Giorgadze

In the third row stand from the left: (Third) Assistant Giorgi Chakhunashvili, (Fifth) Assistant Tamaz Gozalishvili, Postgraduate student Davit Telia, Assistant Nugzar Uberi, Postgraduate student Marine Giorgadze, Laboratory Assistant Lia Kvatadze, Who in Georgian pediatrics and not only in Georgia, have made a flawless contribution to the development of their directions.



The Belt The Road Five European Countries, Georgia, Mongolia, Israel Academic Exchange



European center of traditional Chinese medicine (TCM) in Prague, Czech and xi'an, China

The Belt and Road Medical Communication——Georgian



Georgian Pediatrics is 100 years old



”Children’s rights must be defended since embryo”