Medical research at the Mexican Institute of Social Security: Seven decades of work, achievements, and challenges

Moisés Mercado,¹ Javier Torres,² Fernando Guerrero-Romero,³ Mardia López-Alarcón⁴ and Héctor Mayani⁵*

¹Endocrine Diseases Medical Research Unit, Mexico City; ²Infectious and Parasitic Diseases Medical Research Unit, Mexico City; ³Biomedical Research Unit of Durango, Durango; ⁴Nutrition Medical Research Unit, Health Research Coordination, Instituto Mexicano del Seguro Social, Mexico City; ⁵Oncological Diseases Medical Research Unit, Mexico City. Health Research Coordination, Instituto Mexicano del Seguro Social, Mexico

Abstract

Since its foundation, more than 75 years ago, the Mexican Institute of Social Security (IMSS) has carried out multidisciplinary research—biomedical, clinical and epidemiological—focused on understanding and solving the medical problems that afflict its beneficiaries (more than 50% of the Mexican population). Initially, research was the result of individual and isolated efforts. In the 1960s, a small number of researchers formed the first research groups. Currently, 240 full-time scientists work at five centers and 40 research units located in different states of Mexico. In addition, approximately 270 doctors carry out clinical research at different primary, secondary and tertiary care units. During these seven decades, IMSS scientists have made relevant contributions to medicine, which have not only helped increase knowledge on the etiopathogenesis of numerous diseases, but also their diagnosis, prognosis and treatment. This article presents an overview of medical research carried out at IMSS, based on a historical approach and a review of some of the most relevant contributions in different fields of research.

KEY WORDS: IMSS. Biomedical research. Clinical research. Epidemiological research.

La investigación médica en el Instituto Mexicano del Seguro Social: siete décadas de trabajo, logros y retos

Resumen

Desde su fundación, hace más de 75 años, el Instituto Mexicano del Seguro Social (IMSS) realiza investigación multidisciplinaria —biomédica, clínica y epidemiológica— enfocada a entender y resolver los problemas médicos que aquejan a sus derechohabientes (más de 50 % de la población mexicana). En un inicio, la investigación fue resultado de esfuerzos individuales y aislados. En la década de 1960, un número reducido de investigadores conformó los primeros grupos de investigación. Actualmente, 240 científicos de tiempo completo trabajan en cinco centros y 40 unidades de investigación ubicados en distintos estados de México. Además, aproximadamente 270 médicos efectúan investigación clínica en las distintas unidades de primer, segundo y tercer nivel de atención. Durante estas siete décadas, los científicos del IMSS han realizado aportaciones relevante para la medicina, las cuales no solo han ayudado a incrementar el conocimiento acerca de la etiopatogenia de numerosas enfermedades, sino también al diagnóstico, pronóstico y tratamiento de ellas. En este artículo se presenta un panorama general sobre la investigación médica que se desarrolla en el IMSS, a partir de un enfoque histórico y de la revisión de algunas de las contribuciones más relevantes en los distintos campos de la investigación.

PALABRAS CLAVE: IMSS. Investigación biomédica. Investigación clínica. Investigación epidemiológica.

Correspondence:

*Héctor Mayani

E-mail: hectormayaniv@gmail.com

Date of reception: 17-06-2021

Date of acceptance: 24-06-2021

DOI: 10.24875/GMM.M21000594

Gac Med Mex. 2021;157:454-462

Contents available at PubMed

www.gacetamedicademexico.com

0016-3813/© 2021 Academia Nacional de Medicina de México, A.C.. Published by Permanyer. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

At the beginning of the 20th century, life expectancy in the world was 31 years; currently, it is 72 years¹. This increase is largely the result of advances in medicine, which, in turn, is the product of research. Medical research comprises at least three types of investigation: biomedical, clinical, and epidemiological. Biomedical research is focused on understanding and characterizing mechanisms and processes at the genomic, genetic, molecular, cellular, and physiological levels. The subject of study can be a gene, a protein, a cell, or a process. In clinical research, the subject of study is the individual. This type of research includes studies focused on the prevention, diagnosis, or treatment of a disease. Finally, in epidemiological research, the study subject can range from a small group of people to entire populations. Through it, understanding patterns, causes, risk factors and forms to control diseases is sought.

Since its foundation more than 75 years ago, the Mexican Institute of Social Security (IMSS – *Instituto Mexicano del Seguro Social*) has carried out multidisciplinary research –biomedical, clinical and epidemiological – focused on understanding and solving the medical problems that afflict its beneficiaries. In this article, we present an overview, from our perspective, on medical research activities that take place at IMSS, based on a historical approach and a review of some of the most relevant contributions in different fields of medicine.

The Mexican Institute of Social Security

Founded in 1943, the IMSS is the largest health institution in Mexico; it offers care services to more than 69 million people, which corresponds to 55% of the population. Throughout the national territory, it has 1,527 family medicine units, 249 secondary care hospitals and 25 high-specialty medical units. The number of people who work at IMSS exceeds half a million, out of which approximately 50% correspond to health-care personnel.

Historical perspective of research at IMSS

Incipiently, research at IMSS began at the end of the 1940s. Driven by the initiative and efforts of Doctors Ignacio Morones Prieto and Bernardo Sepúlveda, research at IMSS began as works that were

complementary to health-care activities. During those early years, scientific activity consisted of isolated efforts carried out at different hospitals, without any articulation between each other. It was with the creation of the National Medical Center, in 1961, that a research environment was generated, which favored the interaction of different groups. Thus emerged the first line of research in reproductive biology. One of the most important products of this line of work was the development of a contraceptive “mini-pill,” based on a reduced dose of progestogen².

With the purpose to integrate and strengthen scientific research at IMSS, the Scientific Research Department was created in 1966, by the initiative of Dr. Jorge Martínez Manatou, who was its first director. This department was integrated with the participation of gynecologists, endocrinologists, pathologists and biochemists. Subsequently, it was joined by specialists in immunology, pharmacology and genetics.

The research projects were funded with resources from IMSS itself and by the Ford Foundation. The acquisition of equipment and the supply of materials began, then, in order to integrate a propitious infrastructure that would make the development of different research projects feasible. One of the first acquisitions was an electronic microscope, a piece of equipment that symbolized the beginning of investigation as an activity of importance for the institution. During the following years, the number of research groups at IMSS gradually increased as research was consolidating. The Scientific Research Department became the National Coordination for Medical Research (CNIC – *Coordinación Nacional de Investigación Médica*) and, subsequently, it turned into the Health Research Coordination (CIS – *Coordinación de Investigación en Salud*).

Throughout all that time, outstanding doctors, committed to the development of research, led the Scientific Research Department, the CNIC, and the CIS. Among them are doctors Carlos Beyer, Juan García, Fernando Flores, Arturo Zárate, Ignacio Madrazo, Onofre Muñoz, Homero Martínez, Dante Amato and Fabio Salamanca. It should be mentioned that, during Dr. Onofre Muñoz administration, the presence of research centers and units at IMSS spread to different states of the country, which contributed to the broad national coverage of research groups that are available today. On the other hand, it is important to highlight the pioneering work carried out by doctors Roberto Kretschmer, Armando Isibasi, Luis Benítez, Salvador Armendares, Fabio Salamanca, Salvador

Villalpando, Marcos Velasco, Francisco Velasco, Jesús Kumate, Arturo Zárate, Xavier Lozoya, José Sánchez Corona, Salvador Saíd, Alfredo Fera and Pablo Hernández, among others.

Current status

At present, research at IMSS is developed in 40 units and five research centers, distributed throughout the country. The institution has 240 researchers dedicated full time to scientific activity and approximately 270 doctors who dedicate part time to carrying out clinical or epidemiological research. Of the just over 500 researchers the IMSS has, approximately 70% belong to the National System of Researchers.

Health research activities are directed, promoted, and regulated by the CIS, currently headed by Dr. César Raúl González Bonilla. Annually, this scientific community publishes more than 800 scientific articles in specialized journals and graduates around 100 master's degree and doctoral students in various areas of health. Priority problems such as obesity, diabetes, cancer, and emerging infectious diseases, among others, are addressed in a multidisciplinary and multicenter manner, through intra- and extra-institutional collaborations, in which national and foreign institutions do participate. The infrastructure and knowledge on cutting-edge technologies, such as genomics, cell biology, electron microscopy, and cytometry, have allowed some of the units and research centers to offer diagnostic and prognostic tests that clinical laboratories cannot perform, which has an impact to the benefit of thousands of patients.

Contributions to medical knowledge

During the past 70 years, the IMSS has carried out quality and impact research in various areas of medical knowledge. For the purposes of this paper we highlight, as an example, some of those contributions.

Genetics

Genetics, in particular cytogenetics, is one of the areas that began to significantly be developed at IMSS since 1960. In 1971, Armendares, Salamanca and Frenk, researchers at the National Medical Center Children's Hospital, observed the presence of chromosomal alterations in children (1-60 months of age) with severe malnutrition³. This work, published in the *Nature* journal, was one of the first in the world to

demonstrate structural chromosomal alterations as a consequence of poor nutrition and established the basis for the development of a program on genetic studies in the Mexican pediatric population. This same research group identified various alterations in the chromosomal number and structure in pediatric patients^{4,5}. In parallel, the group headed by José María Cantú and José Sánchez Corona, from *Centro Médico de Occidente*, in Guadalajara, described the cytogenetic findings of the entity known as Cantú syndrome (OMIM entry #239850), characterized by hypertrichosis, macrosomia at birth and various facial and anatomical alterations⁶. To date, more than 30 cases have been reported in international medical literature.

Oncology

Due to its high incidence and mortality, cancer constitutes one of the priority areas of research at IMSS. Given its high frequency in Mexico and the world, cervical cancer has been the focus of priority attention of various IMSS scientific groups, and numerous multicenter trials have been carried out at the national level. Through these studies, the frequency of human papillomavirus (HPV) subtypes (causal agent of this neoplasm) has been determined, and its prevalence and distribution patterns have been shown to be different from those reported in other regions of the world⁷. Considering that there are commercially available vaccines that are widely applied in the general population, this finding has important implications. In another multicenter study, coinfections with different HPV genotypes were observed to apparently play a "protective" role in infected women⁸.

During the past few years, gastric cancer has become an oncological problem in the world. The highest mortality rates associated with this type of neoplasm occur in two regions of the world: Asia and Latin America, with *Helicobacter pylori* infection being the main risk factor. Research carried out at the Infectious and Parasitic Diseases Medical Research Unit (UIM – *Unidad de Investigación Médica*) has contributed to the understanding of the pathophysiology of this disease by identifying mutations or alterations in gene expression in patients who suffer from this type of cancer^{9,10}. This has contributed to the identification of useful markers for the prevention or early diagnosis of gastric cancer.

As for hematological neoplasms, studies carried out by the Oncological Diseases UIM have contributed to the understanding of the biology of different types of

leukemia. This group reported that, in chronic myeloid leukemia, treatment with IMATINIB (a drug that inhibits the BCR-ABL protein, characteristic of this type of leukemia) eliminates the vast majority of leukemic cells, but not the cells that initiate the neoplasm, which not only do survive, but can expand in in vitro cultures¹¹, which is a finding with implications in the treatment of this type of leukemia. This same group demonstrated that mesenchymal stromal cells of the bone marrow of patients with myelodysplastic syndrome, considered a pre-neoplastic stage, exhibit genetic and functional alterations, which may have implications in treatment response¹². This study was one of the first to demonstrate that not only hematopoietic cells are abnormal in some hematological neoplasms, but that bone marrow microenvironment is also altered. Recently, the onco-immunology group at *Centro de Investigación Biomédica de Oriente* (CIBIOR), in Puebla, reported that cortactin (a protein that binds to actin and participates in cell adhesion and migration processes) plays a relevant role in the pathophysiology of childhood acute lymphoblastic leukemia. This protein participates in tissue migration and disease relapse, which is why it constitutes a diagnostic and prognostic marker for this disease¹³.

Pituitary adenomas are one of the most common types of intracranial tumors. In most cases, they occur sporadically and their etiopathogenesis is poorly understood. The Endocrine Diseases UIM research group recently demonstrated, through a transcriptomic and epigenetic study, that this type of tumors can have three different cellular origins, according to the transcription factor that determines their differentiation¹⁴. This finding may contribute to the development of more efficacious therapies for this type of neoplasms.

Microbiology and immunology

Given the importance of *H. pylori* as the main risk factor for gastric cancer, multicenter and multinational studies have been carried out at the Infectious and Parasitic Diseases UIM in order to understand the evolutionary adaptation of the bacterium to different human populations in America¹⁵. The genomic approach of these studies provides highly relevant information that will help to understand the physiology of this bacterium, its interaction with humans, and to explain the differences in gastric cancer risk between different American countries¹⁶.

Tuberculosis constitutes one of the most common infectious diseases in the world. Susceptibility to this disease largely depends on the innate immune system response to mycobacterial infection. The Zacatecas Biomedical Research Unit has shown that LL-37, an antimicrobial peptide, plays a highly important role in this process, since it acts as an immunomodulator of macrophages during *Mycobacterium tuberculosis* infection, controlling the production of pro-inflammatory and anti-inflammatory cytokines¹⁷. Characterization of the physiology of *M. tuberculosis* and of the immune response to this infection will contribute to the development of more effective therapeutic regimens.

One of the leading groups in the area of immunology has undoubtedly been that of Immunochemistry UIM. This group has worked for more than 30 years on the study of the immune response to bacterial and viral infections, aimed at the development of vaccines. Headed by Dr. Armando Isibasi, this group found that porins, which are proteins located on the outer membrane of *Salmonella typhi*, the bacterium responsible for typhoid fever, may be a target for generating immune protection against this pathogen¹⁸. Porins have also shown protective activity in humans¹⁹. Based on these observations, this research group has worked on the development of a vaccine against typhoid fever and other types of salmonellosis.

On the other hand, the Immunology UIM group investigates the role of the prolactin hormone as an immunomodulatory agent. The works of this group have shown that prolactin participates in CD4 T lymphocytes and B lymphocytes activation, promoting the production and secretion of interleukin-2 and interferon-gamma²⁰, as well as the physiological implications of prolactin in different nosological entities.

Nutrition, metabolic syndrome, obesity, and diabetes

Breastfeeding has important effects on the development and growth of children. Studies at Nutrition UIM demonstrated that breastfeeding reduces the frequency and severity of respiratory and gastrointestinal infections, and protects infants' growth, allowing them to grow at similar percentiles to those of infants in developed countries^{21,22}. They have also shown that interventions at neonatal stage based on docosahexaenoic acid (DHA) supplementation attenuate the inflammatory response mediated by interleukin-1 β , its

clinical evolution and protect the nutritional status of neonates with sepsis²³.

Obesity and metabolic syndrome at pre- and pubertal stages are increasingly prevalent, and their early detection and treatment are crucial to prevent the development of cardiovascular and cerebrovascular comorbidities at later stages of life in these patients. Studies carried out at the Nutrition UIM about the prevalence of disorders such as dyslipidemia, insulin resistance and metabolic syndrome, have demonstrated that the composition of dietary and cell membrane polyunsaturated fatty acids, as well as DHA supplementation, can have an impact on decreasing insulin resistance, dyslipidemia, and hyperandrogenemia in girls²⁴⁻²⁷.

Collaborative studies are carried out at Specialty Hospital Clinical Epidemiology UIM and at *Siglo XXI* National Medical Center Biochemistry UIM in order to define obesity and diabetes molecular epidemiology in Mexico. Among them, collaborative studies with national and foreign institutions in which the association between single-nucleotide polymorphisms of certain genes, such as *ABCA1* and *MGEAS-14*, and susceptibility to develop type 2 diabetes^{2,28,29}, as well as the association between the melanocortin receptor gene^{30,31} and the development of obesity have been identified in Mexican children and adults stand out. Currently, obesity and type 2 diabetes are considered pro-inflammatory conditions. In this area of knowledge, researchers from the Endocrine Diseases, Clinical Epidemiology and Biochemistry research units have carried out experimental and clinical studies on the inflammatory profile in obesity and diabetes³²⁻³⁵.

Morbid obesity constitutes a growing health problem, the management of which requires a multidisciplinary approach. In 2012, the *Siglo XXI* National Medical Center Specialty Hospital Morbid Obesity Clinic was created, in which the joint effort of the endocrinology, internal medicine and surgery departments and of the Endocrine Diseases UIM converge. This multidisciplinary clinic, undoubtedly the largest in Mexico, constitutes an important source of clinical information and biological material that have allowed the performance of several studies, both clinical and biomedical. Among them, long-term follow-up of patients undergoing bariatric surgery³⁶, the definition of the pro-inflammatory profile of patients with morbid obesity³⁷, determination of the role of the growth hormone receptor in adipose tissue body distribution³⁸, and a study on the prevalence of obstructive sleep apnea in people with morbid obesity stand out³⁹.

Researchers from the Durango Biomedical Research Unit have studied, for almost 20 years, the role of magnesium in obesity, hypertension, diabetes and metabolic syndrome. Through controlled clinical trials, they demonstrated that the use of supplements of this trace mineral improves practically all the components of metabolic syndrome, both in children and adults⁴⁰⁻⁴³. Another contribution of this group of researchers is the development of the triglyceride/glucose index as a reliable and low-cost biomarker for insulin resistance screening⁴⁴.

Finally, it is important mentioning that although type 1 diabetes is considerably less common than type 2 diabetes, IMSS clinical and biomedical researchers have made important contributions that include the immunopathogenesis of this disease⁴⁵ and the demonstration that those who suffer from it are also metabolic syndrome bearers⁴⁶.

Chronic kidney disease

For more than 20 years, the Nephrologic Diseases UIM has been recognized as one of the leading groups in Mexico in the study of chronic kidney disease. One of the most important contributions of this group is the demonstration, through a clinical trial that included nearly 1000 patients, that creatinine clearance is not an appropriate predictor of mortality in people with end-stage renal failure on replacement therapy. This finding led to a drastic change in dialysis prescription, with a shift towards comprehensive clinical assessment rather than a numerical value, such as urea clearance. Similar results were obtained in a parallel study in patients on hemodialysis^{47,48}. Subsequent studies at the same Unit showed that fluid overload is associated with inflammation^{49,50}, malnutrition, systolic and diastolic myocardial dysfunction^{51,52} and higher rates of mortality, comorbidities, and costs⁵³, especially in patients with diabetes, in whom the peritoneum does not allow adequate ultrafiltration.

Atherogenesis, cardio- and cerebrovascular disease

Over the past 10 years, Thrombosis, Hemostasis and Atherogenesis UIM researchers, in collaboration with clinical specialists, both from *Siglo XXI* National Medical Center and *La Raza* National Medical Center, have carried out important translational research on the pathophysiology of endothelial dysfunction and

susceptibility to developing cardio- and cerebrovascular disease⁵⁴⁻⁵⁶. Among these investigations, two recently published studies stand out. The first one demonstrates the existence of single-nucleotide polymorphisms of genes that encode angiotensin-converting enzyme and angiotensinogen, which are specifically associated with the risk of cerebrovascular ischemic events in Mexican patients⁵⁷. The second explores *AOX*, *LPA*, *MMP9*, and *TPO* genes single-nucleotide polymorphisms and their relationship with increased susceptibility to atherothrombosis in Mexican adults⁵⁸.

Neurological diseases

One of the most solid contributions of the Neurological Diseases UIM is subarachnoid neurocysticercosis pharmacological treatment with praziquantel⁵⁹. On the other hand, perhaps the best known (and also the most controversial) contribution of IMSS neuroscientists is the treatment of advanced Parkinson's disease with adrenal medulla autologous transplantation^{60,61}. Experimental and clinical studies on traumatic spinal cord injury pathophysiology and surgical and pharmacological treatment are carried out at this same Unit⁶²⁻⁶⁴.

Contributions to patient care

In addition to the numerous contributions in the generation of scientific knowledge, which is reflected on the publication of significant articles in journals with a high impact factor and multiple citations, the work carried out at different IMSS Research Centers and Units has importantly contributed to patient care; below, some representative examples are described.

The Nutrition UIM has worked on the description of the composition of human breast milk and exclusive breastfeeding adequate time. Their findings are part of a guidance document published by the World Health Organization. Together with *Siglo XXI* National Medical Center Children's Hospital, this Unit has collaborated to the establishment and management of the milk bank, which is mainly used in patients hospitalized at the Neonatal Intensive Care Unit. On the other hand, it has collaborated to the introduction of enriched milk formulas to the IMSS Essential Foods List.

The Nephrologic Diseases UIM has worked on the design and implementation of peritoneal dialysis programs in patients with chronic kidney failure. It has

also contributed to the international guidelines for peritoneal dialysis, which were published by the World Health Organization. Furthermore, its contribution includes the design of strategies, both for resource optimization in patients receiving renal replacement therapy (peritoneal dialysis and hemodialysis), and for reducing the rate of peritoneal infections in patients with chronic kidney failure treated with peritoneal dialysis. At *Siglo XXI* National Medical Center Specialty Hospital Clinical Epidemiology UIM, institutional programs and guidelines have been developed for the prevention, diagnosis and comprehensive treatment of diabetes, obesity and metabolic syndrome. Another of its contributions has been an optimization of resources for the prevention, diagnosis and treatment of metabolic disorders. This Unit interacts and collaborates with family medicine units in the prevention, diagnosis and treatment of metabolic disorders. In turn, the Endocrine Diseases UIM created the Morbid Obesity Multidisciplinary Clinic, with more than 100 bariatric procedures annually, and has worked on the development of multidisciplinary clinics for complex endocrine diseases such as thyroid cancer, acromegaly, Cushing, non-functioning adenomas and type 1 diabetes.

The *Centro de Investigación Biomédica del Sur*, in Xochitepec, Morelos, has worked for more than 30 years on the generation of drugs extracted from plants with medicinal properties. Starting from extracts of species such as *Solanum chrysoticum* and *Ageratina pichinchensis*, it has developed antifungal agents. From extracts of *Hibiscus sabdariffa* and *Galphimia glauca*, it developed an antihypertensive and an anxiolytic, respectively. It is important to note that clinical trials have been carried out in all cases, with promising results. Another important biotechnological development is that achieved by the Immunochemistry UIM. Researchers from this unit developed a polyvalent experimental vaccine against *Salmonella*, which was tested in phase I clinical trials, with encouraging results. It is important highlighting that this research group is collaborating with other groups and institutions, both national and foreign, in the development of vaccines against various diseases, including COVID-19.

A research program focused on the incidence of childhood acute lymphoblastic leukemia was created at CIBIOR Onco-immunology Laboratory, which seeks to delve into the etiopathogenesis of the disease and contribute useful tools for its diagnosis, prognosis and treatment. To that end, a multidisciplinary and

multi-institutional group of researchers and doctors has been formed, led by Dr. Rosana Pelayo, from CIBIOR, with the purpose to contribute to decrease the incidence of this disease and increase post-treatment survival rates.

The latest example of research work that has had an impact on the care of IMSS beneficiaries corresponds to the umbilical cord blood Hematopoietic Cell Bank, which was created based on the research carried out at Oncological Diseases UIM. This bank was established in 2005 and, to date, it has approximately 1500 units in storage, out of which more than 160 have been used. With said units, more than 120 transplants have been carried out, mainly in pediatric patients, for the treatment of various hematological, metabolic and neoplastic diseases⁶⁵⁻⁶⁷.

Challenges and future perspectives

Scientific research at IMSS has focused on two aspects: generation of new knowledge that helps understanding the origin and progression of diseases, and use of this knowledge to improve treatment and comprehensive care of IMSS beneficiaries, as well as to support the authorities in decision-making. Constant change in epidemiological trends, population growth and emerging health problems, together with the need to work with limited financial resources, has made it necessary for health research activities at IMSS to be preferentially directed at addressing priority health problems; however, the commitment to continue conducting competitive research and to continue training new generations of researchers who take on the challenge of producing knowledge and using it to the benefit of IMSS beneficiaries should not be lost.

Health research is not a luxury, but a necessity that every country should recognize and accept. However, for quality research to be carried out, it should comprise among its activities the training, aptitude, and enthusiasm of the researchers who carry it out, as well as of the authorities that support it. The commitment of the former is to critically recognize the research necessities and to carry it out as best as possible. The commitment of the latter is to provide the necessary assistance and resources for research activities to be carried out.

The inclusion of research within health-care activities at IMSS has been a gradual and continuous process that, to date, translates into a great scientific structure, both human and physical, which is among the most solid in Mexico. Maintaining, consolidating, and

strengthening the research structure at IMSS is undoubtedly one of the relevant challenges for the quality of medical care of Mexican workers to be preserved.

Final thoughts

Since the dawn of medicine, medical practice has been conceived as the indissoluble result of the doctor-patient binomial. Today, the most solid health institutions in the world have consolidated the doctor-research-patient trinomial. Its foundation is that, as a result of research, the doctor acquires and applies new knowledge, skills and technologies to the benefit of patient health. In the field of modern medicine, it is essential to understand the importance of the doctor-research-patient trinomial and, consequently, the structure of research in health institutions should be supported and strengthened.

Funding

This research has not received any specific grant from agencies of the public, commercial or non-profit sectors.

Conflict of interests

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

References

1. Prentice T. Health, History and Hard Choices: Funding Dilemmas in a Fast-Changing World. USA: World Health Organization/University of Indiana; 2006.
2. Instituto Mexicano del Seguro Social. Contribuciones del IMSS a la Medicina Mundial. Pasado, Presente y Futuro. Mexico: Instituto Mexicano del Seguro Social/Instituto Politécnico Nacional; 2018.
3. Armendarés S, Salamanca F, Frenk S. Chromosome abnormalities in severe protein calorie malnutrition. *Nature*. 1971;232:271-3.
4. Armendarés S, Buentello L, Salamanca F, Cantú-Garza JM. A dicentric Y chromosome without evidence of sex chromosomal mosaicism, 46, XYqdic, in a patient with features of Turner's syndrome. *J Med Genet*. 1972;9:96-100.
5. Salamanca F, Buentello L, Sánchez J, Armendarés S. A patient with 44 chromosomes. *Ann Genet*. 1985;28:130-2.

6. Cantú JM, García-Cruz D, Sánchez-Corona J, Hernández A, Nazara Z. A distinct osteochondrodysplasia with hypertrichosis individualization of a probable autosomal recessive entity. *Hum Genet.* 1982;60:36-41.
7. Salcedo M, Piña-Sánchez P, Vallejo-Ruiz V, Monroy-García A, Aguilar-Lemarroy A, Cortés-Gutiérrez EI, et al. Human papillomavirus genotypes among females in México: a study from the Mexican institute for Social Security. *Asian Pac J Cancer Prev.* 2014;15:10061-6.
8. Aguilar-Lemarroy A, Vallejo-Ruiz V, Cortés-Gutiérrez EI, Salgado-Bernabé EM, Ramos-González NP, Ortega-Cervantes L, et al. Human papillomavirus infections in Mexican women with normal cytology, precancerous lesions, and cervical cancer: type-specific prevalence and HPV coinfections. *J Med Virol.* 2015;87:871-84.
9. Partida-Rodríguez O, Torres J, Flores-Luna L, Camorlinga M, Nieves-Ramírez M, Lazcano E, et al. Polymorphisms in TNF and HSP-70 show a significant association with gastric cancer and duodenal ulcer. *Int J Cancer.* 2010;126:1861-8.
10. Pérez-Rodríguez M, Partida-Rodríguez O, Camorlinga-Ponce M, Flores-Luna L, Lazcano E, Gómez A, et al. Polymorphisms in HLA-DQ genes, together with age, sex, and *Helicobacter pylori* infection, as potential biomarkers for the early diagnosis of gastric cancer. *Helicobacter.* 2017;22.
11. Chávez-González A, Ayala-Sánchez M, Sánchez-Valle E, Ruiz-Sánchez E, Arana-Trejo RM, Vela-Ojeda J, et al. Functional integrity in vitro of hematopoietic progenitor cells from patients with chronic myeloid leukemia that have achieved hematological remission after different therapeutic procedures. *Leuk Res.* 2006;30:286-95.
12. Flores-Figueroa E, Arana-Trejo RM, Gutiérrez-Espíndola G, Pérez-Cabrera A, Mayani H. Mesenchymal stem cells in myelodysplastic syndromes: phenotypic and cytogenetic characterization. *Leuk Res.* 2005;29:215-24.
13. Velázquez-Ávila M, Balandrán JC, Ramírez-Ramírez D, Velázquez-Ávila M, Sandoval A, Felipe-López A, et al. High cortactin expression in B-cell acute lymphoblastic leukemia is associated with increased transendothelial migration and bone marrow relapse. *Leukemia.* 2019;33:1337-48.
14. Taniguchi-Ponciano K, Andonegui-Elguera S, Peña-Martínez E, Silva-Román G, Vela-Patiño S, Gómez-Apo E, et al. Transcriptome and methylome analysis reveals three cellular origins of pituitary tumors. *Sci Rep.* 2020;10:19373.
15. Muñoz-Ramírez Z, Pascoe B, Méndez-Tenorio A, Mourkas E, Sandoval-Motta S, Pérez-Pérez G, et al. A 500-year tale of co-evolution, adaptation, and virulence: *Helicobacter pylori* in the Americas. *ISME J.* 2020;15:78-92.
16. Muñoz-Ramírez ZY, Méndez-Tenorio A, Ikuko K, Bravo MM, Rizzato C, Thorell K, et al. Whole genome sequence and phylogenetic analysis show *Helicobacter pylori* strains from Latin America have followed a unique evolution pathway. *Front Cell Infect Microbiol.* 2017;7:50.
17. Torres-Juárez F, Cárdenas-Vargas A, Montoya-Rosales A, González-Curiel I, García-Hernández MH, Enciso-Moreno JA, et al. LL-37 immunomodulatory activity during *Mycobacterium tuberculosis* infection in macrophages. *Infect Immun.* 2015;83:4495-503.
18. Isibasi A, Ortiz V, Vargas M, Paniagua J, González C, Moreno J, et al. Protection against *Salmonella typhi* infection in mice after immunization with outer membrane proteins isolated from *Salmonella typhi* 9,12,d,Vi. *Infect Immunol.* 1988;56:2953-9.
19. Blanco F, Isibasi A, González CR, Ortiz V, Paniagua J, Arreguín C, et al. Human cell mediated immunity to porins from *Salmonella typhi*. *Scand J Infect Dis.* 1993;25:73-80.
20. Chávez-Rueda K, Hernández J, Centeno E, Leano's-Miranda A, Legorreta-Haquet MA, Blanco-Favela F. Identification of prolactin as a novel immunomodulator on the expression of costimulatory molecules and cytokine secretions on T and B human lymphocytes. *Clin Immunol.* 2005;116:182-91.
21. López-Alarcón M, Villalpando S, Fajardo A. Breast-feeding lowers the frequency and duration of acute respiratory infection and diarrhea in infants under six months of age. *J Nutra.* 1997;127:436-43.
22. Villalpando S, López-Alarcón M. Growth faltering is prevented by breast-feeding in underprivileged infants from México city. *J Nutra.* 2000;130:546-52.
23. López-Alarcón M, Bernabe-García M, del Valle O, González-Moreno G, Martínez-Basile A, Villegas R. Oral administration of docosahexaenoic acid attenuates interleukin-1 β response and clinical course of septic neonates. *Nutrición.* 2012;28:384-90.
24. López-Alarcón M, Perichart-Perera O, Flores-Huerta S, Inda-Icaza P, Rodríguez-Cruz M, Armenta-Álvarez, et al. Excessive refined carbohydrates and scarce micronutrients intakes increase inflammatory mediators and insulin resistance in prepubertal obese children independently of obesity. *Mediators Inflamm.* 2014;2014:849031.
25. Barbosa-Cortés L, Villasis-Keever MA, del Prado-Manríquez M, López-Alarcón M. Adiposity and insulin resistance in children from a rural community in Mexico. *Arch Med Res.* 2015;46:214-20.
26. López-Alarcón M, Inda-Icaza P, Márquez-Maldonado MC, Armenta-Álvarez A, Barbosa-Cortés L, Maldonado-Hernández J, et al. A randomized control trial of the impact of LCPUFA-w3 supplementation of body weight and insulin resistance in pubertal children with obesity. *Pediatr Obes.* 2019;14:e12499.
27. López-Alarcón MG, Vital-Reyes VS, Hernández-Hernández FI, Maldonado-Hernández J. The role of LCPUFA ω 3 on the obesity-associated hyperandrogenemia of pubertal girls: secondary analysis of a randomized clinical trial. *J Pediatr Endocrinol Metab.* 2020;33:347-54.
28. Cameron E, Martínez-Marina V, Chan A, Valladares A, Simmons L, Wachter N, et al. MGEA5-14 polymorphisms and Type 2 diabetes in Mexico city. *Am J Hum Biol.* 2007;19:593-6.
29. Villarreal-Molina MT, Flores-Dorantes MT, Arellano-Campos O, Villalobos-Companan M, Rodríguez-Cruz M, Millar-García A, et al. Association of the ATP-binding cassette transporter A1 R230C variant with early-onset Type 2 diabetes in a Mexican population. *Diabetes.* 2008;57:509-13.
30. Vázquez-Moreno M, Zeng H, Locia-Morales D, Peralta-Romero J, Asif H, Maharaj A, et al. The melanocortin 4 receptor p.Ile269Asn mutation is associated with childhood and adult obesity in Mexicans. *J Clin Endocrinol Metab.* 2020;105:dgz276.
31. Vázquez-Moreno M, Locia-Morales D, Valladares-Salgado A, Sharma T, Pérez-Herrera A, González-Dzib R, et al. The MC4R p.Ile269Asn mutation confers a high risk for Type 2 diabetes in the Mexican population via obesity dependent and independent effects. *Sci Rep.* 2021;11:3097.
32. Cruz M, García-Macedo I, García-Valerio Y, Gutiérrez M, Medina-Navarro, R, Durán G, et al. Low adiponectin levels predict Type 2 diabetes in Mexican children. *Diabetes Care.* 2004;27:1451-3.
33. Ferreira-Hermosillo A, Molina-Ayala MA, Ramírez-Rentería C, Vargas G, González B, Isibasi A. Inflammatory cytokine profile associated with metabolic syndrome in adult patients with Type 1 diabetes. *J Diabetes Res.* 2015;2015:972073.
34. Villeda-González JD, Gómez-Olivares JC, Baiza-Gutman LA, Manuel-Apolinar L, Damasio-Santana L, Millán-Pacheco C, et al. Nicotinic acid reduces inflammation and oxidative stress via the cholinergic system in fructose-induced metabolic syndrome in rats. *Life Sci.* 2020;250:117585.
35. Zurita-Cruz J, Villasis-Keever M, Manuel-Apolinar L, Damasio-Santana L, Wakida-Kusunaki GH, Padilla-Rojas M, et al. Resistin/uric acid index as a prognostic factor in adolescents with obesity after lifestyle intervention. *J Pediatr.* 2020;219:38-42.
36. Cadena-Obando D, Ramírez-Rentería C, Ferrera-Hermosillo A, Albarán-Sánchez A, Sosa-Eroza E, Molina-Ayala M, et al. Are there really any predictive factors for a successful weight loss after bariatric surgery? *BMC Endocr Disord.* 2020;20:20.
37. Gómez-Zamudio JE, Mendoza-Zubieta V, Ferreira-Hermosillo A, Molina-Ayala M, Valladares-Salgado A, Suárez-Sánchez F, et al. High thyroid stimulating hormone levels increase proinflammatory and cardiovascular markers in patients with extreme obesity. *Arch Med Res.* 2016;47:476-82.
38. Espinosa E, Salame L, Marrero-Rodríguez D, Romero-Nieves AH, Cuenca D, Castelán-Martínez D, et al. Expression of the growth hormone receptor isoforms and its correlation with the metabolic profile in morbidly obese subjects. *Endocrine.* 2019;63:573-81.
39. Cervantes-Theruel J, Albarrán-Sánchez A, Rodríguez-Pérez V, Espinosa-Cárdenas E, Ramírez-Rentería C, Ferreira-Hermosillo A. Utility of the STOP-Bang and Epworth scales and the neck-to-height ratio to detect severe obstructive apnea-hypopnea syndrome in severe obesity. *Surg Obes Relat Dis.* 2021;17:257-62.
40. Guerrero-Romero F, Jaquez-Chairez FO, Rodríguez-Morán M. Magnesium in metabolic syndrome: a review based on randomized double blind clinical trials. *Magnes Res.* 2016;29:146-53.
41. Guerrero-Romero F, Flores-García A, Saldaña-Guerrero S, Simental-Mendía LE, Rodríguez-Morán M. Obesity and hypomagnesemia. *Eur J Intern Med.* 2016;34:29-33.
42. Simental-Mendía LE, Simental-Mendía M, Sahebkar A, Rodríguez-Morán M, Guerrero-Romero F. Effect of magnesium supplementation on lipid profile: a systematic review and meta-analysis of randomized controlled trials. *Eur J Clin Pharmacol.* 2017;73:525-36.
43. Rodríguez-Morán M, Simental-Mendía LE, Gamboa-Gómez CI, Guerrero-Romero F. Oral magnesium supplementation and metabolic syndrome: a randomized double-blind placebo-controlled clinical trial. *Adv Chronic Kidney Dis.* 2018;25:291-6.
44. Guerrero-Romero F, Simental-Mendía LE, González-Ortiz M, Martínez-Abundis E, Ramos-Zavala MG, Hernández-González SO, et al. The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. *J Clin Endocrinol Metab.* 2010;95:3347-51.
45. Gómez-Díaz RA, Aguilar MV, Meguro EN, Márquez RH, Magaña EG, Martínez-García MC, et al. The role of natural killer T (NKT) cells in the pathogenesis of Type 1 diabetes. *Curr Diabetes Rev.* 2011;7:278-83.
46. Ferreira-Hermosillo A, Ramírez-Rentería C, Molina-Ayala MA, Mendoza-Zubieta V. Utility of the waist-to-height ratio, waist circumference and body mass index in the screening of the metabolic syndrome in adult patients with Type 1 diabetes mellitus. *Diabetol Metab Syndr.* 2014;6:32-43.
47. Paniagua R, Amato D, Vonesh E, Correa-Rotter R, Raos A, Morán J, et al. Effects of increased peritoneal clearances on mortality rates in peritoneal dialysis: ADEMEX, a prospective, randomized, controlled trial. *J Am Soc Nephrol.* 2002;13:1307-20.

48. Paniagua R, Amato D, Vonesh E, Mujais S, Horl WH. Predictive value of brain natriuretic peptides in patients on peritoneal dialysis: results from the ADEMEX trial. *Clin J Am Soc Nephrol*. 2008;3:407-15.
49. Vicente-Martínez M, Martínez-Ramírez L, Muñoz R, Ávila M, Ventura MJ, Rodríguez E, et al. Inflammation in patients on peritoneal dialysis is associated to increased extracellular fluid volume. *Arch Med Res*. 2004;35:220-4.
50. Ávila-Díaz M, Ventura MJ, Valle D, Vicente-Martínez M, García-González Z, Cisneros C, et al. Inflammation and extracellular volume expansion are related to sodium and water removal in patients on peritoneal dialysis. *Perit Dial Int*. 2006;26:574-80.
51. Prado-Uribe MC, Ventura MJ, Ávila-Díaz M, Mora CJ, Méndez-Durán A, Villanueva-Noches D, et al. Low triiodothyronine is associated with N-terminal pro-brain natriuretic peptide and mortality in dialysis patients. *Nefrología*. 2017;37:598-607.
52. Sánchez V, Paniagua R, Prado MD, Mora C, Orihuela O, Martínez-Baca F, et al. High prevalence of diastolic dysfunction in incident patients on peritoneal dialysis: association with low thyroid hormones. *Nephron*. 2017;135:120-8.
53. Paniagua R, Ventura MJ, Ávila-Díaz M, Hinojosa-Heredia H, Méndez-Durán A, Cueto-Manzano A, et al. NT-proBNP, fluid volume overload, and dialysis modality are independent predictors of mortality in ESRD patients. *Nephrol Dial Transplant*. 2010;25:551-7.
54. Jiménez-Rosales A, Amaya-Chávez A, García MV, Camarillo-Romero E, Huitrón-Bravo GG, Majluf-Cruz A. Association of inflammatory and oxidative stress biomarkers in subjects with cardiovascular risk. *Am J Ther*. 2013;20:422-31.
55. Camarillo-Romero E, Domínguez-García MV, Amaya-Chávez A, Camarillo-Romero MS, Talavera-Piña J, Huitrón-Bravo G, et al. Effects of a physical activity program on markers of endothelial dysfunction, oxidative stress, and metabolic status in adolescents with metabolic syndrome. *ISRN Endocrinol*. 2012;2012:970629.
56. Rivera-García BE, Esparza-García JC, Aceves-Chimal JL, Leaños-Miranda A, Majluf-Cruz A, Isordia-Salas I. Platelet glycoprotein IIIa PIA1/A2 polymorphism in young patients with ST elevation myocardial infarction and idiopathic ischemic stroke. *Mol Cell Biochem*. 2013;384:163-71.
57. Isordia-Salas I, Santiago-Germán D, Cerda-Mancillas MC, Hernández-Juárez J, Bernabé-García M, Leaños-Miranda A, et al. Gene polymorphisms of angiotensin-converting enzyme and angiotensinogen and risk of idiopathic ischemic stroke. *Gene*. 2018;688:163-70.
58. Camacho-Mejorado R, Gómez R, Torres-Sánchez LE, Hernández-Tobías EA, Noris G, Santana C, et al. AOX5, LPA, MMP9 and TPO gene polymorphisms increase atherothrombosis susceptibility in middle-aged Mexicans. *R Soc Open Sci*. 2020;7:190775.
59. Proaño JV, Madrazo I, Avelar F, López-Félix B, Díaz G, Grijalva I. Medical treatment for neurocysticercosis characterized by giant subarachnoid cysts. *N Engl J Med*. 2001;345:879-85.
60. Madrazo I, Drucker-Colín R, Díaz V, Martínez-Mata J, Torres C, Becerril JJ. Open microsurgical autograft of adrenal medulla to the right caudate nucleus in two patients with intractable Parkinson's disease. *N Engl J Med*. 1987;316:831-4.
61. Madrazo I, León V, Torres C, Aguilera MC, Varela G, Álvarez F, et al. Transplantation of fetal substantia nigra and adrenal medulla to the caudate nucleus in two patients with Parkinson's disease. *N Engl J Med*. 1988;318:51.
62. Grijalva I, Guízar-Sahagún G, Castañeda-Hernández G, Mino D, Maldonado-Julian H, Vidal-Cantú G, et al. Efficacy and safety of 4-aminopyridine in patients with long-term spinal cord injury: a randomized, double-blind, placebo-controlled trial. *Pharmacotherapy*. 2003;23:823-34.
63. Grijalva I, García-Pérez A, Díaz J, Aguilar S, Mino D, Santiago-Rodríguez E, et al. High doses of 4-aminopyridine improve functionality in chronic complete spinal cord injury patients with MRI evidence of cord continuity. *Arch Med Res*. 2010;41:567-75.
64. Buzoianu-Anguiano V, Rivero-Orsorio J, Orozco-Suárez S, Vega-García A, García-Vences E, Sánchez-Torres S, et al. Single versus combined therapeutic approaches in rats with complete chronic spinal cord injury. *Front Neurol*. 2020;11:136-40.
65. Novelo-Garza B, Limón-Flores A, Guerra-Márquez A, Luna-Bautista F, Juan-Shum L, Montero I, et al. Establishing a cord blood banking and transplantation program in Mexico: a single institution experience. *Transfusion*. 2008;48:228-36.
66. Guerra-Márquez A, Novelo-Garza B, Malagón-Martínez A, Limón-Flores A, Luna-Bautista F, Juan-Shum L, et al. Cord blood banking and transplantation at the Mexican Institute of Social Security: the first five years. *Transfusion*. 2011;51:328-32.
67. Guerra-Márquez A, Peñaflor K, Mayani H. Cord blood banking and transplantation at the Mexican institute of social security: thirteen years of experience. *Arch Med Res*. 2020;51:54-62.