2023

OKAN'S ANATOMY

İstanbul Okan Üniversitesi Tıp fakültesi

TIP FAKÜLTESİ BİLİMSEL ARAŞTIRMA TOPLULUĞU

BROKEN HEART SYNDROME

INFECTIVE ENDOCARDITIS

An overview of Buerger disease

AĞUSTOS 2023

OUBAT Topluluğu Olarak Yaptığımız Etkinlikler

Tasarım:Beyzanur Nişancıoğlu

Yeni Dönemde Sizlerleyiz !

Değerli Meslektaşlarım, Sevgili Öğrenciler;

2013 yılında kurulan İstanbul Okan Üniversitesi Tıp Fakültesi, 2014 yılında ilk öğrencilerini Tuzla Kampüsümüzde kabul etmiş; 2020 yılında ise ilk mezunlarını vermiştir. Ülkemizin kalbi ve en güzide şehirlerinden olan İstanbul'da dünya standartlarında bir kurum olma hedefi ile her yıl hızla ilerlemekte olan fakültemizin, gerek genişleyen öğretim üyesi kadrosu; gerekse 1100'ü aşan öğrenci sayısı ve 4. Dönemi geride bırakan mezun hekimlerimiz ile giderek büyüyen bir aile olduğunu belirtmekten gurur duyuyorum. Bilim ve eğitimde öncü olmayı hedefleyen kadromuz ve gelişime açık yönetim an- layışımız ile çağa uygun nitelikte hekimler yetiştirmek ve yüksek standartlarda sağlık hizmetlerinin sunulması yolunda geçtiğimiz 2022-2023 Eğitim ve Öğretim yılında da ulusal uluslararası kalite stan- dartlarını yakalayan bir kurum olma yolunda emin adımlarla ilerlemeye çalıştık. Halen; fakültemiz- in tıp eğitim müfredatını Ulusal Çekirdek Eğitim Müfredatı (UÇEP) çerçevesinde değerlendirip re- vize etmeye çalışıyor; başvuruda bulunduğumuz Tıp Fakültesi Eğitim Akreditasyonunun (TEPDAD) gereklerini yerine getirmek için çaba gösteriyoruz. Tüm bu süreçlerimizin gerçekleşmesinde yüksek motivasyonları ve özverileri ile çalışarak katkı sunan başta İstanbul Okan Üniversitesi Tıp Fakültesi Akademik ve İdari Personeline, öğrencilerimize, velilerimize ve tüm paydaşlarımıza en içten teşek- kürlerimi sunar; 2023-2024 Akademik Yılının tüm Okan Tıp Ailesine sağlık ve esenlik ve başarı get- irmesini dilerim.

Prof. Dr. Selçuk Mercan - İstanbul Okan Üniversitesi Tıp Fakültesi Dekanı

Editörden Mesaj Var!

Tıp bilimi günümüzde dünyanın en önemli bilim dallarından biri olarak kabul edilmekte ve başta doktorlar olmak üzere sağlık alanında çalışan tüm kişiler, toplum bilincini artırarak toplum sağlığını yükseltmeye ve hastalıkların yayılmasını önlemeye çalışmaktadır. bu nedenle sağlık ve tıp alanında yapılan en son keşifler ve araştırmalar hakkında güçlü bilgiler vermek ve bunları toplum insanına sunmak, hastalıkların önlenmesinde çok yardımcı olabilir. Doktorlar, hastalıkların önlenmesi ve tedavisi alanında her zaman yararlı bir rol oynamıştır.Bunun en bariz örneklerinden biri, Corona pandemisi döneminde öne çıkan doktorların toplumun kurtarıcıları olarak kabul edilme rolüdür . Tüm sağlık çalışanları gibi tıp öğrencileri de toplum bilincini artırmada faydalı olmalıdır.Bu nedenle Okan Üniversitesi tıp fakültesi öğrencileri olarak bizler, sağlık bilimleri alanındaki güncel bilgilerden bazılarını derleyip kolay ve anlaşılır bir şekilde okuyucularımıza sunmaya çalıştık.

Okan's Anatomy 23' Editörü
Amir Mahdi Akbari

İçindekiler

Bu dergi İstanbul Okan Üniversitesi Öğrenci Dekanlığı tarafından düzenlenmiştir.

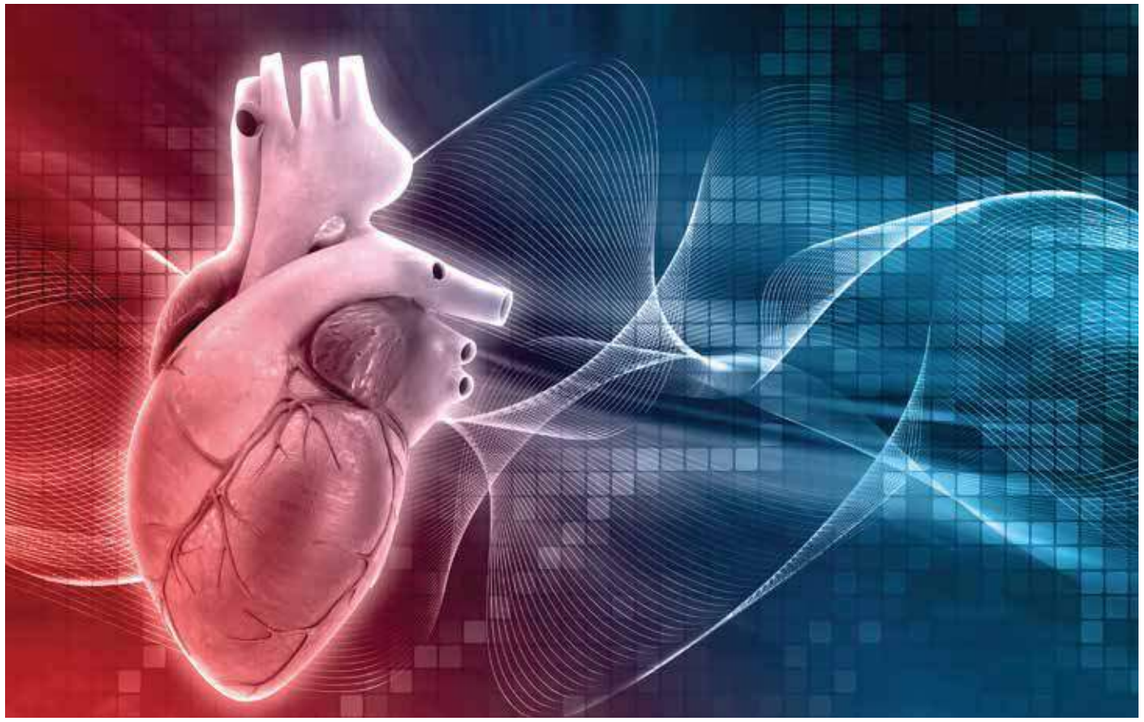
Infective Endocartiditis

i have to appericiate Dr.MEHDI MESKINI ,the assistant professor of department of microbiology at okan university ,school of medicine , for helping me in the writting of this article .

Infective endocarditis (IE) remains a rare condition but one with high associated morbidity and mortality. The cause is typically a bacterial infection and less commonly a fungal infection. With an ageing population and increasing use of implantable cardiac devices and heart valves, the epidemiology of IE has changed. It has an annual incidence of 3–10/100,000 of the population with a mortality of up to 30% at 30 days. 1 Mostaghim AS, Lo HYA and Khardori N. A retrospective epidemiologic study to define risk factors, microbiology, and clinical outcomes of infective endocarditis in a large tertiary-care teaching hospital.

2 Murdoch DR, Corey GR, Hoen B et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. Arch Intern Med 2009; 169:463–73 The epidemiology of IE has gradually changed over the years with healthcare-associated IE now accounting for 25–30% of contemporary cohorts as a result of a greater use of intravenous lines and intracardiac devices. Fernandez-Hidalgo N, Almirante B, Tornos P et al. Contemporary epidemiology and prognosis of health care-associated infective endocarditis. Clin Infect Dis 2008; 47:1287–97. The bacteria most commonly involved are streptococci or staphylococci. Infective Endocarditis – Cardiovascular Disorders". Merck Manuals Professional Edition. September 2017. Retrieved 11 December 2017 Staphylococcus aureus is now the most prevalent cause of IE in most studies at 26.6% of all cases, followed by viridans group streptococci at 18.7%, other streptococci at 17.5% and enterococci at 10.5%. Selton-Suty C, Celard M, Le Moing V et al. Preeminence of Staphylococcus aureus in infective endocarditis: a 1-year population-based

survey. Clin Infect Dis 2012; 54:1230–9 These organisms together account for 80–90% of all cases of endocarditis. High-dose antibiotics are the cornerstone of treatment for infective endocarditis DeSimone DC, Gersh BJ, Anavekar NS (May 2020). "Infective Endocarditis: A Contemporary Review". Mayo Clinic Proceedings.The most frequent causative microorganisms in order are Staphylococcus aureus (S. aureus), streptococci, coagulase-negative staphylococci (CoNS), and Enterococci both in Turkey and globally. Additionally, Brucella spp. is the fifth most common causative agent of IE in Turkey. Coxiella burnetii, which is one of the leading causes of blood culture-negative IE globally, has been identified in some case reports from our country and, therefore, it must be in the differential diagnosis. Although Bartonella spp. and Tropheryma whipplei are frequently the causes of blood culturenegative IE globally, and there are no available data about these causative agents in Turkey.Research concerning these agents should be carried out. Gramnegative bacilli and fungi are often causative agents of healthcare-associated IE. In patients who underwent implantation of intracardiac prosthetic devices such as prosthetic heart valves in the last decade, Mycobacterium chimaera should be kept in mind as a possible pathogen for blood culture-negative IE(Consensus Report on Diagnosis, Treatment and Prevention of Infective Endocarditis by Turkish Society of Cardiovascular Surgery (TSCVS), Turkish Society of Clinical Microbiology and Infectious Diseases (KLIMIK), Turkish Society of Cardiology (TSC), Turkish Society of Nuclear Medicine (TSNM), Turkish Society of Radiology (TSR), Turkish Dental Association (TDA) and Federation of Turkish Pathology Societies (TURKPATH) Cardiovascular System Study Group



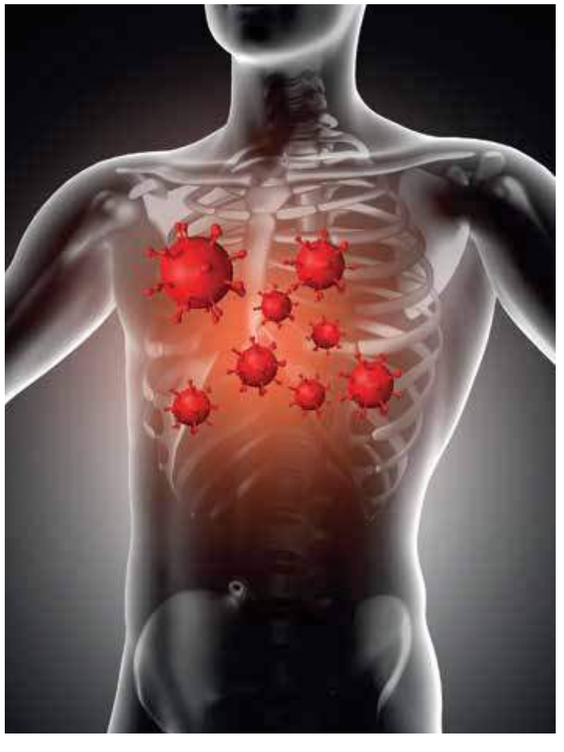
Infective endocarditis is more frequently seen in patients wiath a previous episode of IE, a valvular heart disease, a congenital heart disease, any intracardiac prosthetic material, intravenous drug use (IVDU),chronic hemodialysis treatment, solid organ, and hematopoietic stem cell transplantation, compared to healthy population.(Consensus Report on Diagnosis, Treatment and Prevention of Infective Endocarditis by Turkish Society of Cardiovascular Surgery (TSCVS), Turkish Society of Clinical Microbiology and Infectious Diseases (KLIMIK), Turkish Society of Cardiology (TSC), Turkish Society of Nuclear Medicine (TSNM), Turkish Society of Radiology (TSR), Turkish Dental Association (TDA) and Federation of Turkish Pathology Societies (TURKPATH) Cardiovascular System Study Group: (diagnosis of IE is still difficult (Habib G, Derumeaux G, Avierinos J-F, Casalta J-P, Jamal F, Volot F, et al. Value and limitations of the duke criteria for the diagnosis of infective endocarditis. J Am Coll Cardiol. 1999;33(7) IE is a rare infection with an annual incidence ranging from 3 to 10 cases per 100,000 people [6]. While Gram-positive cocci, such as streptococci and staphylococci, are the predominant IE etiology (80–90% of the cases), the incidence of Gram-negative IE ranges from 1.3% to 10% with most cases attributed to HACEK microorganisms.

Cardiobacterium hominis endocarditis incidentally diagnosed following an aortic valve replacement surgery:this disease is reported to be twice as common in men as in women. Today, the average age of patients with infective endocarditis is over 65 years, which is probably due to the increasing prevalence of predisposing factors such as artificial valves, acquired valve disease, diabetes mellitus and hemodialysis in this group of people (de Sa DDC, Tleyjeh IM, Anavekar NS, Schultz JC, Thomas JM, Lahr BD, et al., editors. Epidemiological trends of infective endocarditis: a population-based study in Olmsted County, Minnesota. Mayo Clinic Proceedings; 2010). In developed countries, the annual prevalence of IE is estimated at 3–9 patients per 100,000 people, an increase that has been seen since 1970–2013 [Wu Z, Chen Y, Xiao T, Niu T, Shi Q, Xiao Y. Epidemiology and risk factors of infective endocarditis in a tertiary hospital in China from 2007 to 2016. BMC Infect Dis. 2020]. In one study, they found that the mean age at the time of IE episodes were younger than those reported from developed countries, although the mean age increased during this period.

The proportion of old patients with IE increased gradually in this period, which was more obvious in developed countries [9, 11]. Erichsen et al. [12] found that the incidence increased substantially for elderly IE patients between 1994 and 2011, with the highest incidence rate of 3.38 for patients over 80 years old at IE onset. In Oliver et al.' s report [13], 49% of IE patients were over 65 years old and 11.2% were over 80 years old.) Epidemiology and risk factors of infective endocarditis in a tertiary hospital in China from 2007 to 2016(The incidence of IE is approximately 6/100,000 people worldwide. There are no data about the incidence of IE in Turkey, which is predicted to be higher in our country due to higher incidences of both valvular diseases and nosocomial bacteremia(Consensus Report on Diagnosis, Treatment and Prevention of Infective Endocarditis by Turkish Society of Cardiovascular Surgery (TSCVS), Turkish Society of Clinical Microbiology and Infectious Diseases (KLIMIK), Turkish Society of Cardiology (TSC), Turkish Society of Nuclear Medicine (TSNM), Turkish Society of Radiology (TSR), Turkish Dental Association (TDA) and Federation of Turkish Pathology Societies (TURKPATH) Cardiovascular System Study Group diagnosis of IE is still difficult (Habib G, Derumeaux G, Avierinos J-F, Casalta J-P, Jamal F, Volot F, et al. Value and limitations of the duke criteria for the diagnosis of infective endocarditis. J Am Coll Cardiol. 1999;33(7)

The diagnosis of infective endocarditis relies on the duke criteria, which were originally described in 1994 and modified in 2000. Clinical features and microbiological examinations are the first steps to diagnose an infective endocarditis. Imagining is also crucial. Echocardiography is the cornerstone of imaging modality in the diagnosis of infective endocarditis. Alternative imaging modalities as computer tomography, magnetic resonance imaging, and positron emission tomography/computer tomography (PET/CT) with 2-[18F] fluorodeoxyglucose (FDG) are playing an increasing role in the diagnosis and management of infective endocarditis.Hubers, Scott A.; DeSimone, Daniel C.; Gersh, Bernard J.; Anavekar, Nandan S. (May 2020). "Infective Endocarditis: A Contemporary Review". Mayo Clinic Proceedings Infective endocarditis is divided into the three categories of acute, subacute, and chronic based on the duration of symptoms.[8] Acute infective endocarditis refers to the presence of signs and symptoms of infective endocarditis that are present for days up to six weeks.[8] If these signs and symptoms persist for more than six weeks but less than three months, this is subacute infective endocarditis. [8] Chronic infective endocarditis refers to the presence of such signs and symptoms when they persist for more than three months.[DeSimone DC, Gersh BJ, Anavekar NS (May 2020). "Infective Endocarditis: A Contemporary Review". Mayo Clinic Proceedings. 95 (5): 982–99] Subacute bacterial endocarditis (SBE) is often due to streptococci of low virulence (mainly viridans streptococci) and mild to moderate illness which progresses slowly over weeks and months (>2 weeks) and has low propensity to hematogenously seed extracardiac sites. Acute bacterial endocarditis (ABE) is a fulminant illness over days to weeks (<2 weeks), and is more likely due to Staphylococcus aureus, which has much greater virulence or disease-producing capacity and frequently causes metastatic infection. [Mitchell RS, Kumar V, Robbins SL, Abbas AK, Fausto N (2007). Robbins Basic Pathology (8th ed.). Saunders/Elsevier. pp. 406] This classification is now discouraged, because the ascribed associations (in terms of organism and prognosis) were not strong enough to be relied upon clinically. The terms short incubation (meaning less than about six weeks) and long incubation (greater than about six weeks) are preferred. [Morris AM (January 2006). "How best to deal with endocarditis". Current Infectious Disease Reports] The treatment of the condition could be difficult, because the species can form biofilms on native and prosthetic heart valves and cause vegetation, which could result in an additional functional dysfunction of the valve.

The optimum therapy still remains debatable, and combination of antifungal therapy and surgical debridement has suggested to bring about better prognosis (Terrien 3rd CM, Edwards NM. Ann Thorac Surg 2017 infective endocarditis should remain high on the differential in all patients on TPN who develop fever as it is the most common presenting symptom [Sankar NP, Thakarar K, Rokas KE: Candida infectiveendocarditis during the infectious diseases and substance use disorder syndetic: a six-year case series. Open Forum Infect Dis. 2020,].Although the percentage of it is low in the population but still it is a life treating disease for humans, especially children.



Broken Heart Syndrome

Pelinsu Buket Yalçınkaya

Think again when you are about to hurt someone's feelings, as you can actually break their heart. Broken heart syndrome (stress-induced cardiomyopathy/Takotsubo cardiomyopathy) is atemporary and reversible form of heart failure that can occur after a person experiences severeemotional or physical stress. This heart attack-like pathology was first described by a Japanesescientist in 1991. BHS is named after an octopus trap because of the shape change of the leftventricle. Stress cardiomyopathy is now a well-recognized cause of acute heart failure, lethalventricular arrhythmias, and ventricular rupture .(1). The symptoms of this condition are similarto those of acute myocardial infarction, except for the absence of obstructive lesions in thecoronary arteries and the presence of left ventricular apical ballooning. Takotsubo syndromeoccurs predominantly in post-menopausal women.

Cause and Triggers:

Although the exact cause of broken heart syndrome is unknown, researchers have linked therelease of stress hormones (adrenaline and noradrenaline) as a response to triggers, to thetemporary dysfunction of the heart muscle. Some of the triggers that can cause extremesympathetic activation include emotional stress, physical stress, medical procedures likebronchoscopy, gastroscopy, or endotracheal intubation, and substance abuse (cocaine oramphetamine).

Symptoms:

Patients with Takotsubo syndrome typically present with: Acute chest pain of cardiac origin (angina) Breathlessness· Palpitations due to sinus tachycardia or arrhythmia· Nausea, vomitingSweating, dizziness, or faintingIn more severe cases, patients may present with: Pre-syncope or syncope due to ventricular tachyarrhythmias Severe left ventricular outflow tract obstruction (LVOTO) Cardiogenic shock Patients may describe a wave of pressure from the chest to the neck and into the head,consistent with the acute catecholamine and hypertensive surge and frequently associated withdiaphoresis and heightened anxiety.

Diagnosis:

Biomarkers, ECG, cardiac catheterization, and blood tests are some of the procedures used indiagnosis. Biomarkers: In 90% of the BHS patients, cardiac troponin levels are elevated. Duringthe acute phase of Takotsubo syndrome, serum cardiac natriuretic peptides (BNP or NT-proBNP)are almost always elevated. Cardiac catheterization is a procedure that involves inserting acatheter into a blood vessel in your arm or leg and threading it up to your heart to measure thepressure in your heart and look for blockages. Blood tests are used to check for cardiac enzymesthat are released during a heart attack. Also, cardiac imaging, including echocardiography andCMR with LGE, helps exclude MI and other possible conditions.

Treatment:

A specific feature of Takotsubo syndrome is the recovery of normal cardiac function. Thetreatment of broken heart syndrome should be supportive care to sustain life while relieving theunderlying stress and to minimize complications during recovery. Medications such as betablockers(regulate heart rate) and ACE inhibitors(blood pressure) can be used to reduce bloodpressure and improve heart function. In severe cases complicated by progressive circulatoryfailure and cardiogenic shock, early mechanical support should be provided.

Prevention:

The best way to prevent broken heart syndrome is to manage stress effectively and to seek help when needed. This may include stress-reducing activities such as exercise, meditation, and relaxation techniques. It is also important to seek medical attention promptly if you experience any symptoms of chest pain, shortness of breath, or irregular heartbeat

Duchenne Musküler Distrofi

Ayşe Nur Balcı

Duchenne musküler distrofi (DMD), kas hücrelerinin sağlam kalmasına yardımcı olan distrofin adı verilen bir proteinin değişmesi nedeniyle ilerleyici kas dejenerasyonu ve zayıflığı ile karakterize edilen X kromozomuna bağlı genetik bir hastalıktır. (1) DMD, erken çocukluk döneminde ortaya çıkan ve etkilenen erkek çocuklarda proksimal kas zayıflığı ve baldır hipertrofisi ile karakterize olan, çocuklarda en sık görülen musküler distrofidir. Hastalar genellikle 12 yaşında tekerlekli sandalyeye bağlı hale gelir. DMD hastalığı, her 3.500 ila 5.000 erkek çocuğundan birinde görülmekte ve her yıl dünya çapında 20 bin yeni tanı konulmaktadır. Ortalama yaşam süresi 26'dır; ancak bazıları 30'lu veya 40'lı yaşlarına kadar yaşayabilir.

Çocuklarda DMD semptomları çoğunlukla 6 yaşına gelmeden fark edilecektir. Bacak kasları genellikle ilk etkilenen kaslardır. Bu nedenle hastalar kendi yaşlarındaki diğer çocuklardan sonra yürümeye başlayacaklardır. Yürümeye başladıklarında, sıklıkla düşebilir ve merdiven çıkmakta, yerden kalkmakta zorluk çekebilirler. Birkaç yıl sonra yürüme paytaklaşabilir veya parmak uçlarında yürümeye başlayabilirler. DMD ayrıca kalbe, akciğerlere ve vücudun diğer bölgelerine zarar verebilir. Yaşlandıkça çocuklarda skolyoz, bacaklarda kontraktür,baş ağrısı, öğrenme ve hafıza ile ilgili problemler, nefes darlığı,uyku hali, odaklanmada zorluk gibi semptomlar gözlenebilir. Kas problemleri zaman zaman kramplara neden olabilir, ancak genel olarak DMD ağrılı değildir.

Hastamız mesane ve bağırsaklarını kontrol etmeye devam edecektir. Bozukluğu olan bazı çocukların öğrenme ve davranış sorunları olmasına rağmen, DMD çocuğun zekasını etkilemez. DMD tanısı sıklıkla 3-5 yaş arasında konulur. Genel olarak DMD tanısı şu sıralama ile yapılır:

1)Belirti ve semptomları gözlemleme
2)Enzim seviyelerini belirlemek için kan testleri (kreatin kinaz vb.)
3)Bir uzmana yönlendirme
4)Genetik test
5)Kas Biyopsisi (gerekirse)

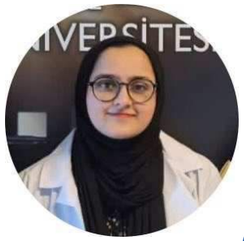
DMD'den şüphelenme durumunda birçok teste başvurulabilir. Bu testler:
Kreatin Kinaz Kan Testi: Kaslarınız hasar gördüklerinde kreatin kinaz salgılarlar, bu nedenle yüksek seviyeler DMD'yi gösterebilir. Seviyeler tipik olarak 2 yaşına kadar zirve yapar ve normal aralığın 10 ila 20 katından fazla olabilir.
Genetik Kan Testi: Distrofin geninin tamamen veya neredeyse tamamen yokluğunu arayan bir genetik kan testi, DMD tanısını doğrulayabilir.
Kas Biyopsisi: Uyluk veya baldırlarındaki bir kastan kas dokusunun küçük bir örnek alınabilir.
Elektrokardiyogram (EKG): DMD vakaların %50'sinde kalbi etkilediğinden, DMD'nin karakteristik belirtilerini aramak ve çocuğun kalp sağlığını kontrol etmek için EKG yapmak önemlidir.(5)

DMD tedavisinde yeni stratejiler bulma yolunda çalışmalar hala devam etmektedir. Özellikle CRISPR/Cas9 sistemi ile ilgili çalışmalar bu konudaki verileri artıracaktır. Burada ilaç denemelerinden, gen ve hücre tedavisine kadar farklı çabalar mevcuttur. Genel olarak amaç DMD'li çocuklarda motor fonksiyonları korumak, yaşam süresini uzatmak, yaşam kalitesini artırmaktır.

Kortikosteroidler DMD tedavisinde kullanılmaktadır. Bu tür ilaçlar kas yıkımını yavaşlatarak ve kas gücünü koruyarak hastalığın seyrini geciktirler. Fizik tedavi ve atellerle eklem sertlikleri önlenebilir. İleri dönemde ise destek cihazlarla yaşam kalitesi artırılabilir. Solunum kaslarının hasarı sonucu, hastalar solunum desteğine ihtiyaç duyabilir, hatta daha iyi akciğer fonksiyonları için cerrahi müdahale (ör. skolyoz) gerekli olabilir (6)

Umuyoruz ki hiçbir çocuk geleceğine koşmakta zorlanmaz ve kesin tedavisi mümkün olmayan diğer genetik hastalıklarla birlikte Duchanne Musküler Distrofi çözüme kavuşur.

The Relationship Between Gut Health & Cognitive Function

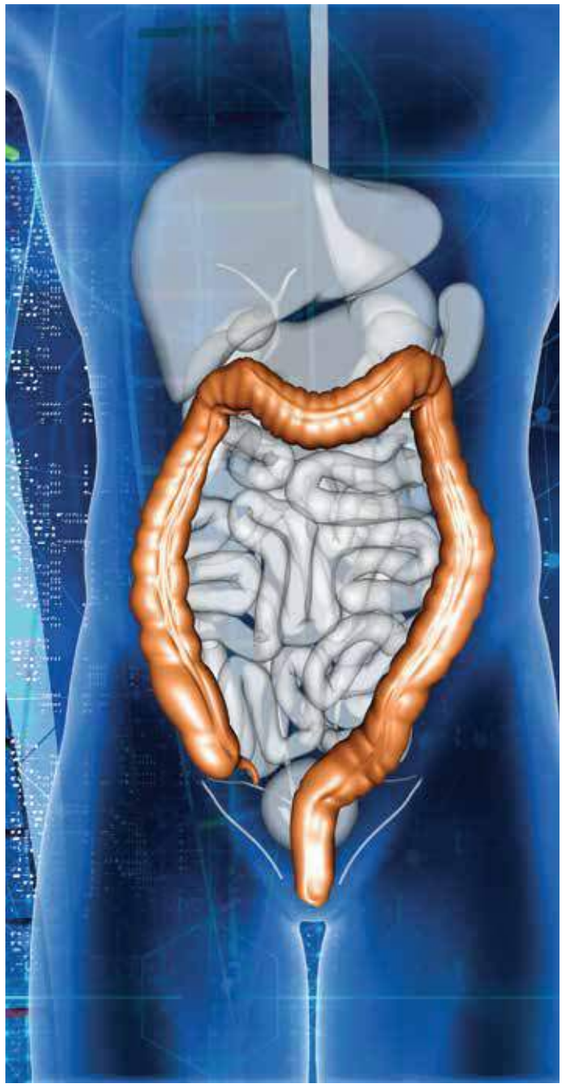


Amna Atiq

The gut-brain axis involves many complex bidirectional pathways of communication that we are just beginning to understand. New studies are continuing to emerge about this complicated yet fascinating phenomenon.

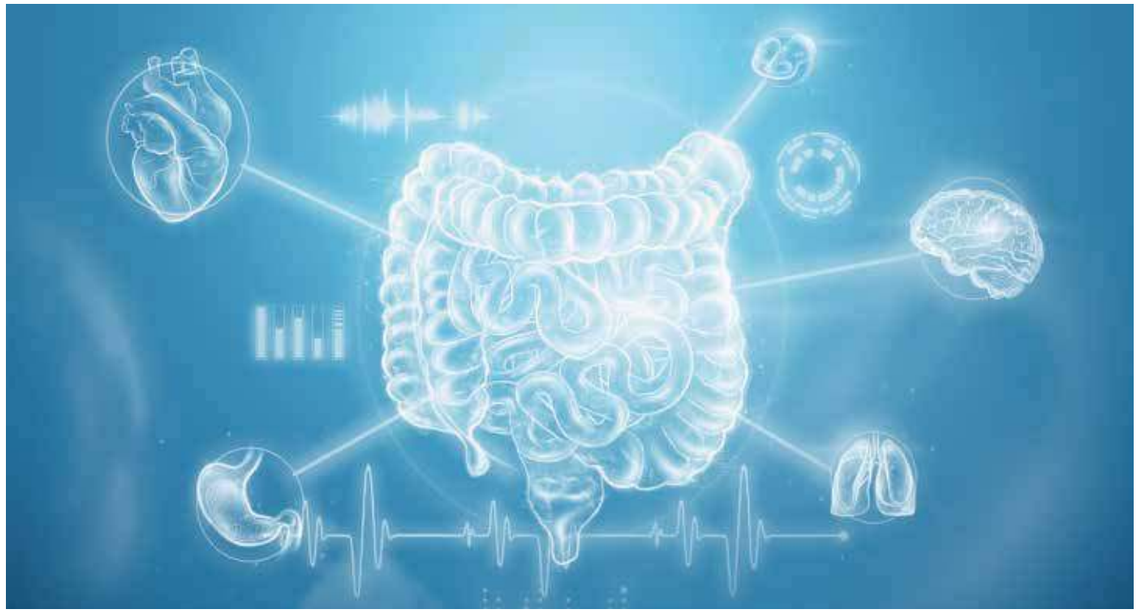
The Inhabitants of the Gut

The gut or gastrointestinal tract contains many microorganisms such as bacteria, pathogens, fungi, parasites, protozoa, and viruses. Some of these microorganisms play vital roles in maintaining overall health. (1) The gut microbiota, referring to the bacteria, archaea, and eukarya in the gut, has a symbiotic relationship with the human body. The microbiota provides many benefits such as maintaining the gut epithelium, harvesting energy from indigestible food, modulating im munity, and providing protection from pathogens. These mechanisms can be disturbed by dysbiosis, which refers to the imbalance in bacterial composition. Dysbiosis can cause various physiological changes in the human body and can be observed in several diseases such as those related to metabolism and the nervous system. (2)



Neurodegenerative Disorders and the Gut

There are several diseases in which gut abnormalities and neurodegenerative disorders go hand in hand.
Studies have found alterations in gut microbiota in patients diagnosed with Parkinson's disease, Huntington's disease, Alzheimer's disease, and Amyotrophic lateral sclerosis (ALS). Gastrointestinal symptoms of ALS have been found to occur before neurological symptoms, indicating that the disorder is linked to both the gut and the nervous system. Neurodegenerative diseases lead to cognitive impairment, therefore poor gut health could be linked to cognitive dysfunction. (1)



Can Improved Gut Health Improve Cognitive Function?

The gut microbiota synthesizes essential neurotransmitters needed for the homeostasis of the central nervous system. Examples of these neurotransmitters are tryptophan, brain-derived neurotrophic factor (BDNF), Gamma-aminobutyric acid (GABA), and short-chain fatty acids (SCFA). BDNF promotes the growth and survival of neurons. Low levels of this protein are associated with various neurodegenerative disorders.

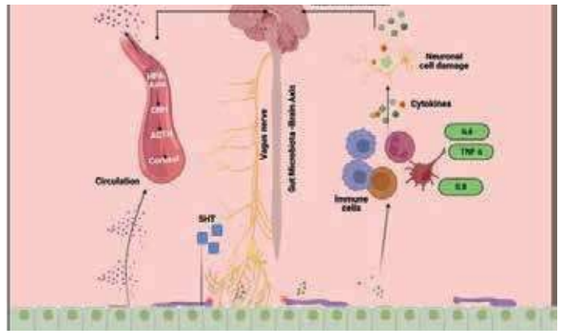


Figure 1. The gut and the brain interact via the neural, endocrine, metabolic, and immunological mechnisms. (3)

Some probiotics can stimulate BDNF production in the gut. (3) Probiotics are living microorganisms that are present in several foods such as yogurts and fermented milk. (4) They have been found to benefit gut health by strengthening the intestinal barrier and regulating bacterial composition. (5)

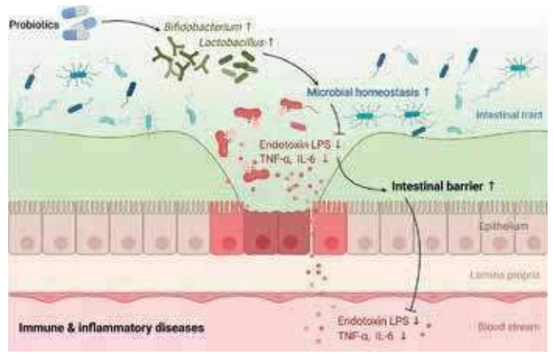


Figure 2. Probiotics strengthen the intestinal barrier and prevent gut leakage. (5)

In the future, manipulating the gut microbiome with probiotics to improve gut health and cognitive function could potentially be used to treat various diseases. However, this is a relatively new field of study and further research is required to draw any definitive conclusions.

Conclusion

It can be concluded that gut health plays an important role in overall health and well-being. Improving it can enhance the quality of life of people with various diseases. One way to achieve this is by choosing the right diet. For example, the Mediterranean and Nordic diets lower the risk of cognitive decline. (6) As research progresses in this field of study, the potential of using the gut-brain axis to cure many incurable diseases may be revealed.

Öldürmek İçin Doğmak

"Seri Katil" Geni MAO-A ve Suça Yatkınlık/Şiddet İlişkisi

Hasan Yaman

Şiddet ve "Tahrip Etme Dürtüsü" canlılık ve varoluşun ilk zamanlarından beri süregelen ve Sigmund Freud'un psikanalitik kuramında da açıkladığı gibi insan doğasını oluşturan iki temel içgüdüden birisidir(Eros ve Tanatos).Tanatos yani bir diğer ismiyle "ölüm içgüdüsü" Freud'a göre yaşamın tahrip edilmesi ve sona erdirilmesine yönelik enerjidir(1).Bu perspektifte göre de saldırganlık ve şiddet primer olarak kişinin kendisini tahrip etmeye yönelik ölüm içgüdüsünün diğer insanlara yönlendirilmesinden kaynaklanmaktadır.(1)

Şiddet'in kökenlerinin ve şiddete sebep olan koşulların doğası da şiddet kavramının kendisi kadar ilgi çekici ve merak konusudur.Son yıllardaki tıbbi ve genetik keşifler sayesinde şiddeti ve nedenlerini daha iyi kavramış durumdayız.Bu yazıda da yapılan yeni çalışmalarla düşük aktivite gösterdiğinde ve belli şartlar altında şiddet ve agresyonla ilişkilendirilen bir enzim olan MAO-A enzimi (Monoamin Oksidaz A) ve onu kodlayan gen MAOA'yı inceleyeceğiz.

Monoamin Oksidaz A Geninin Özellikleri

MAOA geni veya bir diğer ismiyle "savaşçı gen"/"seri katil geni" insan genomunda X kromozomunun kısa kolundaki 11.3 pozisyonunda bulunur(2).MAOA geninin kodladığı MAOA enziminin hücredeki görevi dopamin,nörepinefrin,serotonin gibi amin yapıdaki nörotransmitterlerin sinyal iletimi sonrası yıkımıdır.Bu amin yapıdaki nörotransmitterler insan davranışlarının şekillenmesinde başat rol oynayan biyokimyasallardır.Literatürdeki bazı çalışmalarda gösterildiği üzere MAOA geninin normalden az aktivite gösteren MAOA-L varyantındaki anomaliler yükselmiş seviyede agresyon ve fiziksel şiddetle ilişkilendirildi(4).Hollandalı bir ailenin nesilleri boyunca erkek üyelerinin gösterdiği anormal agresif davranışlar da bu genin 8.ekzonundaki delesyon nokta mutasyonunun neden olduğu düşük ekspresyondaki Monoamin-oksidaz A aktivitesi yani bir diğer deyişle MAOA-L ile ilişkilendirildi(4).Çocuklar üzerinde yapılan bir araştırmada ise eziyet görmüş ve ihmal edilmiş olup MAOA-L varyantına sahip olanlarda suç işlemeye yatkınlık durumu gözlendi(4).Sadece insanlardan ibaret olmamakla birlikte fareler üzerinde yapılan bir çalışmada da fonksiyon dışı kalmış MAOA geninin yüksek seviyede agresiflikle korele olduğu kayıtlara geçti(2).Öyle ki bu genetik durum etkisini adli vakalarda da gösterdi;2009 yılında ABD'de ve 2010 yılında İtalyada iki davada kanıt olarak sunuldu.2009 yılındaki davada birinci derece cinayetten yargılanan faili idam cezasından kurtarıp 32 yıl hapse mahkum etti,İtalyadaki mahkemede ise suçlunun cezasını 9 yıldan 8 yıla indirdi(2)(7).

Sonuç ve Etik İkilemler

Önceki bölümde bahsedilen veriler ışığında beyin fırtınası yapacak olursak ortaya bazı etik ve hukuki problemler çıkıyor: "Şiddet suçları işlemiş fakat MAOA-L durumundan muzdarip insanları yargılarken bu genetik durum ne kadar dikkate alınmalı?"

"Bu fizyopatolojik durum insanın biliş ve karar verme/muhakeme/yargı yeteneğine ne kadar ket vuruyor,failler özgür iradeleri üzerinde ne kadar kontrol sahibi?"
"Çevresel etmenleri göz ardı etmemekle birlikte toplumun Ted Bundy, Jeffrey Dahmer, Andrei Chikatilo gibi suçluları yaratmasında genetik kodlarımızın ne kadar payı var?"
"Bu tür durumlardan muzdarip insanlara Fizikçi J.Robert Oppenheimer'ın da dediği gibi "dünyaları yıkan ölümün ta kendisi"şeklinde bakıp toplumdan izole mi etmeliyiz yoksa planlı ve programlı tedavilerle ve altyapısı gelişmiş sağlık kompleksleriyle topluma yeniden mi kazandırmaya çalışmalıyız?"

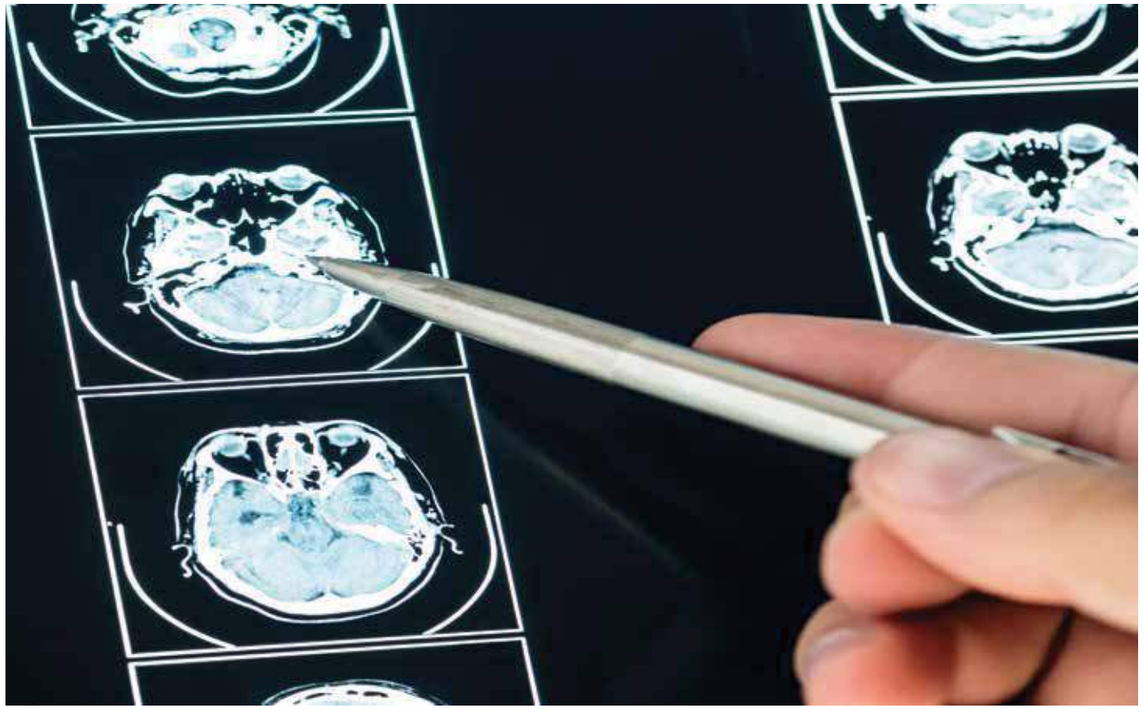
Bilim tarihini inceleyecek olursak görürüz ki her yeni buluş ve gelişme beraberinde daha büyük sorular ve ikilemler doğurmuştur.Son yıllardaki moleküler biyoloji ve genetikteki gelişmelerden dolayı bu sorular insanoğlunun birincil varoluşuna ve canlılığı oluşturan temel dinamiklere kadar derinleşmiştir.Bu durumla paralel olarak etik sorulara verdiğimiz cevaplar da bir o kadar önem kazanmıştır.Bu tür soruların cevaplarını daha sağlıklı verebilmek için psikiyatri,genetik ve adli bilimlere bilim dünyasında verilen önem artmalı ve yapılan çalışmalar teşvik edilmelidir.

The Effect of Oxandrolone

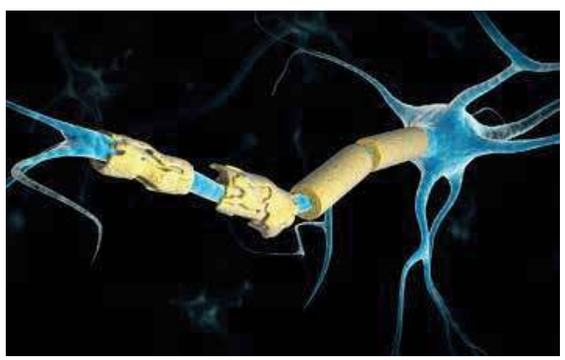
On The MS Patients

Amir Mahdi Akbari

Multiple sclerosis (MS) is the most common demyelinating disease, in which the insulating covers of nerve cells in the brain and spinal cord are damaged. This damage disrupts the ability of parts of the nervous system to transmit signals, resulting in a range of signs and symptoms, including physical, mental, and sometimes psychiatric problems. Specific symptoms can include double vision, blindness in one eye, muscle weakness, and trouble with sensation or coordination.]
MS takes several forms, with new symptoms either occurring in isolated attacks (relapsing forms) or building up over time (progressive forms).
In the relapsing forms of MS, between attacks, symptoms may disappear completely, although some permanent neurological problems often remain, especially as the disease advances. While the cause is unclear, the underlying mechanism is thought to be either destruction by the immune system or failure of the myelin-producing cells. Proposed causes for this include genetics and environmental factors, such as viral infections.
MS is usually diagnosed based on the presenting signs and symptoms and the results of supporting medical tests. No cure for multiple sclerosis is known. Treatments attempt to improve function after an attack and prevent new attacks. Physical therapy and occupational therapy can help with people's ability to function. Many people pursue alternative treatments, despite a lack of evidence of benefit. The long-term outcome is difficult to predict; better outcomes are more often seen in women, those who develop the disease early in life, those with a relapsing course, and those who initially experienced few attacks. Multiple sclerosis is the most common immune-mediated disorder affecting the central nervous system. Nearly one million people have MS in the United States in 2022, and in 2020, about 2.8 million people (about the population of Mississippi) were affected globally, with rates varying widely in different regions and among different populations. The disease usually begins between the ages of 20 and 50 and is twice as common in women as in men. MS was first described in 1868 by French neurologist Jean-Martin Charcot. The name "multiple sclerosis" is short for multiple Cerebro-spinal sclerosis, which refers to the numerous glial scars (or sclerae – essentially plaques or lesions) that develop on the white matter of the brain and spinal cord. Oxandrolone, sold under the brand names Oxandrin and Anavar, among others, is an androgen and anabolic steroid (AAS) medication which is used to help promote weight gain in various situations, to help offset protein catabolism caused by long-term corticosteroid therapy, to support recovery from severe burns, to treat bone pain associated with osteoporosis, to aid in the development of girls with Turner syndrome, and for other indications. It is taken by mouth. ALSO is a synthetic analog of testosterone, used to preserve or restore muscle mass in different clinical conditions and to promote beneficial clinical outcomes in the treatment of wasting and catabolic disorders. The indications for using oxandrolone, and generally all anabolic drugs, are neuromuscular diseases and catabolic muscular conditions. As oxandrolone is already 5a-reduced, it is not a substrate for 5a-reductase, hence is not potentiated in androgenic tissues such as the skin, hair follicles, and prostate gland. This is involved in its reduced ratio of anabolic to androgenic activity. Due to the substitution of one of the carbon atoms with an oxygen atom at the C2 position in the A ring, oxandrolone is resistant to inactivation by 3ahydroxysteroid dehydrogenase in skeletal muscle. This is in contrast to DHT and is thought to underlie the preserved anabolic potency with oxandrolone. Because it is 5a-reduced, oxandrolone is not a substrate for aromatase, hence cannot be aromatized into metabolites with estrogenic activity. Oxandrolone similarly possesses no progestogenic activity



AS we know Oxandrolone is a synthetic analog of testosterone, used to preserve or restore muscle mass in different clinical conditions and to promote beneficial clinical outcomes in the treatment of wasting and catabolic disorders. The indications for using oxandrolone, and generally all anabolic drugs, are neuromuscular diseases and catabolic muscular conditions. We will test the hypothesis that Oxandrolone, added to a physical rehabilitation program, could increase muscle and nerve protein synthesis and improve strength and motor control. demonstrated that, after a local spinal injury, typical alpha-motoneurons can reinnervate a skeletal muscle by regenerating axons after peripheral nerve graft. The emerging branches are kept together by Schwann cell basal lamina scaffolds, suggesting an increase in the synthesis of myelin proteins. The increase in muscle mass, strength, and motor control induced by Oxandrolone may be due to the increased protein synthesis in the muscles and in myelin of the motoneurons. Neuroactive steroids, like progesterone, dihydroprogesterone, tetrahydro progesterone testosterone, and dihydrotestosterone are involved in the control of gene expression of myelin proteins in the peripheral nervous system and are also capable to influence peripheral glial elements and their specific products like myelin membranes. In the adult injured spinal cord and motoneurons, either by disease or by experimentally induced trauma, an axonal repair (due to myelin associated inhibitors) is observed, and the axons may extend over very long distances; these capabilities persist even in neurons reprogrammed from very aged human cells. This process appears to be responsive to exogenous and/or endogenous androgen. This finding might be of relevance for new therapeutic approaches for recovery of motoneuron function and muscle reinnervation, rebuilding the peripheral myelin in demyelinating disease. As a case report that has been reported in 2015 about 5-year-old man with a severe demyelinating neuropathy presented with spastic tetra paresis, muscle weakness, spasticity, and instability during de ambulation.
=A strength test, a walking test, and sensory nerve conduction velocity (SNCV) and compound muscle action potential (CMAP) for the median and sural nerves were assessed.
There is no more evidence about the effect of it on the MS patients, but it can be helpful on them depending on the researchers that have been done in the past .



Beyond the Tremors:

The Psychological Impact of Parkinson's Disease

Seyed Amir Ali Moeineddini

Parkinson's disease (PD) is a neurodegenerative disorder that primarily affects the motor system, causing tremors, rigidity, and bradykinesia. However, the impact of PD extends beyond the physical symptoms, affecting the psychological well-being of patients. The psychological impact of PD is a complex issue that involves various factors, including depression, anxiety, cognitive impairment, and social anxiety.

Depression and anxiety are common in patients with PD. According to Asif et al [3]., the prevalence of depression and anxiety in PD patients is higher than in the general population. The study found that the young population was more susceptible to anxiety, and depression was significantly higher in females.

The impact of PD on the quality of life (QoL) of patients is well documented. Schrag et al [5]. found that patients with akinetic rigid PD had worse QoL scores than those with tremor-dominant disease, mainly due to impairment of axial features. Karlsen et al [1]. reported that PD patients had higher distress scores than healthy elderly people for all the Nottingham Health Profile dimensions.

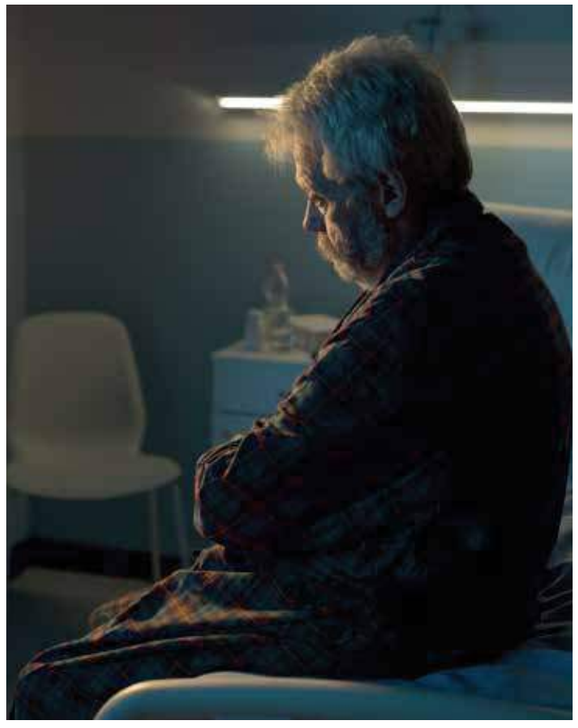
The treatment of psychological issues in PD patients is essential to improve their QoL. Schrag et al [8]. proposed a randomised placebo-controlled trial to evaluate the effectiveness of escitalopram and nortriptyline on depressive symptoms in PD patients. The study aims to recruit 408 people with PD with subsyndromal depression, major depressive disorder, or persistent depressive disorder and a Beck Depression Inventory-II score of 14 or above.

In conclusion, PD has a significant psychological impact on patients, caregivers, and their families. Depression, anxiety, cognitive impairment, and social anxiety are common psychological issues that affect PD patients. Caregivers of PD patients also experience psychological distress. The impact of PD on the QoL of patients is well documented. The treatment of psychological issues in PD patients is essential to improve their QoL.

Saha [2] reported that patients with disfiguring diseases experience significant distress in social interaction, and they may also develop social anxiety either related to or secondary to PD. Nash et al [6]. found that cognitive and behavioural factors contribute to social anxiety in PD patients. These associated factors have not yet been explored in idiopathic PD, where disease severity and motor symptoms might also influence the experience of social anxiety.

Cognitive impairment is another psychological issue that affects PD patients. A study by Aarsland et al [9]. found that disturbances of cognition and emotion are common in PD patients. Cho and Byeon [10] reported that cognitive disorder by PD is known to be very common. Cognitive and neuropsychiatric symptoms may surpass motor symptoms as the major factors impacting patient quality of life [7].

Caregivers of PD patients also experience psychological distress. Aarsland et al [4]. found that mental symptoms in PD patients are important contributors to caregiver distress. Using linear regression analysis, patient predictors of caregiver distress were depression, functional and cognitive impairment, agitation, aberrant motor behaviour, and delusions.



Meningitis

Amir Mahdi Akbari

Meningitis is acute or chronic inflammation of the protective membranes covering the brain and spinal cord, collectively called the meninges. (1) The most common symptoms are fever, headache, and neck stiffness. Other symptoms include confusion or altered consciousness, nausea, vomiting, and an inability to tolerate light or loud noises.Young children often exhibit only nonspecific symptoms, such as irritability, drowsiness, or poor feeding. A non-blanching rash (a rash that does not fade when a glass is rolled over it) may also be present.(2)

The inflammation may be caused by infection with viruses, bacteria or other microorganisms. Noninfectious causes include malignancy (cancer),subarachnoid haemorrhage, chronic inflammatory disease (sarcoidosis) and certain drugs.(3) Meningitis can be life-threatening because of the inflammation's proximity to the brain and spinal cord; therefore, the condition is classified as a medical emergency. (3)

A lumbar puncture, in which a needle is inserted into the spinal canal to collect a sample of cerebrospinal fluid (CSF), can diagnose or exclude meningitis.(4)

Most common bacterial causes of meningitis in the United States are(5)

- Streptococcus pneumoniae (incidence in 2010: 0.3/100,000)
- Group B Streptococcus
- Neisseria meningitidis (incidence in 2010: 0.123/100,000)
- Haemophilus influenzae (incidence in 2010: 0.058/100,000)
- Listeria monocytogene

Bacterial meningitis during the neonatal period is still one of the most devastating conditions, with a morbidity rate of 20% to 60%.(6)The nationwide mortality can be as high as 40% in treated cases in the first month of life, and up to 10% beyond the neonatal period. Multiple factors contribute to the susceptibility of infants to this illness. The immune immaturity of infants is the biggest contributor, especially preterm infants. Because infants do not receive their first set of immunizations until 2 months of age, the risk is high for bacteremia, possibly resulting in bacterial meningitis.Those populations at highest risk are preterm infants, males, the indigent population, and infants in daycare. Also, children of mothers with a history of a sexually transmitted infection, including genital herpes, and mothers who test positive for group B streptococcus are at high risk. Mothers who have eaten certain types of foods may be at risk for passing Listeria infection to their newborns, another pathogen found in the neonatal population. Gram-negative rods, most commonly Escherichia coli, contribute to significant mortality. Group B streptococcus continues to be the most common pathogen causing meningitis in the neonatal period.

Neonates are especially prone to meningitis and sepsis due to their cellular and humoral immune immaturity. They are at high risk for bacterial infections, with 10% to 20% of febrile infants younger than 3 months having a serious bacterial infection. Bacteremia is twice as likely to occur in the first month of life.In developed countries, culture-proven neonatal meningitis is estimated at 0.3 per 1000 live births, but this is likely underestimated. For infants in the neonatal intensive care unit (NICU), of those evaluated for sepsis, only 30% to 50% have a lumbar puncture done, and 75% of the time it occurs after the initiation of broad-spectrum antibiotics. As such, the culture results may be affected by this.(7) The mortality rate is about 10% to 15%, and the morbidity remains high. Up to 50% of infants who survive the illness develop chronic neurological sequelae, including seizures, cognitive deficiencies, motor problems, as well as hearing and visual impairment.(8)In developing countries, the incidence is higher, at 0.8 to 6.1 per 1000 live births, with a mortality rate of up to 58%.(7) Reporting in some of these countriesis suspect, and the incidence is likely higher.Multiple sources report that in the last 40 years, the mortality of this disease has dropped tremendously. However, despite the multitude of advances in neonatology and medicine, morbidity has not changed.

Calorie Restrictions and Eating Disorders:

An Overview

Shough (Maryam) Alharata

One of the most promising dietary interventions for extending the human lifespan is calorie restriction (CR), which involves reducing calorie intake to a level that does not compromise general health. However, it is important to recognize that calorie restriction can intersect with disordered eating patterns and potentially contribute to the development or exacerbation of eating disorders. This article explores the complex relationship between calorie restriction and eating disorders, shedding light on the potential risks and considerations involved.

Understanding Calorie Restriction:
Caloric restriction involves reducing energy intake below typical daily requirements and is often pursued for weight loss, body composition changes, or health optimization. It refers to the act of onsistently maintaining a pattern of consuming fewer calories on average, ensuring that essential nutrients are not compromised. While modest calorie restrictions can be implemented safely in a controlled and supervised context, extreme or prolonged restrictions may have detrimental effects. Eating disorders are severe mental health conditions characterized by disturbed eating behaviors and attitudes toward food, weight, and body shape. Anorexia nervosa, bulimia nervosa, and binge eating disorder are the three most prevalent eating disorders. Anorexia nervosa (AN) is primarily identified by self-induced malnutrition and significant weight loss, which can lead

to cachexia. When body weight falls below a predetermined level, AN is deemed a health risk in accordance with diagnostic criteria.
For adults, this danger is observed when the body mass index (BMI) falls below 17.5 kg/m^2, while for children and adolescents, it corresponds to being below the 10th percentile of BMI for age. Bulimia nervosa (BN) is characterized by recurring periods of uncontrollable cravings for high-calorie foods. The use of laxatives and/or diuretics improperly, self-induced vomiting, and periods of strict fasting alternate with these episodes while Binge eating disorder (BED) is characterized by recurrent episodes of overeating and a loss of control over eating habits.

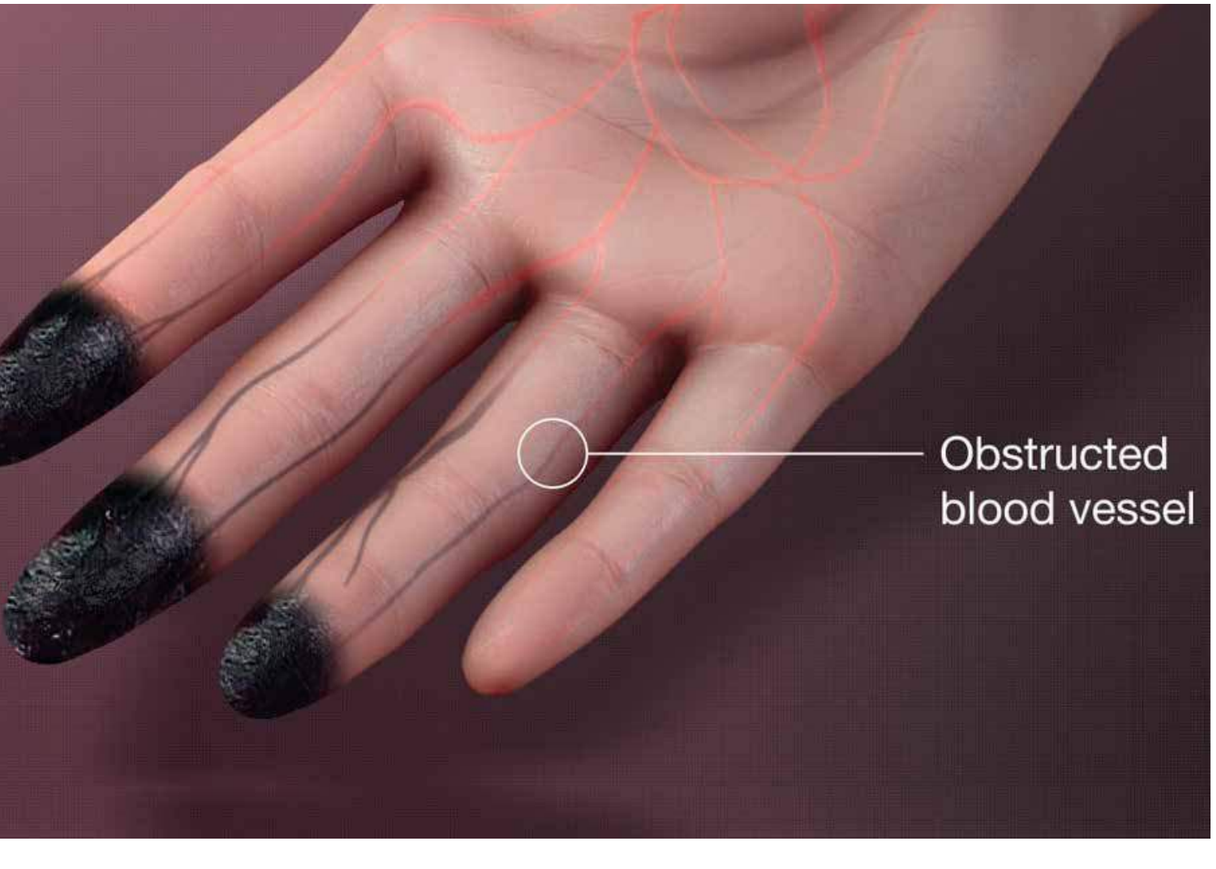
The presence of complex psychological and physiological factors underscores the importance of recognizing these illnesses and understanding how to address them effectively.

Calorie Restriction and Eating Disorders:

1. **Triggering and Exacerbating Factors:**
   - Calorie restriction can act as a trigger for individuals susceptible to disordered eating behaviors, especially those with a perfectionistic mindset or body image concerns.
   - Restrictive eating patterns can exacerbate pre-existing eating disorders, reinforcin obsessive thoughts about food and weight control. For individuals with anorexia, the restriction of calories and excessive exercise are employed as coping mechanisms to address emotional needs and pain, often driven by a fear of obesity.
2. **Reciprocal Relationship:**
   - Caloric restriction has the potential to trigger the development of eating disorders, while conversely, eating disorders often coincide with the practice of caloric restriction.
3. **Physiological Impact:**
   - Long-term calorie restriction interferes with healthy physiological functions and causes metabolic changes, hormonal imbalances, and nutrient deficiencies.
   - Knuckle calluses, tooth enamel deterioration, enlarged salivary glands, cardiomegaly (ipecac poisoning), hypochloremia, hypokalemia, metabolic alkalosis (from vomiting), and increased salivary amylase can present in patients with bulimia nervosa.

Clinical Considerations and Recommendations:

1. **Early Detection and proactive Intervention:**
   - Healthcare professionals should be vigilant in recognizing warning signs of disordered eating behaviors and closely monitor individuals engaging in calorie restriction for prolonged periods.
   - Early intervention and appropriate treatment can help prevent the progression of eating disorders and associated complications
2. **Balanced Approach:**
   - Enhancing physical and mental health can be safely and effectively achieved through healthy eating, exercise, and adopting appropriate energy balance behaviors. It is crucial to note that these interventions should not involve the promotion of negative body image, shaming individuals, or perpetuating social stigma.
3. **Integrated Care**
   - Addressing both the psychological and physiological aspects of eating disorders linked to calorie restriction requires an interdisciplinary approach involving mental health professionals, registered dietitians, and doctors. Understanding the complex relationship between calorie restriction and eating disorders is essential for healthcare professionals and individuals striving for a balanced approach to nutrition and overall well-being. By promoting education, early intervention, and collaborative care, we can mitigate the risks to mental and physical health when calorie restriction is practiced without proper guidance and in vulnerable individuals.



An Overview of **Buerger's Disease**

Bayan Taleb

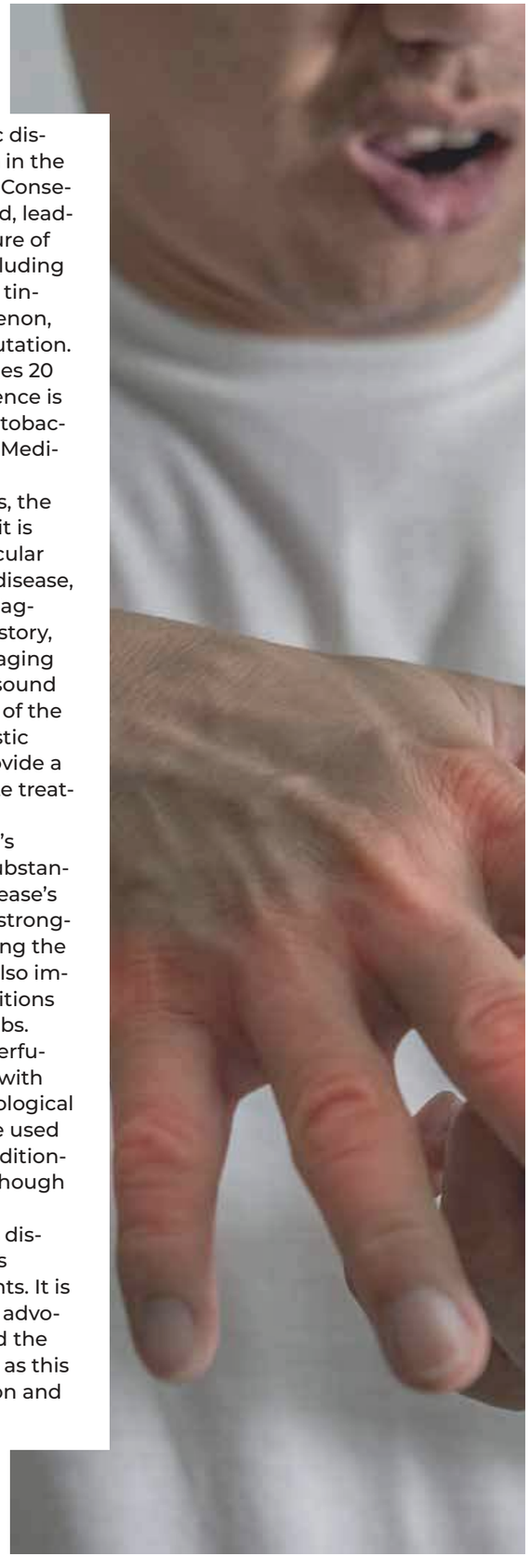
In the realm of medicine, there exists a myriad of mysteries that still eludes our understanding. Amongst these medical enigmas lies Buerger's Disease, a rare condition that has challenged the medical community for decades. Although Buerger's Disease, also known as Thromboangiitis Obliterans, was first identified by Dr. Leo Buerger more than a century ago, our understanding of this condition remains limited, with no known cure or definitive pathogenesis identified to date.

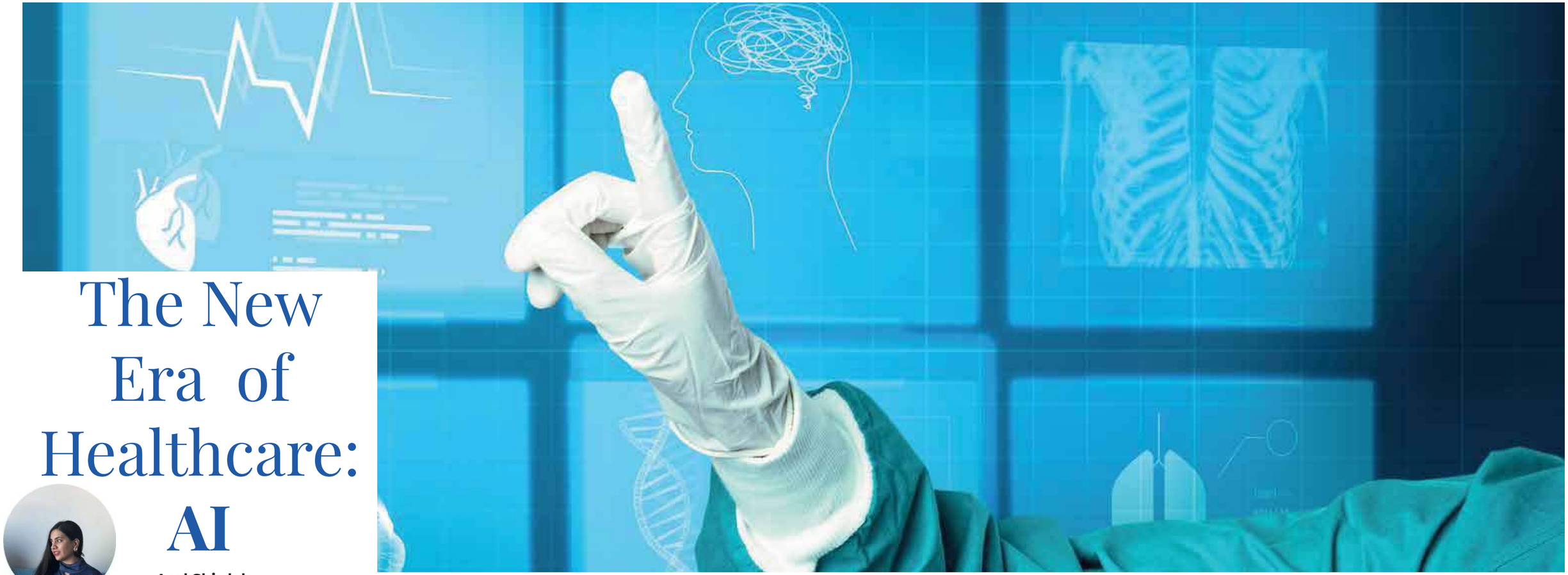
At its core, Buerger's Disease is a nonatherosclerotic disorder that triggers inflammation and clot formation in the small and medium blood vessels of the extremities. Consequently, these vessels become narrowed or occluded, leading to tissue damage and necrosis. The clinical picture of Buerger's Disease showcases various symptoms including painful ulcerations of the fingers and toes, pain and tingling in the limbs, claudication, Raynaud's phenomenon, and in severe cases, gangrene, which requires amputation. This condition predominantly afflicts young men ages 20 to 45 who engage in heavy smoking, and its occurrence is more common in regions with a high prevalence of tobacco use such as the Middle East, Eastern Europe, the Mediterranean Region, and Southeast Asia.

As is often the case with obscure medical conditions, the diagnosis of Buerger's Disease can be difficult, and it is not uncommon for it to be confused with other vascular disorders. Hence, to accurately diagnose Buerger's disease, healthcare professionals rely on a comprehensive diagnostic approach. This includes a detailed medical history, a thorough physical examination, and advanced imaging techniques such as arteriograms and Doppler ultrasound of the extremity, which offer a visual representation of the affected blood vessels. By integrating these diagnostic methods, medical practitioners can successfully provide a precise diagnosis, paving the way for the appropriate treatment to be administered.

Despite the absence of a definitive cure for Buerger's Disease, several treatments are available that can substantially alleviate the symptoms and decelerate the disease's progression. Smoking and tobacco use cessation is strongly recommended as it is the cornerstone to controlling the disease and impeding possible complications. It is also imperative to avoid cold temperatures and other conditions that decrease blood flow in the upper and lower limbs. Vasodilators could be necessary to increase blood perfusion to the tissues especially if the patient presents with concurrent Raynaud phenomenon. Other pharmacological agents include prostaglandin analogs, which can be used to relieve pain and treat ischemic complications. Additionally, in severe cases, surgery may be required even though it is not common.

In light of the existing knowledge gaps of Buerger's disease, researchers persist in their efforts to unravel its underlying mechanisms and discover new treatments. It is worth noting that healthcare professionals strongly advocate for the cessation of all forms of tobacco use and the avoidance of the exposure to secondhand smoking, as this is crucial in limiting the exacerbation of the condition and alleviating its symptoms.





The New Era of Healthcare: AI

Asal Shirdel

Artificial intelligence, also known as AI, is a discipline within computer science that is capable of analyzing intricate medical data. Its potential to exploit significant relationships within a data set can be employed in a wide range of clinical situations, such as diagnosis, therapy, and forecasting results. (AN Ramesh, 2004).

The healthcare industry has been undergoing a major transformation in recent years, with advancements in technology driving innovation across the sector. One of the most significant developments has been the rise of artificial intelligence (AI) and its applications in medicine. AI is revolutionizing the way we approach healthcare, from diagnosis and treatment to research and development.

The field of AI in medicine is vast, with many different technologies and applications. However, for now, we will focus specifically on deep learning. Deep learning is a type of machine learning algorithm that uses neural networks to analyze large amounts of data and make predictions or decisions based on that data. In healthcare, deep learning has shown great promise in a variety of applications, including medical image analysis, disease diagnosis, drug discovery, and clinical decision support

One of the primary applications of AI in healthcare is improving the accuracy of diagnosing. Deep learning algorithms can analyze vast amounts of medical data, including imaging tests, to detect patterns that may be too subtle for the human eye to identify. This can lead to earlier and more accurate diagnose of conditions such as cancer and heart disease.

SomE of the specific applications of deep learning in X-ray analysis include:

1. Machine learning models can automatically analyze and diagnose X-ray images for specific diseases such as pneumonia or lung cancer with high accuracy.
2. The detection of anomalies or abnormalities in X-ray images can be enhanced through the use of computer vision techniques, which can identify subtle differences that may be imperceptible to human radiologists.
3. Image segmentation in X-ray images can be facilitated through advanced computational techniques, which can accurately categorize various regions of interest, such as bone or tissue, to aid in diagnosis.
4. Clinical decision-making can be improved through the use of artificial intelligence algorithms that analyze X-ray images. These algorithms can identify concerning areas and provide recommendations for follow-up tests or procedures, ultimately improving patient outcomes.

The interpretation of the chest radiograph can be challenging due to the superimposition of anatomical structures along the projection direction. This effect can make it very difficult to detect abnormalities in particular locations (for example, a nodule posterior to the heart in a frontal CXR), to detect small or subtle abnormalities, or to accurately distinguish between 2 different pathological patterns. For these reasons, radiologists typically show high inter-observer variability in their analysis of CXR image. (ErdiÇallı, 2021)

AI and Machine Learning in Drug Discovery :

The process of discovering and developing new drugs is a critical area of research for chemical scientists and the pharmaceutical industry. However, it faces obstacles such as poor effectiveness, delivery to unintended targets, high expenses, and time consumption. Moreover, the abundance and complexity of data from areas such as genomics, proteomics, microarrays, and clinical trials present further challenges to the drug discovery pipeline. Artificial intelligence and machine learning have modernized this field, with artificial neural networks and deep learning algorithms providing novel solutions to these challenges (Rohan Gupta # 1) (Rohan Gupta # 1, Artificial intelligence to deep learning: machine intelligence approach for drug discovery, 2021) However, the potential uses of AI in medicine extend far beyond just these applications. AI is also being explored for its potential to improve patient outcomes through personalized medicine, to enhance the efficiency of healthcare operations through automation, and to address public health challenges through data analysis and predictive modeling. (Helen K Brittain, 2017).

Pluripotent Kök Hücre Kullanımı ile Kalp Rejenerasyonu

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Kardiyovasküler hastalıklar, dünya genelinde hastalığa bağlı ölümlerin en sık nedenidir (Go vd., 2013). Farmasötik, perkütan ve cerrahi müdahaleler ile kardiyak atakların tekrarlamasının önüne geçilmeye çalışılsa dainı azaltmış olsa'da, bu durum için kalp nakli dışındaki bir tedavilerin etkinliği yoktur ya da çok düşüktür. Kardiyomiyositler iskemik olaylar gibi durumlarda ve diğer olaylarla hasarlandığında hasar gördüğünde, kalan canlı kardiyomiyositlerin çoğalma kapasitesinin sınırlı olması sınırlıdır ve ölü kardiyomiyositlerin yerini kontraktil olmayan fibröz doku alması nedeniyle kalp yetmezliği gelişimine yol açan fonksiyonel bozulmalar meydana gelir. Kalp yetmezliği morbiditesindeki artış oranları göz önünde bulundurulduğunda, kalp rahatsızlığı için yeni ve güncel terapi tedavilerin geliştirilmesi, üzerinde çalışılması gereken konulardandırmeye acil bir ihtiyaç vardır. Rejeneratif tıp, kalp hastalıklarının tedavisinde umut vadedici tedavi seçeneklerinden biridir. İlk klinik deneyler, kemik iliği kaynaklı hücrelerin ve kalp kök hücrelerinin kalp transplantasyonunda işlevsel faydaları sağladığın ortaya koymuştur. Ancak bu hücresel tedaviler, kalp yetmezliği için mevcut standart tedaviler arasında yer almamaktadır (Chien vd., 2019; Murry & MacLellan, 2020).

Embriyonik ve uyarılmış pluripotent kök hücreleri (sırasıyla ESC'ler ve iPSC'ler) içeren pluripotent kök hücreler (PSC'ler), sınırsız denebilecek kardiyojenik kapasiteleri ile kalp hastalıklarında rejeneratif tıp alanında büyük potansiyele sahiptir. Klinik öncesi pek çok çalışma, PSC'den türetilen kardiyomiyositlerin (PSC-CM'ler), transplantasyon sonrası fonksiyonel faydalarını ortaya koymuştur. Bu hücrelerin kullanımı, kardiyovasküler hastalıkların modellenmesine izin vererek, insan hastalık mekanizma çalışmalarına yeni bir bakış açısı kazandırarak tedavi stratejilerine katkı sağlar (Kadota vd., 2020).

İnsan pluripotent kök hücreleri (hPSC'ler) sınırsız bir şekilde kendini yenileyebilir ve kardiyomiyositleri de içeren üç germ tabakasına farklılaşabilir. Bu yetenekleri ile gerektiği kadar hPSC'den türetilen kardiyomiyosit (hPSC-CM'ler) hazırlanabilir. Elde edilen kanıtlar, hPSC-CM'lerin hasarlı kalplerin yeniden kasılması ve konakçı ile aşı kardiyomiyositleri arasında boşluk bağlantılarının oluşumu üzerindeki yararlı etkilerini ortaya koymaktadır (Liu vd., 2018; Shiba vd., 2016). Yapılan son çalışmalar, enfarktüs sonrası kasılma fonksiyonunun iyileşmesi açısından hPSC-CM'lerin, iskelet miyoblastları ve mezenkimal kök hücreler gibi diğer somatik hücrelerden üstün olduğunu göstermektedir (Ishida vd., 2019). Kalp yetmezliği için yeni nesil kök hücre tedavisinde hPSC-CM'lerin kullanımına yönelik klinik çalışmalara başlanmıştır. Bu derleme, kalp rejenerasyonu için hPSC-CM'lerin mevcut durumunu ve güncel çalışmaları özetlemekte ve tartışmaktadır (Kadota vd., 2020).

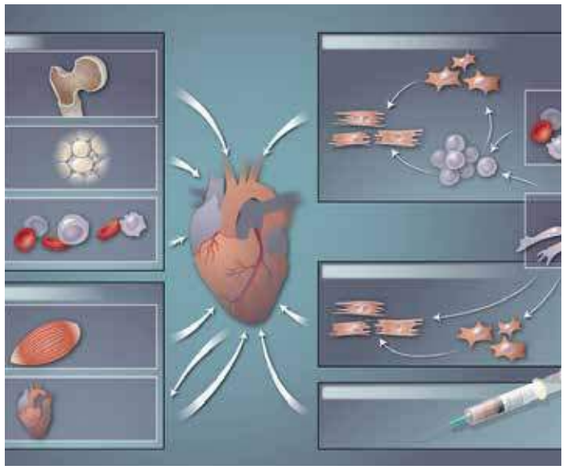
Kalp, fonksiyonlarını yerine getirebilmek için yüksek mitokondriyal aktiviteye ve yapısal proteinlere gereksinim duyması nedeniyle genetik hastalıklar açısından riski altındadır. İnsan kalp hastalıklarını modelleme teknikleri, hastaya özgü insan kaynaklı pluripotent kök hücre kaynaklı kardiyomiyositlerin (hiPSC-CM'ler) geliştirilmesiyle son beş yılda önemli ölçüde ilerlemiştir (Burridge vd., 2012). Çok sayıdaki genetik ve çevresel faktörlü kalp hastalığını doğru bir şekilde özetlediği gösterilmiştir (Matsa vd., 2014; Sharma vd., 2014a).

Japonya'da insan iPSC-CM'leri (hiPSC-CM'ler) kullanılan ilk klinik çalışmalar ile birlikte yeni tedavi stratejilerinde PSC-CM'lerin kullanılmaya başlandığı kritik bir sürece girilmiştir. Bu derlemede aynı zamanda, kalp rejenerasyonu için PSC-CM'lerin kullanımı hakkında güncel bilgileri, bakış açılarını özetlemek amaçlanmaktadır (Chien vd., 2019; Murry & MacLellan, 2020).

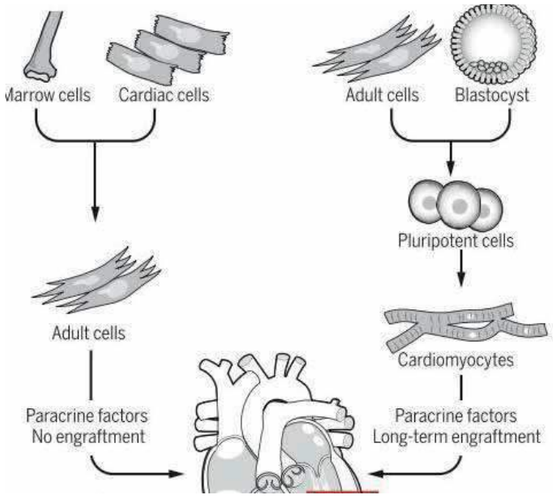
Bir hastalık fenotipinde, uzun süreli hiPSC kültürü ve kriyoprezervasyonu, hiPSC'lerin kardiyomiyositlere farklılaşması ve hastalığa sahip bireylerden hiPSC'lerin oluşturulması gibi laboratuvar aşamaları bulunmaktadır (Burridge vd., 2015). Bu aşamaya ulaşabilmek için, insan pluripotent kültüründe, yeniden programlama ve kardiyak farklılaşmada önemli ilerlemelerin kaydedilmesi gerekmektedir. İnsan somatik hücrelerinin hiPSC'lere yeniden programlanması için, retroviral ve lentiviral ekspresyondan başlanarak, kendi kendini kopyalayan epizomal plazmidlerden tek bir kodon optimize mini intronik plazmide (CoMIP) doğru ilerleyen gen iletimi metodolojisi teknikleri kaydedilmiştir (Diecke vd., 2015).

CoMiP'de, insan OCT4, SOX2 ve KLF4 cDNA sekansları, yüksek seviyeli ekspresyon için en uygun olanlar ile değiştirilir ve transfeksiyon verimliliğini artırmak için minimum boyutlu bir omurga ile bir plazmid kullanılabilir. Bu teknik, eksojen DNA dizilerinin entegrasyonu olmadan yeniden programlamaya izin verir, böylece hedef hücre genomunun bütünlüğünü korur. İkinci büyük gelişme ise hiPSC'leri kültürlemek için kullanılabilen basit, kimyasal olarak tanımlanmış, serum/albüminsiz bir ortamın sadece sekiz bileşenden oluştuğu keşfidir (E8) (Chen vd., 2011), yeniden programlama için uyumlu olacak şekilde değiştirilebilir (E7). Bu durumun gelişimi, hiPSC kültürlerinin kalitesini önemli ölçüde iyileştirir (kendiliğinden farklılaşan hücreleri ortadan kaldırarak) ve yeniden programlamayı, kültür maliyetini ve karmaşıklığını azaltır. Yakın zamanda, hiPSC-CM (pluripotent kök hücre kaynaklı kardiyomiyositlerin) farklılaşmasının, gösterildiği gibi, serum veya büyüme faktörlerine ihtiyaç duymadan, kimyasal olarak tanımlanmış bir ortam ve küçük moleküller kullanılarak gerçekleştirilebileceği gösterilmiştir. Bu metodolojinin çok sayıda hiPSC hattının farklılaştırılması için güvenilir ve tekrarlanabilir olduğu kanıtlanmıştır (Burridge vd., 2014). Son olarak, TNNT2 (troponin T) ve ACTN2 (α-aktin) için immünofloresan boyama tekniğinin bilinen bir yapısal fenotipi tespit edebildiği ve Fluo-4AM ile kalsiyum görüntüleme kullanılarak fonksiyonel bir fenotipin tespit edilebileceğini gösterilmiştir (Burridge vd., 2015).

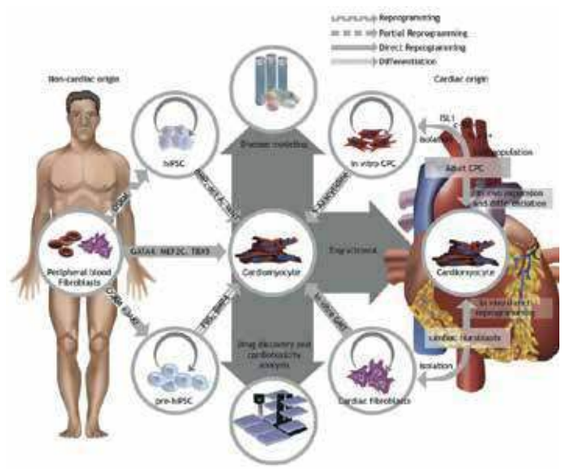
Bu derlemede, bahsedilen üç durumun (yani, CoMIP, kimyasal olarak tanımlanmış yeniden programlama ve kimyasal olarak tanımlanmış farklılaşma) birleştirilerek somatik hücrelerin bir hastadan izole edilebileceğini, hiPSC'lere yeniden programlanabileceğini ve hiPSC-CM'lere farklılaştırılabileceğini göstermeyi amaçladık. Hücreler, immünofloresan ve kalsiyum görüntüleme kullanılarak fenotipik olarak karakterize edilebilmektedir (Burridge vd., 2015).



Şekil 1: Kardiyovasküler doku onarımı için yetişkin ve pluripotent kök hücreler (Matsa vd., 2014).



Şekil 2: Kardiyak kök hücre tedavisi (Murry & MacLellan, 2020)



Şekil 3: Allogeneic transplantation of iPS cell-derived cardiomyocytes regenerates primate hearts (Burridge vd., 2012).

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