Special Issue. Ophthalmol. Cases. Hypotheses, (2024), 5:2

33

**SPECIAL ISSUE**

***New Ophthalmic Research***

**Baku-2024**

**ISBN:** 978-9952-559-53-8

**DOI:** 10.30546/2788-516X.2024.1010.

**Copyright © 2024**

**Editorial Ofϐice Address:** HAT Medicine Clinic. AZ1011 89A Hasan Bey Zardabi Street, Baku, Azerbaijan.

**Contacts:** Phone: +994 50 200 03 79, **E-mail:** of ice@ophthalmolcases.com **Website:** https://ophthalmolcases.com

**License**: Creative Commons Attribution 4.0 International License.

Journal of Ophthalmology Cases & Hypotheses allows readers to read, download, copy, distribute, print, search, or link to the full texts of itsarticles and allows readers to use them for any other lawful purpose.

Published in AZERBAIJAN.

Prepared and designed by: “GPARC GROUP” LLC

2

**SPECIAL ISSUE**

**GUEST EDITORS**

**Professor Vitovska Oksana**

*Bogomolets National Medical University, Kyiv, Ukraine*

**Suleyman Kaynak, MD, PhD**

*Retina Ophthalmic Research Center, Department of Ophthalmology, Izmir, Turkiye*

**Nikolay P. Pivovarov, MD, PhD**

*Professor, Ophtahlmologist, Pescara Corso Vittorio Emmanuele*

*406 Studio Oculistico Renato Minicucci, Italy*

This Special Issue is the publication of the Journal Ophthalmology Cases & Hypotheses (OCH), (ISSN 3006-1237,E-ISSN 2788-516X) published online in the open-access.

(Available at: https:// https://ophthalmolcases.com)

OCH**®**

3

**SPECIAL ISSUE**

**PREFACE**

This article presents an innovative perspective on the emergence of human diseases, particularly eye diseases, through the lens of Chaos Theory. The authors propose that all cells in the body are arranged in fractal patterns, and diseases arise when these fractal structures are disrupted. The foundation of this disruption is an imbalance among epithelial cells, the microbiota, and surrounding immunoglobulins, collectively termed the “triumvirate,” drawing an analogy with ancient Roman history.

The triumvirate concept is groundbreaking, as it posits that this symbiotic relationship regulates all organs and tissues, functioning as a “clinical attractor.” This self-sustaining system of interactions between the microbiota, mucosal membranes, and antibodies is hypothesized to maintain the balance and health of various body tissues. The identi ication of ive clinical attractors – the gut, urogenital, respiratory, ocular, and aural attractors –further re ines our understanding of disease mechanisms.

Particularly compelling is the hypothesis that peptides on the surface of MHC-1 of somatic cells are epitopes of the microbiota. This suggests that each cell type, depending on its evolutionary history, harbors speci ic microbiota-related antigens. The example of peptides associated with MHC-1 cells of the optic nerve and visual tract underscores the potential for targeted therapeutic interventions. The notion that restoring the balance between the ocular microbiota and surrounding antibodies can halt the progression of optic nerve atrophy and improve visual function is particularly promising.

Overall, this theory offers a paradigm shift in understanding the origin and treatment of human diseases, providing a novel framework that integrates microbiota-immune interactions and fractal biology. This article is a valuable contribution to the ield, presenting a comprehensive and innovative approach that warrants further exploration and validation.

Likewise, I would like to express my appreciation for the tremendous efforts made by the author, Rasim V. Hajiyev MD, PhD, Professor, who submitted the paper to this special issue. I also sincerely thank the Guest Editors of this Special Issue and the editorial team of the Journal Ophthalmology Cases & Hypotheses (OCH).

**Professor Vitovska Oksana**

*Bogomolets National Medical University, Kyiv, Ukraine*

4

**SPECIAL ISSUE**

This article offers an insightful and progressive hypothesis linking microbiota imbalance to the development of both ocular and systemic diseases. Through a robust review of existing literature combined with the authors’ own research, the paper advocates for a shift from traditional reductionist views in medicine to a model that embraces the complexities of chaotic systems. This approach illuminates the intricate relationships between microbiota, human epithelial cells, and immunoglobulins.

The paper introduces a pioneering perspective on disease genesis, emphasizing the chaotic and fractal nature of cellular organization. It suggests that the arrangement of cells in fractal patterns is fundamental tohealth, and that diseases may stem from disruptions in these patterns. Central tothis disruption is an imbalance in the “triumvirate” of mucosal cells, microbiota, and immunoglobulins—a term evocatively borrowed from Roman history to describe their interdependent relationship.

The hypothesis posits that the fractal structure of cellular arrangement, when disrupted, leads to disease. This disruption is intricately linked toan imbalance among the epithelial cells that interface with the external environment, the microbiota, and the immune system’s antibodies. By framing this relationship as a clinical attractor, the article offers a novel framework for understanding how changes in micro lora can in luence disease states across the body, not just in the eyes but systemically.

This review does more than just challenge existing paradigms; it proposes a comprehensive model that could revolutionize our understanding of health and disease. The integration of chaos theory into systemic medicine provides a valuable lens through which we can re-examine the complexities of human health. This article is a signi icant contribution to the ield, offering new avenues for research and potential therapeutic strategies that could be particularly transformative in the realm of ophthalmology.

**Suleyman Kaynak, MD, PhD**

*Retina Ophthalmic Research Center, Department of Ophthalmology, Izmir, Turkiye*

5

**Ophthalmology Cases & Hypotheses** Volume 5, Number 2, 2024

**DISCLAIMER**

The opinions and information contained in this publication are those of the authors of the respective articles and not necessarily those of the editors, proofreaders, or the the Journal of Ophthalmology Cases & Hypotheses (OCH).

Consequently, we assume no liability or risk that may be incurred as a consequence, directly or indirectly, of the use and application of any of the contents of this publication.

6

**OPHTHALMOLOGY CASES AND HYPOTHESES®**

**CONTENTS**

*Rasim V. HAJIYEV*

**A new theory of the emergence of eye diseases based on the imbalance**

**of human microbiota. A critical review of the literature** ..........................................8 DOI: 10.30546/2788-516X.2024.1010.

**CORRECTIONS** ....................................................................................................................................24

**EDITORIAL OFFICE**

Inam M. GULIYEV, Associate Managing Editor

Full text articles and new content alerts can be found online at https://ophthalmolcases.com

***Publisher’s Note:*** *We stay neutral with regard to jurisdictional claims in published maps and institutional afϔiliations.*

7

**ORIGINAL ARTICLE**

Special Issue, (2024), 5:2:8-23

**A NEW THEORY OF THE EMERGENCE OF EYE DISEASES BASED ON THE IMBALANCE OF HUMAN MICROBIOTA. A CRITICAL REVIEW OF THE LITERATURE**

**Rasim V. Hajiyev MD, PhD, Professor** HAT Medicine Clinic, Baku, Azerbaijan

**Received:** 16.02.2024 **Accepted:** 21.04.2024 **Printed:** 07.08.2024

**Citation:** Hajiyev R., A new theory of the emergence of eye diseases based on the imbalance of human microbiota. A critical review of the literature. Special Issue. 2024 (Journal of Ophthalmology Cases and Hypotheses. ). 8-23, doi: 10.30546/2788-516X.2024.1010.

**ABSTRACT**

**Purpose**

Based on a critical review of the literature, as well as our own research and observations on the causes of eye diseases (dry eye syndrome, glaucoma, retinal diseases, optic neuropathy), we propose a new hypothesis about the role of microbiota imbalance in the development of both ocular and systemic diseases. This review attempts to move away from the existing reductionist approach. It attempts to explain that the laws of Chaos underpin systemic medicine.

**Conclusions and importance**

From the new perspective of Chaos, the emergence of all human diseases, particularly eye diseases, is considered.All cells in the body are arranged in the form of fractals. In diseases, the fractal structure of cell arrangement is disrupted.

The basis for the emergence of diseases and the disruption of the fractal structure of cells lies in the imbalance between the epithelial cells of humans that come into contact with the external environment, the microbiota, and the surrounding immunoglobulins. This symbiosis between mucosal cells, microbiota, and immunoglobulins is called the “triumvirate,” by analogy with ancient Roman history.

This triumvirate regulates all organs and tissues of the body. This entire system represents a “clinical attractor.” The term “clinical attractor” re lects the idea of a self-sustaining system where interactions between the microbiota, mucosal membranes, and surrounding antibodies regulate various tissues in the body.

There are ive clinical attractors in the body: gut attractor, urogenital attractor, respiratory attractor, ocular attractor, and aural attractor.

It is hypothesized that peptides on the surface of MHC-1 of somatic cells are epitopes of the microbiota. Each cell of an organ or tissue in the human body has MHC-1 on its surface, which is an epitope of a speci ic microbiota. The speci ic antigenic determinant of the microbiota on the cells of the conjunctiva, choroid, and retina depends on the evolutionary history of that speci ic tissue.

For example, a peptide associated with MHC-1 cells of the optic nerve and visual tract is characteristic of the ocular microbiota. Restoring the balance between the ocular microbiota and the surrounding antibodies can stop the progression and improve the visual functions of patients with optic nerve atrophy.

This theory provides a new perspective on the origin and treatment of all human diseases.

**Keywords:** Microbiota, optic neuropathy, af inity, peptide exchange, adaptive immunity, major histocompatibility complex, epitope, systems biology, chaos, fractals, dry eye disease

8

© 2024 OCH. Journal of Ophthalmology Cases & Hypotheses / Published by Hat Medicine Clinic

Special Issue. Ophthalmol. Cases. Hypotheses, (2024), 5:2

**Access this article online** **Focus on a singular factor**

**Quick Response Code:** **Website:** https://ophthalmolcases.com

10.30546/2788-516X.2024.1010.

**Address for correspondence:**

Rasim V. Hajiyev MD, PhD, Professor HAT Medicine Clinic, Baku, Azerbaijan

Email: rasim.gadjiev@gmail.com

When the human body is viewed as a collection of components, the natural inclination of medicine is to isolate the single factor that is most responsible for the observed behavior. Much like a mechanic who repairs a broken car by locating the defective part, physicians typically treat disease byidentifying that isolatable abnormality. Implicit within this practice is the deeply rooted belief that each disease has a potential singular target for medical treatment. For infection, the target is the pathogen; for cancer, it is the tumor; and for gastrointestinal bleeding, it is the bleeding vessel or ulcer.

The alternative explanation that has received much recent attention, due to systems biology, is

**Introduction**

Since Descartes and the Renaissance, science, including medicine, has taken a distinct path in its analytical evaluation of the natural world.1,2 This approach can be described as one of “divide and conquer,” it is rooted in the assumption that complex problems are solvable by dividing them into smaller, simpler, and thus more tractable units. Because the processes are “reduced” into more basic units, this approach has been termed “reductionism” and has been the predominant paradigm of science over the past two centuries. Reductionism pervades the medical sciences and affects how we diagnose, treat, and prevent diseases.

The surgery operates on a reductionist level. The triumph of reductionism was the discovery of the DNA molecule by Watson and Crick.3

While it has been responsible for tremendous successes in modern medicine, there are limits to reductionism, and an alternative explanation must be sought to complement it.

While the implementation of clinical medicine is systems-oriented, the science of clinical medicine is fundamentally reductionist. This is shown in four prominent practices in medicine: (1) the focus on a singular, dominant factor, (2) emphasis on homeostasis, (3) inexact risk modi ication, and (4) additive treatments. 4

the systems perspective

While the success of this approach is undeniable, it leaves little room for contextual information

**Emphasis on homeostasis**

The homeostasis principle was discovered by Walter Bradford Cannon in 1929. 5 “The homeostasis principle is the property of a physiological system to regulate its internal environment to a given set point in the presence of a speciﬁc stimulus producing changes in that variable” 6

The control activity in the body is guaranteed by the arrangement of the control center (composed by nervous and endocrine systems), sensors, and effectors. For decades, homeostasis has been a vital, guiding principle for medicine

Since then, homeostasis has been incorporated into clinical practice. Illness is de ined as a failed homeostatic mechanism, and treatment requires physicians to substitute for this failed mechanism by correcting deviations and placing parameters within normal range.

Consequently, emphasis is placed on static stability/normal ranges and not on dynamic stable states, such as oscillatory or chaotic (seemingly random but deterministic) behavior. Circadian rhythms7,8 are an example of chaotic behavior. Failure to include these dynamic states in the homeostasis model may lead to treatments that are either ineffective or even detrimental. 9

9

A new theory of the emergence of eye diseases based on the imbalance of human microbiota. A critical review of the literature

**Inexact risk modiϐication**

Since disease cannot always be predicted with certainty, health professionals must identify and modify risk factors. The common, unidimensional, “one-riskfactor to one-disease” approach used in medical epidemiology, however, has certain limitations.

Doctors are trying to identify risk factors for diseases, such as hypertension, through scienti ic research.10 But it is impossible to take into account all risk factors for hypertension.11

**Additive treatments**

In reductionism, multiple problems in a system are typically tackled piecemeal. Each problem is partitioned and addressed individually. In coronary artery disease, for example, each known risk factor is addressed individually,whether it be hyperlipidemia or hypertension.

Cardiologists treat coronary artery disease with one method, while gastroenterologists treat intestinal ulcers with a different method. And in principle, these diseases may be based on the same cause.

**Limitations to Current Medical Science**

The science underlying our medical practices, from diagnosis to treatment to prevention, is based on the assumption that information about individual parts is suf icient to explain the whole. But there are circumstances in which the complex interplay between parts yields a behavior that cannot be predicted by the investigation of the parts alone. The failure to account for these circumstances is the common denominator for the explanations of why the aforementioned practices are, in many cases, inadequate.

So how should these complexities be addressed? Is there a formal method that can explain how the pieces create the whole? How do weshift our lens from the parts to the system?

**Systems biology**

The answers to these questions may come from a relatively new branch of science called systems biology or systems medicine12,13,14,15,16

10

But this system also does not work. It doesn’t work because the laws of Chaos are not taken into account. Although it must be admitted that there are studies devoted to the theory of chaos in medicine.17,18,19

But these studies do not answer the question of how the human body works and why diseases occur. The fact is that the theory of Chaos does not

it well into the modern idea of medicine in general.

**Chaos theory from new positions**

We believe that systemic medicine is based on the laws of Chaos. Chaos theory was called by Feynman himself one of the three triumphs of the 20th century, along with the theory of relativity and quantum mechanics. In 2013, the journal Nature stated that this is one of the most important misunderstood theories of the 20th century.20

Lorenz an American mathematician and meteorologist was the pioneer of the chaos theory. He studied weather patterns he began to realize that they did not always change as predicted. Minute variations in the initial values of variables in his twelve-variable computer weather model would result in grossly divergent weather patterns. This sensitive dependence on initial conditions came to be known as the butter ly effect21

Chaos theory explains that within the visible randomness of complex, chaotic systems, there are inherent repetition, patterns, self-organization, interconnectedness, self-similarity, and constant feedback loops.

**Fractals**

Today, fractals form part of the visual identity of chaos. As in initely complex objects that are self-similar across all scales, they represent dynamical systems in all their glory

The birth of fractal geometry is usually associated with the publication of Mandelbrot’s book in 1977.22 Fractal geometry describes structures that repeat at different scales with similar or identical shapes. In organic matter, cellular structures and enzymes23 often exhibit fractal characteristics due

© 2024 OCH. Journal of Ophthalmology Cases & Hypotheses / Published by Hat Medicine Clinic

Special Issue. Ophthalmol. Cases. Hypotheses, (2024), 5:2

to their hierarchical organization and repetitive structural elements across different levels. This is because fractal geometry re lects universal principles of organization and formation in

complex systems, whether organic or inorganic.

Quantitative analysis of the branching of the respiratory tract showed that it has a fractal structure.24

The fractal structure is also characteristic of liver tissue. 25,26 Cells of the gastrointestinal system also have a fractal structure.27

Thus, we see that all cells of the human body are in the form of fractals. Violation of the fractal structure leads to the occurrence of diseases. We can see this in the example of eye angiography (Figure. 1,2,3.).

**Figure 1.** *Normal fractal structure of the eye’s capillaries.*

**Figure 2, 3.** *In retinal diseases, the normal structure of the capillaries changes. Chaos ensues*

We have hypothesized that the fractal structure of the body’s cells is maintained by the state of equilibrium between the body’s microbiota and the surrounding immune cells – immunoglobulins. Let’s examine the theory of Chaos in more detail.

**Laws of dialectical materialism in the theory of Chaos**

The laws described in Chaos coincide with the laws of dialectical materialism. The second law of dialectical materialism states that everything in the world obeys the principle of unity and the struggle of opposites.28

An atom maintains its structure due to the ‘struggle’ between the positively charged nucleus and the negatively charged electrons orbiting around it. Each elementary particle corresponds to an antiparticle; both have almost identical characteristics, except that they have opposite electric charges. If the particle is neutral, then the antiparticle is also neutral, but they may differ in other characteristics.

It is in the struggle of opposites (The Unity of Opposites) that particles are born and their opposites immediately arise.

We can observe manifestations of these laws in the example of the retina. The retina consists of an outer layer (red color Figure. 4), which includes the pigment epithelium layer and the photoreceptor layer, and an inner layer (green

11

A new theory of the emergence of eye diseases based on the imbalance of human microbiota. A critical review of the literature

color, bipolar ganglion cells, Müller cells). These two layers are in opponent relationships with each other (Figure. 4).30

In diabetic retinopathy, only the inner part of the retina is affected, and photoreceptors remain intact.

For the treatment of diabetic retinopathy, we use pan retinal laser coagulation. By destroying the outer layer of photoreceptors, we improve the condition of the inner layer. That is why pan-retinal coagulation is the main method for treating diabetic retinopathy.29

With a high degree of myopia or with “parquet type” (tessellated fundus), diabetic retinopathy does not develop.30

In cases of high myopia or tessellated fundus, diabetic retinopathy does not develop. These two layers of the retina are in opposition to each other. This phenomenon manifests itself throughout the body.

It has been shown that optic ibers from the periphery of the retina go to the superior colliculus, while ibers from the center of the retina go tothe lateral geniculate body.Azerbaijani neurophysiologists have established that these two channels are in an opposing relationship. When one channel is stimulated, the activity of the other channel is suppressed and vice versa.31 It is interesting to note that when gastrointestinal diseases occur, brain diseases or dementia32, are less likely to occur, and vice versa. When there is a gynecological pathology, there may not be any eye diseases. Sometimes gynecological diseases disappear, and optic neuritis,24 or retinal diseases34 may suddenly appear. So throughout the body.

Cells cannot exist without competition with other cells for habitat and food resources. Competitive interactions between cells are the basis of many homeostatic processes in biology.35

This competition also manifests itself in the macroorganism. In recent years, many articles have appeared devoted to the role of microbiota in the occurrence of various human diseases. The human body cannot exist without microbiota (the struggle of opposites).

In particular, the role of gut microbiota in the occurrence of dry eye syndrome36,37 and glaucoma

has been established.38,39,40 An imbalance of the microbiota and the human immune cells surrounding them can lead to various eye diseases: diabetic retinopathy, uveitis, and orbitopathy.41

Studies conducted by some authors on clinical cases in patients suggest the possible role of gut microbiota in the development of retinal diseases. The question arises, how does gut microbiota cause retinal diseases?

**Figure 4.** *The outer part of the retina is colored red, the inner part of the retina is colored green. Yellow represents Müller cells, which contain the yellow pigment lipofuscin. Atrophy of Müller cells in the outer plexiform layer results in hard exudates. 30*

12

**Evolution of the human eye**

To answer this question, we must turn to the evolution of man and the eye.

Considering the aforementioned literature data on the role of microbiota in the occurrence

© 2024 OCH. Journal of Ophthalmology Cases & Hypotheses / Published by Hat Medicine Clinic

Special Issue. Ophthalmol. Cases. Hypotheses, (2024), 5:2

of eye diseases, we believe that the human organism exists thanks to microbiota. Microbes colonize and reside on the mucous membranes of cells that are in contact with the external environment. The aggression of microbes is restrained by immune cells, creating a state of dynamic equilibrium (the struggle of opposites). After unicellular organisms, coelenterates appeared. That is, an environment (intestinal tube) populated bymicroorganisms – microbiota – emerged, which began to regulate all the life activities of the macroorganism.

The immune system of Hydra developed due to the need to control the resident microbiota. Protection against invasive pathogens is secondary compared to the need to regulate commensals.43

The microbiota of the coelenterate gut tube was surrounded by primary immune cells. A state of balance emerged. At that time there was no acquired immunity and the state of equilibrium was maintained by innate immunity.

Authors also review observations that indicate that resident bene icial microbes affect the animal’s behavior by directly interfering with neuronal receptors.44

Also, the formation of the future eye system begins with Hydra. Sensitive opsins were also found in hydra nerve cells. The analysis of the hydraopsin gene suggests that hydraand human opsins have a common origin.46

Box jelly ish, which are also coelenterates, also have eyes. 46,47,48 These are primitive eyes that developed due to the functioning of the gut microbiota. This is why a number of eye diseases are associated with disturbances in gut microbiota. 49,50

The eyes of cuboid jelly ish are primitive, capable of distinguishing light from darkness. Then, in the process of evolution, the eyes improved and other newly formed microbiota began to take part in their development (for example, the microbiota of the genitourinary tract and others).

In addition, the conjunctiva of the eye itself is also populated by microbiota and regulates the

conjunctiva, cornea, and iris. However, since at the beginning of evolution the conjunctiva was regulated by the gut microbiota, its disruption can lead to dry eye syndrome, glaucoma, and AMD.

**The ϐirst clinical attractor**

How does the microbiota of the gastrointestinal tract work? The intestine irst appeared in coelenterates. A typical representative of coelenterates is a hydra. There has been a huge revolution in biology. The body of a living creature has its own microbes. These microbes surround immune cells.

An entirely new dynamic community has emerged, consisting of the intestinal microbiota, surrounding immune cells, and the epithelial cells of the Hydra “gut.” By analogy with ancient Roman history, wegavethis community the name *triumvirate.*

This microbiota not only helps digest food,51 but also regulates all the vital functions of coelenterates. What is an attractor?

An Attractor is a term used to describe any system that remains stable without any changes over time. The simplest attractor is a pendulum-shaped attractor. The attractor is a single point; all trajectories spiral in toward it, like a pendulum slowing down and coming to rest, pulled to the single center of gravity. Complex periodic attractor, indicating a system that repeats itself periodically.

All Hydra cells together with the triumvirate (epithelial cells, microbiota, immune cells) represent the irst gastrointestinal, complex clinical attractor.

A change in one of the components of the “triumvirate” can lead toachange in the functional state of the hydra (by analogy with a person, the appearance of characteristic symptoms or diseases). But then, thanks to the lability of the “triumvirate,” the work of the immune system returns the clinical attractor to its original state.

Thus, it is the gut attractor triumvirate that determines the entire life activity of coelenterates,

13

A new theory of the emergence of eye diseases based on the imbalance of human microbiota. A critical review of the literature

their health, eye condition, timing of division, aggressive. This impacts the cells, causing

reproduction and further evolution.

An interesting question is how an imbalance of the gut attractor microbiota and the antibodies surrounding them can lead to dry eye syndrome, glaucoma or AMD?

**Interaction of microbiota with immunoglobulins**

Our question addresses the complex dynamics between different populations of microbes and the immune system. The competition for resources among microbes and the interaction with antibodies is a multi-layered process.

The microbiota living on mucous membranes is heterogeneous. Various bacteria can be observed there. Even bacteria of the same type differ in their antigenic composition. These microbes compete for resources, for territory. Immunoglobulins appear to be produced by the average determinant of the microbial population.

When different strains of microbes compete for resources, it can alter their numbers and population structure. If more aggressive or extreme forms start to dominate, this can indeed cause a change in the pro ile of immunoglobulins produced. The immune system, particularly B-cells, is capable of adapting to new antigens by producing immunoglobulins speci ic to the new dominant strains.

*This adaptation may involve:*

1. Clonal selection and proliferation of B-cells that are speci ic to new antigens.

2. The process of af inity maturation, where antibodies become more speci ic to the antigens they encounter.

The degree of microbial adherence to antibodies, or avidity, is of paramount importance. If microbes were left unchecked, they could completely destroyall the cells in the body,similar to what happens post-mortem. Immunoglobulins restrain microbial aggressiveness. However, if the antigenic composition of microbes changes, their adherence decreases, making them more

14

changes in their orientation relativeto each other, potentially altering the fractal structure of the cells. These alterations can lead to diseases. The speed at which the immune system can restore the original avidity will determine whether the symptoms will disappear. In other cases, changes in the fractal structure can propagate like a “domino” effect, affecting other areas controlled by this attractor.

Thus, the triumvirate system (cells, microbiota, immunoglobulins) is constantly subject to changes (due to constant changes in avidity between microbiota and immunoglobulins) and this is re lected in the functioning of the corresponding clinical attractor.

Thus, the immune system and microbiota are in constant dynamics.

Changes in one system inevitably led to changes in another. If extreme forms of microbes begin to dominate and the immune system does not keep up with the adaptation to new antigens, this can cause an imbalance that can lead to disease.

Competition among microbes can also in luence the immune response, leading to changes in in lammation levels and cytokine production. Thus, the immune system and microbiota are in constant dynamic interaction, where changes in one system lead to responses in the other.

The description of microbiota as a system that is constantly changing and recovering indeed resembles the behavior of complex attractors in chaotic systems.”

Chaotic systems are characterized by high sensitivity to initial conditions and unpredictable but deterministic behavior. In biological systems, such as the microbiota and the immune system, similar properties can be observed.

The microbiota can change under the in luence of various factors, including diet, environment, and infections, which in turn affects the immune response of the body.52,53,54

These dynamic and unpredictable changes can be considered chaotic because they lead to

© 2024 OCH. Journal of Ophthalmology Cases & Hypotheses / Published by Hat Medicine Clinic

Special Issue. Ophthalmol. Cases. Hypotheses, (2024), 5:2

nonlinear responses and dif iculty in predicting Neurons in the brain are constantly in a state the system’s future behavior. Our comparison of self-sustaining criticality. Any frequent

with a pendulum returning to its original state is also appropriate, since it re lects the idea of a stable state around which a system can oscillate.

Thus, the microbiota and immune system can be viewed as a chaotic system where constant change and adaptation are key characteristics. This highlights the importance of understanding the dynamics of such systems for the development of new treatments and health maintenance.

Our description of the triumvirate of the microbiota, antibodies, and epithelial cells highlights the importance of the interactions between these components in maintaining homeostasis. If we consider them as a single unit, it becomes clear that any disturbance in one of these elements can lead to an imbalance, which then causes pathological conditions. When the immune system fails to quickly adapt to changes in the microbiota or antigenic composition, it can indeed lead to chronic in lammation.

**Self-organised criticality (SOC)**

The last decade and a half has seen an ardent development of self-organized criticality (SOC), a new approach to complex systems.55

“If wekeep pouring grains of sand, a heap will soon form. The heap will become steeper and steeper until the pile of sand reaches a critical state. It is unknown when the next grain might cause an avalanche. A catastrophe will occur, but the system will not leave the critical state. The heap of sand will remain just as steep. It will take very few new grains for another avalanche to occur. Avalanches will continue to occur again and again. Their size can vary, for example, from small landslides to large ones involving 30-40% of the sand. And yet, it will remain in a critical state.

This is a very interesting phenomenon of self-organized criticality. This phenomenon is found everywhere. It is found in evolutionary theory, population dynamics, social phenomena, and medicine.

disturbances can trigger cascading activations of neurons.56

**“Self-organized criticality in immunology**

How can the theory of self-organized criticality be applied tohumans? It manifests in everything, especially in immunity.

With the exception of passive immunity, humans have two main types of immunity—innate and acquired immunity. The former evolved in primitive organisms, and the latter appeared in vertebrates. Innate immunity reacts quickly (between several hours to days), while the latter reacts slowly (days to years).57

The cellular components of innate immunity consist of macrophages, natural killer (NK) cells, and mast cells, while the cellular components of acquired immunity are made up of T and B cells.58

IgM is often associated with the initial stage of infection, as it is produced irst in response to an antigen.59 An increase in IgM levels may indicate a recent infection. IgG, on the other hand, indicates a more mature immune response and can suggest an ongoing or past infection.60

Studying other types of antibodies can also aid in diagnosis. For example, IgE is elevated in allergic reactions and some parasitic infections.61 IgA is important for the protection of mucous membranes and can be linked to immune disorders in these areas.

Humans suffer from a vast number of diseases of the digestive organs, respiratory organs, urogenital organs, and the eyes. All these diseases are related to changes in the balance of immunoglobulins in the blood. However, we cannot determine how changes in the balance of immunoglobulins in the blood in luence the development of hundreds of diseases. Why?

Mammals make ive classes of antibodies, each of which mediates a characteristic biological response following antigen binding.62

15

A new theory of the emergence of eye diseases based on the imbalance of human microbiota. A critical review of the literature

Immunoglobulins circulating in the blood are *body’s own microbiota (epitopes of microbiota* produced against various microbiota present *antigens)*. SIgA located in the mucous

in the human body (gut microbiota, urogenital microbiota, respiratory tract microbiota, ocular and aural microbiota Figure. 5). It is interesting to note that there are 5 types of microbiotas and 5 types of immunoglobulins in the body. Is this a coincidence or not?

**Figure 5.** *Schematic representation of immunoglobulins responsible for different microbiota in the blood.*

**Triumvirate**

We have called the symbiosis of the microbiota, the surrounding secretory immunoglobulins, and the epithelial cells of the mucous membranes

membranes of the microbiota on one side can be bound at one end to the microbiota epitope MHC-1 of the epithelial cell, and at the other end can be bound to microbes in the mucous membranes. That is why they are characterized by dimerism (Figure. 6).

Since these are fragments of the body’s own microbiota, for which immunoglobulins have already been produced, T-killers do not react to them. The immune system of the body monitors this, which in some cases can test epitopes and, when changing the antigen composition of the microbiota or changing its af inity with antibodies, trigger a new immune response.

There is a constant change in the antigens of the microbiota in the body, and accordingly, the hypervariable regions (CDR-complementarity-determining regions) of immunoglobulins that interact with this microbiota are also changing. Even hypervariable regions of immunoglobulins, such as CDR, exhibit fractal geometry.64

that contact the external environment (for example, the epithelium of the digestive tract) a ‘triumvirate,’ by analogy with ancient Roman history. Each epithelial cell contains a major histocompatibility complex (MHC-1) on its surface.

On the surface of MHC class-I complexes, there are peptides that are fragments of intracellular proteins. These peptides can be either self-derived (originating from normal cellular proteins) or non-self (such as viral proteins during infections).

Cytotoxic T-lymphocytes (T-killers) recognize

these peptides through their T-cell receptors (TCR). If the TCR detects a peptide that is different from normal self-peptides (such as a viral or mutant protein), the T-cell becomes activated and can destroy the infected or abnormal cell.63

What are peptides that are fragments of intracellular proteins? *It can be assumed that these are active fragments of antigens of the*

16

**Figure 6.** *Schematic representation of the ‘triumvirate’. Peptides on the surface of MHC-1 are epitopes of the microbiota. Secretory immunoglobulins monitor this, which in some cases can test the epitopes and change their structure when the antigen composition of the microbiota changes*

© 2024 OCH. Journal of Ophthalmology Cases & Hypotheses / Published by Hat Medicine Clinic

Special Issue. Ophthalmol. Cases. Hypotheses, (2024), 5:2

Then the peptide protein of somatic cells immunoglobulin to the antigen. The degree immediately changes. This process occurs of binding (af inity) can be either weaker or

constantly. Moreover, this is characteristic of each clinical attractor with its own microbiota.

stronger. In either case, symptoms of diseases or the diseases themselves may appear

The balance of ocular microbiota helps protect For a clinical attractor, a certain type of

the eye from pathogens, modulates the immune response, and maintains the integrity of the tear ilm. Disruption of this balance can lead to various ophthalmological conditions, such as conjunctivitis, keratitis, and dry eye syndrome

**What ensures the normal balance in the triumvirate?**

1. The total amount of immunoglobulins in the blood is relatively constant. They are all distributed among the iveclinical attractors. Each microbiota is characterized by a certain amount of immunoglobulins. An increase in the amount of immunoglobulins for gut microbiota can lead to a decrease in the amount of immunoglobulins for urogenital microbiota.

2. Each microbiota is characterized by a speci ic type of immunoglobulins. For example, gut microbiota is more characteristic of immunoglobulin type IgA. Although other immunoglobulins can also act there.

3. Af inity. The degree of binding of immunoglobulins to the microbiota can vary. For gut microbiota, low af inity is likely characteristic. This is necessary so that the microbiota also participates in the absorption of food.

**Avidity of immunoglobulins**

1. Each triumvirate of the clinical attractor regulates the tissues and organs under its control. However,these tissues and organs can sometimes affect other triumvirates of other clinical attractors. The appearance of clinical symptoms and diseases occurs in the following cases

2. The avidity of immunoglobulins to the microbiota changes. Secretory immunoglobulins are located on mucous membranes. Each microbiota of a clinical attractor is characterized by a certain degree of binding of the secretory

immunoglobulin may be characteristic. Can you imagine how many possible interactions there are between microbiota and immunoglobulins?

Immunoglobulins are produced for each of these microbiotas. These immunoglobulins are found both on the epithelial cells of the microbiota and circulating in the blood. Thus, the blood contains a whole set of all immunoglobulins. We do not know which of them are responsible for which microbiota. Besides, there are immunoglobulins against various viruses and other bacteria with which the organism has come into contact. This is schematically represented in the drawing (Figure. 5).

Each triumvirate of the clinical attractor regulates the tissues and organs under its control. A change in the balance at the level of the triumvirate can lead to the appearance of certain clinical symptoms and diseases in the tissues and organs under the control of this attractor. Interestingly, the condition of other organs under the control of this attractor improves. For example, with a stomach ulcer (gut attractor), there are usually no serious brain diseases (tumors, Alzheimer’s disease), and vice versa.”

**Relationship between humoral and secretory immunoglobulins**

Immunoglobulins circulating in the blood indeed play a crucial role in our immune response. Most of these immunoglobulins are produced in response to our microbiota, especially on mucous membranes.

Secretory Immunoglobulin A is the predominant mucosal antibody, which binds pathogens and commensal microbes. SIgA is a polymeric antibody, typically containing two copies of IgA that assemble with one joining chain to form dimeric IgA that is bound by the polymeric Ig-receptor ectodomain, called secretory component.67

17

A new theory of the emergence of eye diseases based on the imbalance of human microbiota. A critical review of the literature

Innormal conditions, secretory immunoglobulin A (SIgA) is the principal antibody produced by B cells in the GIT mucosa.68

IgA is the most dominant immunoglobulin class in humans. IgA-producing cells are mainly distributed in the mucosa lining tissues such as the intestine and oral and nasal cavities.69 But there can also be IgG immunoglobulins.70

Secretory immunoglobulins A (sIgA) and humoral immunoglobulins A (IgA) are closely related. IgA in the blood is primarily in monomer form and can penetrate mucous membranes. Once there, they transform into sIgA by binding with the secretory component, which helps IgA move through epithelial cells and stabilizes it on the surface of mucous membranes.71

Thus, humoral IgA produced in response to microbiota can convert into sIgA, playing a crucial role in protecting mucous membranes from pathogens. The connection between them lies in their common origin and functional transformation, providing an effective immune response both in the bloodstream and on mucous surfaces.72

**Interaction between ocular microbiota and gut microbiota**

How can gut microbiota cause dry eye syndrome,37 and glaucoma 73 or AMD?74,75

Consider this with the example of the epithelial cells of the conjunctiva and cornea. A tear ilm is present on their surface. This ilm contains ocular microbiota.76

Therefore, MHC-1 cells of the conjunctiva contain antigenic determinants of ocular microbiota in the form of peptides. But, since the evolutionary development of the eye arose in coelenterates, some MHC-1 cells of the conjunctiva may contain antigenic determinants of gut microbiota in the form of peptides. Therefore, regulation occurs from two different microbiota.

Disturbances in nutrition or competition between microbes in the gastrointestinal tract for resources can lead to an imbalance between the gut microbiota and the surrounding immunoglobulins (changes in the avidity of immunoglobulins with antigens). A disturbance in the antigen composition of the gut microbiota will immediately lead to a change in the

When the antigenic composition of the antigenic determinant present on the MHC-

microbiota changes, it primarily affects the humoral immunoglobulins A (IgA) in the blood. Then the information about the changes is

1 cells of the conjunctiva. This can change the local immunological status and lead to the appearance of symptoms of conjunctivitis or dry

transmitted to secretory immunoglobulins eye syndrome (Figure.7) A (sIgA), which are located on mucous

membranes and have a more direct contact with the microbiota. Thus, the changes start with humoral immunoglobulins and then are passed on to secretory ones.

To further advance our understanding in the

ield of immunology, it is essential to conduct scienti ic studies aimed at identifying and thoroughly describing the mechanisms of

interaction between humoral and secretory immunoglobulins of class A. This will help elucidate their relationship and coordinated involvement in the body’s immune defense.

**Figure 7.** *MHC-1 cells of the conjunctiva contain antigenic determinants of ocular microbiota in the form of peptides. However, since the evolutionary development of the eye arose in coelenterates, some MHC-1 cells of the conjunctiva may contain antigenic determinants of gut microbiota in the form of peptides.*

18

© 2024 OCH. Journal of Ophthalmology Cases & Hypotheses / Published by Hat Medicine Clinic

Special Issue. Ophthalmol. Cases. Hypotheses, (2024), 5:2

**Optic nerve and optic tract**

The ocular attractor regulates the condition of the conjunctiva, the anterior segment of the eye, and the optic nerve, optic tract, and adjacent neurons. The optic nerve and optic tract are also regulated solely by ocular microbiota. This is con irmed by the fact that in the treatment of optic nerve atrophy using the new HAT Medicine method, with the help of minimal antibacterial drugs aimed at partially suppressing the ocular microbiota, there is an improvement in visual acuity and visual ields in all cases.77

This occurs regardless of the cause of optic nerve atrophy (trauma, tumor, glaucomatous atrophy, provided normal intraocular pressure). When treating young patients with optic nerve atrophy and associated neurological disorders using the new method, children’s muscle tone improves dramatically, they become more active, and neurological symptoms decrease (Figure. 8).78

By normalizing the balance between ocular microbiota and the surrounding immunoglobulins, it is possible to achieve remission of optic nerve atrophy and improvement of visual functions.

It is possible that in some cells surrounding neurons, MHC-1 relates tothe peptide determinant of the genitourinary tract microbiota. This assumption is because optic neuritis often occurs in women after menstrual cycle disturbances or genitourinary tract diseases. 79,80,81

**Conclusions**

From the new perspective of Chaos, the emergence of all human diseases, particularlyeye diseases, is considered.

All cells in the body are arranged in the form of fractals. In diseases, the fractal structure of cell arrangement is disrupted.

The basis for the emergence of diseases and the disruption of the fractal structure of cells lies in the imbalance between the epithelial cells of humans that come into contact with the external environment, the microbiota, and the surrounding immunoglobulins. This symbiosis

between mucosal cells, microbiota, and

**Figure 8.** *The optic nerve and optic tract are regulated by the ocular microbiota. The ocular microbiota is also responsible for the areas of the brain located near the optic tract.*

Therefore, MHC-1 of the neurons of the visual pathway, oligodendroglia covering the nerve, and brain cells located near the visual tract are connected to the epitope peptide (antigenic determinant) of the ocular microbiota.

immunoglobulins is called the “triumvirate,” by analogy with ancient Roman history.

This triumvirate regulates all organs and tissues of the body. This entire system represents a “clinical attractor.” The term “clinical attractor” re lects the idea of a self-sustaining system where interactions between the microbiota, mucosal membranes, and surrounding antibodies regulate various tissues in the body.

There are ive clinical attractors in the body: gut attractor, urogenital attractor, respiratory attractor, ocular attractor, and aural attractor.

It is hypothesized that peptides on the surface of MHC-1 of somatic cells are epitopes of the microbiota. Each cell of an organ or tissue in the human body has MHC-1 on its surface, which is an epitope of a speci ic microbiota. The speci ic antigenic determinant of the microbiota on the cells of the conjunctiva, choroid, and retina

19

A new theory of the emergence of eye diseases based on the imbalance of human microbiota. A critical review of the literature

depends on the evolutionary history of that speci ic tissue.

For example, a peptide associated with MHC-1 cells of the optic nerve and visual tract is characteristic of the ocular microbiota. Restoring the balance between the ocular microbiota and the surrounding antibodies can stop the progression and improve the visual functions of patients with optic nerve atrophy.

This theory provides a new perspective on the origin and treatment of all human diseases.

**Ethics**

**Peer-review:** Externally peer-reviewed.

**Conϐlict of Interest:**

No con lict of interest was declared by the author.

**Data availability statement**

The data that support the indings of this study

3. Cobb M. 1953: When Genes Became “Information”. Cell. 2013;153(3):503-506. doi:10.1016/j. cell.2013.04.012

4. Ahn AC, Tewari M, Poon CS, Phillips RS. The limits of reductionism in medicine: could systems biology offer an alternative? PLoS Med. 2006;3(6):e208. doi: 10.1371/journal.pmed.0030208

5. Cannon, W. B., Organization for physiological homeostasis. Physiological reviews 1929; 9: 399– 431

6. Lassoued, A. and O. Boubaker, Modeling and control in physiology. In book:Control Theory in Biomedical Engineering. 2020. pp. 3–42. doi: 10.1016/B978-0-12-821350-6.00001-9.

7. Scheer FA, Czeisler CA. Melatonin, sleep, and circadian rhythms. Sleep Med Rev*.* 2005; 9(1):5-9. doi: 10.1016/j.smrv. 2004.11.004.

8. Poon CS, Merrill CK. Decrease of cardiac chaos in congestive heart failure. Nature. 1997; 2; 389(6650):492-5. doi: 10.1038/39043.

9. Goldberger AL, Amaral LA, Hausdorff JM. et al. Fractal dynamics in physiology: alterations with disease and aging. Proc Natl Acad Sci U S A. 2002 Feb 19;99 Suppl 1(Suppl 1):2466-72. doi:

10.1073/pnas.012579499.

are available from the corresponding author upon reasonable request.

**Funding**

None.

**Study association**

This study is not associated with any thesis or dissertation work.

10. Kannel W. Prevalence and implication of uncontrolled systolic hypertension. Drugs Aging. 2003; 20(4):277–286. doi: 10.2165/00002512-200320040

11. Rose G. The strategy of preventive medicine. Oxford: Oxford University Press; 1994. 160 pp.

12. Kitano H. Looking beyond the details: A rise in system-oriented approaches in genetics and molecular biology. Curr Genet. 2002;4(1):1–10. doi: 10.1007/s00294-002-0285-z.

13. Kitano H. Systems biology: A brief overview.

Science. 2002;295(5560):1662–1664. doi: 10.1126/science.1069492

14. Ehrenberg M, Elf J, Aurell E, Sandberg R,

**References and notes:**

1. Lindberg D. C. The beginnings of Western science: The European scienti ic tradition in philosophical, religious, and institutional context, prehistory to AD 1450. – University of Chicago Press, 2010.:

2. Sweeney K, Kernick D. Clinical evaluation: constructing a new model for post-normal medicine. J Eval Clin Pract. 2002; 8(2):131-138.

doi:10.1046/j.1365-2753.2002.00312.x

Tegner J. Systems biology is taking off. Genome Res. 2003;13(11):2377–2380. doi: 10.1101/ gr.1763203

15. Weston AD, Hood L. Systems biology, proteomics, and the future of health care: Toward predictive, preventative, and personalized medicine. J Proteome Res. 2004 Mar-Apr;3(2):179-96. doi: 10.1021/pr0499693. PMID: 15113093.

16. Federoff HJ, Gostin LO (September 2009).

“Evolving from reductionism to holism: is there

20

© 2024 OCH. Journal of Ophthalmology Cases & Hypotheses / Published by Hat Medicine Clinic

Special Issue. Ophthalmol. Cases. Hypotheses, (2024), 5:2

a future for systems medicine?”. JAMA. 302 (9): 994–6. doi:10.1001/jama.2009. 1264.

17. Kumar A., Hegde B.M. Chaos theory: impact on and applications in medicine. Nitte Univ J Health Sci 2012; 2(4):93-99. doi:10.1055/s-0040-1703623

18. Ferreira B.B., Souza de Paula A., Savi M.A. Chaos

29. Hajiyev R.V. On the pathogenesis of diabetic retinopathy and central retinal vein occlusion. 2011, Baku, Poligraphic production. 71s (russian language)

30. Hajiyev R.V. On the pathogenesis of diabetic

retinopathy, damage to muller cells, diseases

control applied to heart rhythm dynamics Chaos, of opponents, and in lammation: a review.

Solitons and Fractals 2011; 44(80):587-599. doi:10.1016/j.chaos. 2011.05.009

19. Havlin S., Buldyrev S.V., Goldberger A.L. et al.

Ophthalmology Cases and Hypotheses. 2021; 2(2):5-8. doi: 10.30546/2788-516X.2021. 2.2.14

31. Gasanov GG, Gadzhieva NA, Kulgavin LE. Kontrol’

Fractals in biology and medicine. 1995;6:171-201. provedeniia afferentnoĭ impulsatsii cherez doi: 10.1016/0960-0779(95)80025-c. naruzhnoe kolenchatoe telo bodrstvuiushchego

20. Crutch ield, J. Erratum: Between order and krolika so storony verkhnikh bugrov chaos. Nature Phys 9, 382 (2013) .https://doi. chetverokholmiia [Control of conduction of org/10.1038/nphys2639 afferent impulses across the lateral geniculate

21. Lorenz E.N. “Atmospheric predictability as body by the side of the superior colliculus revealed by naturally occurring analogues”. in alert rabbits]. Bull. Eksp Biol Med. 1989 Journal of the Atmospheric Sciences. 1969; 26 (4): Oct;108(10):387-9. Russian. PMID: 2597745

636–646.2. 32. Hajiyev, R.V. On the relationship between

22. Mandelbrot B. The Fractal Geometry of Nature. 1982, United States, W.H.Freeman and Co. ISBN 0-7167-1186-9

23. Sendker FL, Lo YK, Heimerl T, Bohn S. et

diseases of the gastrointestinal tract and the occurrence of dementia in humans (Tesselated Fundus), Ophthalmology Cases & Hypotheses. 2022;

3(2):11-14 doi: 10.30546/2788-516X. 2021.3.2.14

al. Emergence of fractal geometries in the 33. Hajiyev R.V. On The Connection between evolution of a metabolic enzyme. Nature. 2024 In lammatory Diseases of the Female

Apr;628(8009):894-900. doi: 10.1038/s41586-

024-07287-2

Reproductive System and The Occurrence of Optic

Neuritis, Ophthalmology Cases & Hypotheses.

24. Ionescu C., Oustaloup A., Levron F., et al. 2024; 5(1):16-20. doi: 10.30546/2788-A Model of the Lungs Based on Fractal 516X.2024.018.0275

Geometrical and Structural Properties IFAC 34. Mammadova, G. (2023) Sudden decrease in vision

Proceedings Volumes 2009;42(10):994-999.doi.

org/10.3182/20090706-3-FR-2004. 00165

in one eye after sharp pains in the back and lower

abdomen, Ophthalmology Cases & Hypotheses.

25. Gaudio E, Chaberek S, Montella A, et al. Fractal

and Fourier analysis of the hepatic sinusoidal

2023;4(1):16-19. doi: 10.30546/2788-

516X.2023.4.1.16.

network in normal and cirrhotic rat liver. J 35. Johnston LA. Competitive interactions between Anat. 2005;207:107-115. doi.org/10.1111/ cells: death, growth, and geography. Science.

j.1469-7580.2005.00436.x

26. Iannaccone PM. Fractal geometry in mosaic

2009 Jun 26;324(5935):1679-82. doi: 10.1126/

science.1163862. PMID: 19556501

organs: a new interpretation of mosaic pattern. 36. Watane A., Raolji S., Cavuoto K., Galor A.

FASEB J. 1990 Mar;4(5):1508-12. doi: 10.1096/ fasebj.4.5.2307328.

27. Grizzi F, Spadaccini M, Chiriva-Internati M, et

al. Fractal nature of human gastrointestinal

Microbiome and immune-mediated dry eye: a review. BMJ Open Ophthalmology. 2016;7(1). doi:10.1136/bmjophth-000956

37. Moon J, Yoon CH, Choi SH, Kim MK. Can Gut

system: Exploring a new era. World J Microbiota Affect Dry Eye Syndrome? Int J Mol

Gastroenterol. 2023; 29(25): doi: 10.3748/wjg. v29.i25.4036]

28. McGill V.J., Parry W.T. The Unity of Opposites: A

dialectical principle. JSTOR Science and Society.

Sci. 2020 Nov 10;21(22):8443 doi: 10.3390/ ijms21228443. PMID: 33182758

38. Huang L., Hong Y., Fu S. et al. The role of the

microbiota in glaucoma. Molecular Aspects of

1947; 12(4):418-444 Published by: Guilford Press Medicine 2023;94. doi:10.1016/j.mam.2023. 101221

21

A new theory of the emergence of eye diseases based on the imbalance of human microbiota. A critical review of the literature

39. Lee, J.W., Lim, S.H., Shin, J.H., Lee, Y., Seo, J.H. 11, 609765. doi.org/10.3389/ immu.2020. Differences in the eyelid and buccal microbiome 609765

between open-angle glaucoma and uveitic 51. Lenhoff H.M. Digestion of protein in Hydra as

glaucoma. Acta Ophthalmol. 2022;100, e770– e778 doi: 10.1111/aos.14967.

40. AstafurovK, Elhawy E, Ren L. et al. Oral microbiome link to neurodegeneration in glaucoma. PLoS One. 2014 Sep 2;9(9):e104416. doi: 10.1371/journal. pone.0104416.

41. Fu X., Tan H., Huang L. et al. Gut microbiota and eye diseases: a bibliometric study and visualization

analysis. Front. Cell.Infect. Microbiol. 2023; 13(09

studied using radioautography and fractionation by differential solubilities, Experimental Cell Research, 1961; 23(2):335-353. doi.org/10.1016 /0014-4827(61)90043-X.

52. Hasan N., Yang H. Factors affecting the composition of the gut microbiota, and its modulation. Peer.J. 2019; e7502 doi: 10.7717/peerj,7502

53. Zhang P. In luence of Foods and Nutrition on the

Gut Microbiome and Implications for Intestinal

August) doi.org/10.3389/fcimb.2023.1225859 Health. International Journal of Molecular 42. Mammadkhanova, A. (2021) Acute posterior Sciences. 2022; 23(17):9588. https://doi.

multifocal placoid pigment epitheliopathy org/10.3390/ijms23179588)

(APMPPE), its possible relationship with urogenital 54. Bourdeau-Julien, I., Castonguay-Paradis, S., tract disorder and treatment, Ophthalmology Rochefort, G. et al. The diet rapidly and differentially Cases & Hypotheses. 2021; 2(2):9-13. doi: affects the gut microbiota and host lipid mediators

10.30546/2788-516x.2021.2.2.9

43. Thomas C.G. Bosch. Rethinking the role of

in a healthy population. Microbiome 11, 26 (2023).

https://doi.org/10.1186/s40168-023-01469-2

immunity: lessons from Hydra. Trends in 55. Bak P., Tang C., Wiesenfeld K. Self-organized Immunology. 2014; 35(10):495502. doi.org criticality// Phys. Rev. A. 1988. V.38, N1, p.364-3 /10.1016/j.it.2014.07.008. 56. Plenz D., Ribeiro TL, Miller R., Kells PA et al., Self-

44. Kimovich A.V., Bosch T.C.G. Rethinking the Organized criticality in the brain. Section Section

role of the nervous system: lessons from the hydra holobiont. BioEssays 2018; 40(9): doi.

org/10.1002/bies.201800060

on Critical Brain Dynamics, National Institute of Mental Health, National Institutes of Health,

Bethesda, MD, USA p.40

45. MacKenzie D. Eeyless hydra shed light on 57. Medzhitov R., Janeway C.A. Innate immunity: how eyes could have evolved New Scientist. impact on the adaptiveimmune response. Current

2010;205(2751):10. doi.org/10.1016/S0262-

4079(10)60566-0

Opinion in Immunology 1997; 9(1):4-9. https://

doi.org/10.1016/S0952-7915(97)80152-5

46. Bielecki J.,Dam Nielsen S.K., Gösta Nachman G.,Garm, A. Associative learning in the box jelly ish

Tripedalia cystophora, Current Biology 2023;

58. Jee YS. Acquired immunity and moderate physical exercise: 5th series of scienti ic evidence. J Exerc

Rehabil. 2021 Feb 23;17(1):2-3. doi: 10.12965/

33(19):4150-4159. https://doi.org/10.1016/j.

cub.2023.08.056)

jer.2142042.021.

59. Boes M. Role of natural and immune IgM

47. Nilsson D.E., Colley N.J. Comparative Vision: antibodies in immune responses, Molecular Can Bacteria Really See? Current Biology 2016; Immunology 2000;37(18): 1141-1149. doi.

26(9):369-371.doi.org/10.1016/j.cub.2016. 03.025

48. Shubert M. Sight in a single cell The Ophthalmologist

org/10.1016/S0161-5890(01)00025-6.)

60. Seeling M., Pöhnl M., Kara S., et al. Immunoglobulin

G-dependent inhibition of in lammatory bone

2015. https://theophthalmologist.com/ remodeling requires pattern recognition receptor

subspecialties/sight-in-a-single-cell

49. Siddiq MAB, Jahan I, Rasker JJ. Statin in Clinical and

Dectin-1,Immunity 2023;56(5):104601063. doi.

org/10.1016/j.immuni.2023.02.019

Preclinical Knee Osteoarthritis-What E vidence 61. Ansotegui I.J., Melioli G., Canonica G.W. et Exists for Future Clinical Use?-A Literature Review. al. Erratum to IgE allergy diagnostics and Curr Rheumatol Rev. 2023 Jun 5;19(3):270-280. other relevant tests in allergy, a World Allergy doi: 10.2174/1573397118666220930141740 Organization position paper, World Allergy

50. Li, J.J., Yi, S., Wei, L., Ocular microbiota and intraocular in lammation. Front. Immunol*.* 2020;

22

Organization Journal. 2020;13(2):1939-4551. doi.

org/10.1016/j.waojou.2019.100080.

© 2024 OCH. Journal of Ophthalmology Cases & Hypotheses / Published by Hat Medicine Clinic

Special Issue. Ophthalmol. Cases. Hypotheses, (2024), 5:2

62. Alberts B., Johnson A., Lewis J, et al. Molecular biology of the cell. 4th edition 2002, New York:

Garland Science

73. Chen J, Chen DF, Kin-Sang Cho KS, The Role of Gut Microbiota in Glaucoma Progression and

Other Retinal Diseases, The American Journal of

63. Rout P, Caminero F, Iqbal Z, et al. Histology, Pathology, 2023;193,(11):1662-1668. https:// Cytotoxic T Cells. [Updated 2023 Sep 20]. In: doi.org/10.1016/j.ajpath.2023.06.015

StatPearls [Internet]. Treasure Island (FL): 74. Lin P, McClintic SM, Nadeem U, Skondra D. A StatPearls Publishing; 2024 Jan-. Available Review of the Role of the Intestinal Microbiota from: https://www.ncbi.nlm.nih.gov/books/ in Age-Related Macular Degeneration. J Clin

NBK559279/

64. Sendker FL, Lo YK, Heimerl T, Bohn S, et al.

Emergence of fractal geometries in the evolution

Med. 2021 May 12;10(10):2072. doi: 10.3390/ jcm10102072.

75. Luo W, Skondra D. Implication of gut microbiome

of a metabolic enzyme. Nature. 2024 Apr; in age-related macular degeneration. Neural

628(8009):894-900. doi: 10.1038/s41586-024-07287-2.

65. Hajiyev R.V. Prediction of exacerbation of chronic in lammatory diseases. Patent I 2004 0078 Baku

Azerbaijan (in Azeri).

Regen Res. 2023 Dec;18(12):2699-2700. doi: 10.4103/1673-5374.373687.

76. Schlegel I, De Goüyon Matignon de Pontourade CMF, Lincke J-B, Keller I, et al. The Human Ocular

Surface Microbiome and Its Associations with the

66. Hajiyev R.V. Reaction of agglutination in Tear Proteome in Dry Eye Disease. *International* the treatment of chronic prostatitis with *Journal of Molecular Sciences.*2023; 24(18):14091.

antibacterial preparations (to the pathogenesis of chronic prostatitis). Azerbaijan Medical Journal

2014;4:27-32. (in Russian).

https://doi.org/10.3390/ijms241814091

77. Hajiyev R.V. A new approach to the treatment of

optic nerve atrophy as an in lammatory disease.

67. Kumar BS, Parker BW, Malyutin AG, et al. Journal of Life Sciences and Biomedicine. The structures of secretory and dimeric 2023;(1), 56–60. https://doi.org/10.5281/

immunoglobulin A. eLife. 2020 Oct 27;9:e56098.

doi: 10.7554/eLife.56098.)

zenodo.8004390

78. Hajiyev R.V. Treatment of optic nerve atrophy using

68. León ED, Francino MP. Roles of Secretory antibacterial drugs using a new HAT Medicine

Immunoglobulin A in Host-Microbiota Interactions in the Gut Ecosystem. Front Microbiol. 2022 Jun 2;13:880484. doi: 10.3389/fmicb.2022.880484.

69. Takeuchi T., Ohno H. IgA in human health and

method. Materials of the International scienti ic conference dedicated to the 95th birthday of Academician Zarifa Aliyeva, Baku, April 28, 2018,

c. 82-87 (In Russian)

diseases:potential regulator of commensal 79. Hajiyev R.V. On The Connection between microbiota. Fron. Immunol. 2022;13 doi. In lammatory Diseases of the Female

org/10.3389/ immu.2022.1024330

70. Zeng M.Y., Cisalpino D., Varadarajan S., et al. Gut

Reproductive System and The Occurrence of Optic

Neuritis. Ophthalmology Cases & Hypotheses.

Microbiota-Induced Immunoglobulin G Controls 2024; 5(1):16-20.doi: 10.30546/2788-516X. Systemic Infection by Symbiotic Bacteria and 2024.018.0275

Pathogens, *Immunity* 2016; 44(3):647-658. doi. 80. Shchadnykh, M. Punctate inner choroidopathy org/10.1016/j.immuni. 2016.02.006. and spontaneous abortion of the pregnancy,

71. Conley ME, Delacroix DL. Intravascular and mucosal immunoglobulin A: two separate but related systems of immune defense? Ann Intern Med. 1987 Jun;106(6):892-9. doi: 10.7326/0003-4819-106-6-892

72. Conley ME, Delacroix DL. Intravascular and mucosal immunoglobulin A: two separate but related systems of immune defense? Ann Intern Med. 1987 Jun;106(6):892-9. doi: 10.7326/0003-

4819-106-6-892

Ophthalmology Cases & Hypotheses. 2020; 1(1):5-8. doi: 10.30546/2788-516X. 2020.1.1.5

81. Aliyeva, A. and Hajiyev, R. Unusual treatment option for panuveitis, Ophthalmology Cases & Hypotheses. 2021; 2(2):5-8. doi: 10.30546/2788-

516X.2021.2.2.5

23

**CORRECTIONS**

24

**OPHTHALMOLOGY CASES AND HYPOTHESES®**

**GUIDELINES FOR AUTHORS**

Thank you for considering the Ophthalmology Cases & Hypotheses (OCH) journal as a venue for your work. We recommend reviewing the instructions for authors prior to submitting, as manuscripts not adhering to the guidelines will be returned to the author without review.

**Guidelines for Authors to Submit a Manuscript**

The Ophthalmology Cases & Hypotheses (OCH) accepts original research articles, review articles, case reports, hypotheses, clinical images, short commentary, letters tothe Editor, and Medical Ethics on EyeRelated Researches on all the aspects of ophthalmology and eye diseases. This journal publishes the study related to Strabismus, Amblyopia (Lazy Eye), Astigmatism, Blepharitis, Cataracts, CMV Retinitis, Conjunctivitis (Pink Eye), Corneal Ulcer, Detached Retina, Diabetic Retinopathy, Diplopia (Double Vision), Glaucoma, Optic atrophy, Uveitis, Macular Degeneration (AMD), Macular Dystrophy, Ocular Migraine, Ophthalmology, Ptosis (Drooping Eyelid), Retinitis Pigmentosa, Eye disorder in Pregnancy, Uveitis and other eye diseases.

Submissions shall be clear, concise, and well-documented reports. Submissions on speci ic themes are welcomed for publishing in this esteemed Journal. Published manuscripts should have not been accepted or will not be published elsewhere. Manuscripts should be devoid of any ethical problems or malpractice.The paper should be unique and not published elsewhere (except in conference abstracts). All authors should read and approve the authorship responsibility and publication ethics principles presented at our website. All authors further warrant that the undersigned are the sole authors of this work. One author has been entitled as the corresponding author with contact details and postal address. Only papers written in English are considered. The articles should be comprehensible to a reader who is luent in English and should be edited prior to submission to ensure that standard English grammar and usage are observed.

**Article type**

The journal does not publish articles in which the position of the authors does not coincide with the position of the editors, as well as serial articles under the headings “in previous issues” and “in the next issue”.

Each type of publication is de ined as follows:

1. Cases Reports 2. Research Article 3. Review Article

4. Clinical Image Article 5. Short Commentary 6. Hypotheses

7. Medical Ethics on Eye Related Researches 8. Letter to Editor etc.

The research articles should be 4–10 pages, and the review articles should be no more than 12 pages.

25

**Article Requirements:**

**Manuscript Titles**: Tile should be brief and accurate technical enough to explain the content it holds in the manuscript.

**Author(s)**: Author names need to be mentioned as Last name followed by their concern Initials without space or any punctuation.

**Afϐiliation(s)**: Author Af iliations must be provided as: Department, University, Country

**\*Corresponding author**: Last Name followed by Initials, Department, University, Complete Postal Address, Country, Telephone details;

**Original articles**: Should contain a structured abstract, 3-5 keywords, introduction, methods, results, discussion, conclusion, ethical declaration, acknowledgment, funding, and references. There is no restriction on word numbers and supporting documents. RCTs should be registered at any RCT Registries approved by the WHO.

**Case reports** (preferably with a comprehensive literature review): Should contain a structured abstract, 3-5 keywords, introduction, case presentation, discussion, conclusion, ethical declaration, acknowledgment, funding, and references. Informed consent should be obtained from the patients to report their cases. The Journal keeps the right to ask for original signed informed consent.

**Review articles**: Review article, systematic reviews or meta-analysis are most welcome. The protocol of the study should adhere to PRISMA guideline.

**Editorials and letters**: Letters and editorials should be preferably less than 2500 words. Those letters discussing about articles published in the journal should be submitted at most within 6 months after the publication of the main article. Editorials and letters will undergo the peer-review process. These articles have no abstracts.

**Manuscripts should be prepared based on the following segments:**

**Cover letter**that contains the rationale of performing the research and statement that you will not resubmit your article to another journal until the reviewing process will be completed. Also please indicate whether the authors have published or submitted any related papers from the same study to prevent Salami plagiarism.

**Title page** should include title of study, name of authors (with an email address), and their af iliations as the irst page of the manuscript. Complete mailing address, telephone number, and email address of the corresponding author should be mentioned.

**Abstract**, not less than 250 words, structural, concise, and comprehensible to readers. Keywords are used for indexing purposes; three to ive keywords should be selected

**Introduction** should cover a short background of former studies and potential gaps in the literature, and specify the aim of the study.

**Methods** should indicate evidently the stepwise approach taken to acquire the data including statistical analysis. It should be detailed mention inclusion and exclusion criteria and preferably presented in separated subsections. For reports of randomized controlled trials, authors should refer to the CONSORT statement.

**Results** should be presented in chronological order in the text, table, and illustration. Tables and igures must be cited in order in which they appear in the text, and present with the separate legend and reveal all abbreviations. Tables should be simple include titles, descriptions, footnotes and ensure all igures and tables have been cited in the text. Do not present tables with duplicate information in the text of the paper. Figures should be provided only if they add further information. High-resolution igures in TIFF format with dpi of 500 should be presented. If you have reused or adapted igures, tables or sections of text from papers published elsewhere please approach the copyright owner and obtain their permission to re-use those elements.

26

**Discussion** should challenge the outcomes of the research with other publications in the literature in the format of arguments and counterarguments. The limitations and strengths of the study and the implications of the

indings for future study or clinical practice should be presented.

**Conclusion** should present the inal outcome and brief recommendations that have been reached.

**Ethical declaration** consists of ethical approval and con lict of interest that should be presented and reported.

**References** should be complied numerically according to the order of citation in the text. We follow the “Vancouver” style and all references cited in the “reference segment” should be cited in the text.

**Clinical Images**

Clinical images are the pictures that show the clinical indings of a particular case of the patient. The clinical pictures should include questions and answers that should educateor remind readers about an important clinical situation or event. The image should not just describe the picture; however, should be informative enough from a clinical teaching view.

**Formatting guidelines**: The title should be less than ive to eight words. The text describing a clinical question should be within 150 words. The images can be uploaded in .tiff, .jpg or .jpeg format. We recommend using high-quality images. Text should be in one double-spaced electronic document.

**Patient Consent Form**

If the image/ igure of the patient is identi iable then the patient consent form is required. In case, the eyes are masked then the form is not mandatory.

Please click to download patient consent form. Kindly ill the downloaded form and send it along with the manuscript.

**Author identiϐication**

Authors are recommended to use their ORCID ID when submitting an article for consideration or acquire an ORCID ID via the submission process.

**DOI Number**

A DOI number will be available as a unique identi ier on the title page of each article. DOIs are useful for identifying and citing articles published online without volume or issue information (for more information, please see www. doi.org).

**Conϐlict of Interest**

Any con lict of interest related to the manuscript should be declared by authors. These include but not limited to commercial, personal, political, and intellectual aspects. All editors, editorial staff, and reviewers should also report potential con licts related tothe submissions they are working with. All authors are required todisclose potential con licts of interest in the Acknowledgments section of the manuscript by following the Recommendations of the International Committee of Medical Journal Editors (ICMJE) http://www.icmje.org/con licts-of-interest/.

27

**Conϐlicts include the following:**

Financial - funding and other payments, goods and services received or expected by the authors relating to the subject of the work or from an organization with an interest in the outcome of the work

Af iliations - being employed by, on the advisory board for, or a member of an organization with an interest in the outcome of the work

Intellectual property - patents or trademarks owned by someone or their organization Personal - friends, family, relationships, and other close personal connections Ideology - beliefs or activism, for example, political or religious, relevant to the work Academic - competitors or someone whose work is critiqued

**Disclaimer**

All statements expressed herein in our publications are merely those of the author(s) and do not re lect the publisher or editorial board. The publisher and the board members do not endorse any service or product presented in our publications and disclaims any accountability or liability for such materials.

**Copyright**

Published articles are distributed under the Creative Commons Attribution-Non-Commercial 4.0 International License (which permits copy and redistributes the material just in noncommercial usages if the original work is properly cited. Once the manuscript is adopted by Ophthalmology Cases & Hypotheses (OCH), a Copyright Transfer Agreement signed by all the authors should be submitted immediately.

The procedure for submitting your manuscript is easy and quick.Manuscripts for publication should be sent tothe editorial board on the “Make a Submission” page of the website: https://ophthalmolcases.com.Also, submissions can be sent to the Journal Editorial Of ice by email at of ice@ophthalmolcases.com. Acknowledgment(s) to the concern submission will be received within 24 working hours.

The Journal followsICMJE and WAME ethical principles. In case of any ethical malpractice (fraud, plagiarism, etc.), we treat based on the guidelines of WAME, ICMJE, COPE, and all principles presented at this webpage.

**Archiving**

All back articles are made available as full text on the journal website. In the event that the OCH discontinues its publication, its archive of published articles will still remain available on the journal website, to be maintained as an archive website by OCH Press.

HAT Medicine clinic (Azerbaijan) is a publisher of an international peer-reviewed, scholarly, open access journal titled “The Ophthalmology Cases & Hypotheses (OCH)”, since its establishment in 2020.

28

**JOURNAL POLICIES**

**Publication Ethics Policy**

The Ophthalmology Cases & Hypotheses (OCH) welcomes the submission of manuscripts that meet the general criteria of signi icance and scienti ic excellence.

Generally, the receipt of a manuscript will be acknowledged within 2 weeks of submission; authors will be provided with a manuscript reference number for future correspondence. If an acknowledgment is not received in a reasonable period of time, the author should contact the Editorial Of ice.

Papers written in English are considered. If English is not your native language, please consider having your text reviewed by a professional medical editor. All manuscripts are subject to editorial review.

**Statements**

This journal operates on a double-blind review process. Submissions are reviewed by the Editorial Of ice to ensure that they contain all parts. Submissions will be rejected if the author has not supplied all the material and documents as outlined in these author’s instructions. Manuscripts are then forwarded to the Editor-in-Chief, who makes an initial assessment of it. If the manuscript does not appear to be of suf icient merit or is not appropriate for the Journal, the manuscript will be rejected without review.

Manuscripts not compiled under the requirements of the journal will not be accepted for publication.

**Statement of Ethics**

Published research must comply with internationally-accepted standards for research practice and reporting. Manuscripts may be rejected if the editors believethat the research has not been carried out within an appropriate ethical framework, and concerns raised after publication may lead to a correction, retraction, or expression of concern in line with COPE guidelines.

The presentation of manuscripts should follow the Uniform Requirements for Manuscripts Submitted to Biomedical Journals from the International Committee of Medical Journal Editors (ICMJE).

The Ophthalmology Cases & Hypotheses (OCH) journal aims to adhere to the COPE Code of Conduct and Best Practice Guidelines.( https://publicationethics.org/)

**License** to Publish / Open Access and Creative Commons Licensing

This is an open-access journal and articles are distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License (CC BY), which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate

Each author must complete a License to Publish. This license grants Ophthalmology Cases & Hypotheses permission, among other things, to publish and distribute the article. Authors will also need to indicate on the form if they are making their article open access under the CC BY license

29

**Peer review**

Journal uses a double-blind peer review system where reviewers do not know the names of the authors and the authors do not know who reviewed their manuscripts. All contributions will be initially assessed bythe editor for suitability for the journal. Papers deemed suitable are then typically sent toaminimum of two independent expert reviewers to assess the scienti ic quality of the paper. The Editor is responsible for the inal decision regarding acceptance or rejection of articles. In the event that an editor has a con lict of interest with a submitted manuscript or with the authors, the manuscript, review, and editorial decisions are managed by another designated editor without a con lict of interest related to the manuscript. Editors are not involved in decisions about papers which they have written themselves or have been written by family members or colleagues or which relate to products or services in which the editor has an interest.

**Duplicate submission and redundant publication**

Ophthalmology Cases & Hypotheses (OCH) journal consider only original content, i.e. articles that have not been previously published, including in a language other than English. Articles based on content previously made public only on a preprint server, institutional repository, or in a thesis will be considered. Manuscripts submitted to our journal must not be submitted elsewhere while under consideration and must be withdrawn before being submitted elsewhere. Authors whose articles are found to have been simultaneously submitted elsewhere may incur sanctions.

If authors have used their own previously published work, or work that is currently under review, as the basis for a submitted manuscript, they must cite the previous articles and indicate how their submitted manuscript differs from their previous work.

Redundant publication, the inappropriate division of study outcomes into more than one article (also known as salami slicing), may result in rejection or a request to merge submitted manuscripts and the correction of published articles. Duplicate publication of the same, or a very similar, article may result in the retraction of the later article, and the authors may incur sanctions.

**Plagiarism**

The journal may use plagiarism detection software to screen the submissions. Manuscripts that are found to have been plagiarized from a manuscript by other authors, whether published or unpublished, will be rejected and the authors may incur sanctions. If plagiarism is identi ied, the COPE guidelines on plagiarism will be followed.

**Citation manipulation**

Authors whose submitted manuscripts are found to include citations whose primary purpose is to increase the number of citations to a given author’s work, or to articles published in a particular journal, may incur sanctions. Editors and reviewers (https://publicationethics.org/node/19886) must not ask authors to include references merely to increase citations to their own or an associate’s work, to the journal, or to another journal they are associated with.

**Fabrication and falsiϐication**

The authors of submitted manuscripts or published articles that are found to have fabricated or falsi ied the results, including the manipulation of images, may incur sanctions, and published articles may be retracted.

30

**Principles of Transparency and Best Practice in Scholarly Publishing**

The Journal complies with the ICMJE uniform requirements for manuscripts. This is clearly indicated in the Submission Guidelines. Also, our af iliated Journal followstheCOPE guidelines and the Principles of Transparency and Best Practice in Scholarly Publishing. The statements and opinions contained in this journal are solely those of the individual authors and do not necessarily re lect the editor or the publisher’s ones.

**Ethics & advertisement policies**

We endorse the World Association of Medical Editors (WAME) policies in editorial, peer review, advertisement, ethics, informed consent, handling cases requiring corrections, retractions, and editorial expressions of concern. We also respect policies of International Committee of Medical Journal Editors (ICMJE) Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals.

**RESEARCH ETHICS POLICY**

**Human/Animal Rights and Informed Consent**

The Ophthalmology Cases & Hypotheses (OCH) requires that all manuscripts utilizing human subjects for investigation report that all subjects signed a statement of informed consent. Studies conducted in their countries must be compliant with the Health Insurance Portability and Accountability Act (HIPAA). Institutional Review Board (IRB) or Ethics Committee (EC) approval must be obtained if the study utilizes human subjects or reviews medical records. If there is no IRB or Ethics committee, the authors should state whether their study adhered to the tenets of the Declaration of Helsinki. Clinical trials must be registered with one of the public information sites for clinical research. Finally,use of animals must be approvedby the Institutional Animal Care and Use Committee. The Ophthalmology Cases & Hypotheses (OCH) will not publish anymanuscript that has not clearlydemonstrated respect for Human and Animal rights. https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/.

**Clinical Trial Registry**

When publishing clinical studies, Ophthalmology Cases & Hypotheses (OCH) aims to comply with the Recommendations of International Committee of Medical Journal Editors (ICMJE) on trials registration (https:// www.who.int/clinical-trials-registry-platform/the-ictrp-search-portal). Therefore, authors are requested to register the clinical trial presented in the manuscript in a public trials registry, and include the trial registration number in the Methods Section.

31

**https://www.gparc.net/**

Чапаимзаланмышдыр: 31.07.2024.

Юлчц: 70х100 1/16. Чапвяряги: 4,5. Сифариш: 87/24. Сай: 500 ядяд.

Бакы, Az1122, Зярдабипр. 78c Тел: 012/070 4977021

Е-почту: info@ave.az

32

34

© 2024 OCH. Journal of Ophthalmology Cases & Hypotheses / Published by Hat Medicine Clinic