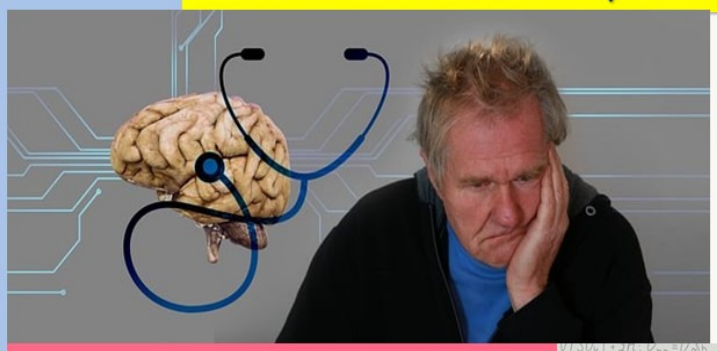
PHARMAMEDICAL TREND ANALYSIS (PMTA)



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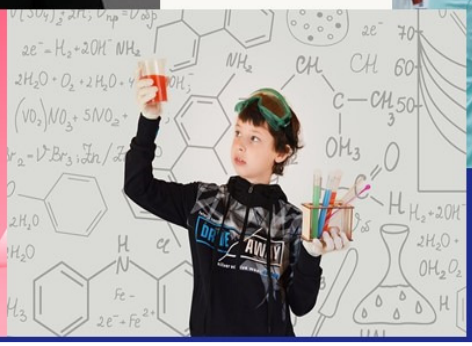

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Medical Section

Secret Key to Extend Lifespan and Cancer-fighting Ability of Human Beings

Deterioration of body organs and the diseases of cancer, diabetes, cardiovascular failure affect the lifespan. However, genetic modification may extend its lifespan and superpower its cancer-fighting cells.

Aging and lifespan of human beings is associated with body organ deterioration or decay and the occurrence of chronic diseases, such as cancer, diabetes, cardiovascular failure and neurodegeneration. In the past decades, a lot of researches have been carried out to develop different biomedical-and biotechnology-related strategies, which have been applied to cure the life-threatening diseases including therapy of cancer and extend lifespan of human beings.

A research team from Taipei Medical University in Taiwan published a research article in the public domain (bioRxiv preprint) in April 21, 2023, which reported that a genetic modification or mutation in a mouse model extended its lifespan, healthspan and superpowered its cancer-fighting cells. The genetically engineered or modified mice had high anti-cancer capability.

The bone marrow mononuclear cells of mice model could be transplanted to ordinary mice to have the anti-cancer capability and extend lifespan characteristics. Using gene expression profiling analysis, the research team has identified changes of the expression of specific proteins and cellular pathways in the leukocytes of mice, which could provide the mice with anti-cancer and/or anti-aging characteristics.

The research team have indicated that the results of this study have significant implication for human health. They would apply them in the near future and if it is successful, they will apply for clinical trials.

Reviewed by Dr Md Anawar Hossain

Reference

Wang, J.-P., Hung, C.-H., Liou, Y.-H., Liu, C.-C., Yeh, K.-H. et al. (2023). Hematopoietic Transfer of the Anti-Cancer and Lifespan-Extending Capabilities of A Genetically Engineered Blood System. bioRxiv preprint, Cold Spring Harbor Laboratory. 10.1101/2023.04.21.537849.

Current Treatment for Alzheimer's Diseases

Medications currently available for treatment of Alzheimer's diseases cannot cure Alzheimer's. Some drugs may help to reduce symptoms of memory loss and confusion for a short time, while other medicines change disease progression helping cognition and function.

The patients with Alzheimer's diseases and their family members should know about the currently available treatment options and medications to treat Alzheimer's diseases. The more they know about Alzheimer's treatment and medications, the better they will be prepared to discuss them with their medical doctors and make informed choices about their treatment plan.

Efficacy of current Alzheimer's drugs

- Current medications cannot cure Alzheimer's disease,
- Some drugs may help to reduce symptoms, such as memory loss and confusion, for a limited time,
- Other medicines change disease progression helping cognition and function,
- Treatments may be available in different forms (pill, patch or other). An experienced medical doctor should monitor people who are taking this treatment.

Types of FDA-approved drugs for Alzheimer's

The U.S. Food and Drug Administration (FDA) has approved medications that fall into two categories:

- Drugs that may change disease progression in people living with Alzheimer's,
- Drugs that may temporarily mitigate some symptoms of the disease.

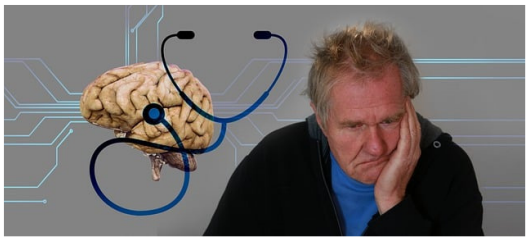
Drugs that may change disease progression

An anti-amyloid antibody drug called aducanumab (Aduhelm™) is the first therapy for the treatment of Alzheimer's disease. The drug was indicated for people living with early Alzheimer's disease, mild cognitive impairment (MCI) or mild dementia due to Alzheimer's disease.

- The drug targets beta-amyloid, a microscopic protein fragment that accumulates in the brain and forms into plaques,
- Removing amyloid from the brain is reasonably likely to reduce cognitive and functional decline in people living with early Alzheimer's,
- Preventing beta-amyloid build-up may provide benefit,
- Side effects include ARIA, headache and fall.

Drugs to reduce cognitive (memory and thinking) symptoms

These drugs are prescribed for patients to treat their symptoms of loss of memory and thinking. These medications cannot stop the damage of brain cells caused by Alzheimer's. But they may help reduce or stabilize symptoms for a limited time. The drugs currently approved to treat cognitive symptoms are cholinesterase inhibitors and glutamate regulators.



A few examples of these drugs include Donepezil Aricept®, Galantamine Razadyne®, Rivastigmine Exelon®, Memantine Namenda®, and Memantine + Donepezil Namzaric®. These drugs are indicated to use for mild to severe dementia due to Alzheimer's diseases. These drugs have some common side effects, such as nausea, vomiting, loss of appetite, muscle cramps and increased frequency of bowel movements. Memantine Namenda® has side effects of headache, constipation, confusion and dizziness.

Non-cognitive (behavioral and psychological) symptoms

Alzheimer's affects not only just memory and thinking, but also causes different behavioral and psychological symptoms that accompany dementia, such as sleep changes. Sleep changes may include difficulty in sleeping, taking daytime naps and/or experiencing other shifts in sleep pattern.

Suvorexant (Belsomra®) is prescribed to treat insomnia in people living with Alzheimer's (mild to moderate).

Reviewed by Dr Md Anawar Hossain

Reference

Alzheimer's Association, 2022. Treatments and Research, https://www.alz.org/help-support/i-have-alz/treatments-research. Accessed on 22/09/2022.

How Depression Causes Abnormal Brain Signals and Transcranial Magnetic Stimulation Restores Normal Flow of Signals

Severe depression could cause an abnormal brain signal and neural activity in patients. Transcranial magnetic stimulation (TMS) can stimulate only one part of the brain without a generalised seizure, can reset the abnormal flow of signal and restore the normal directional flow of brain signal in the patients.

Transcranial magnetic stimulation (TMS) is a widely used technique to treat and cure depression and other mental health conditions. But the mechanism behind this was not fully clear to the doctors and scientists.

Electroconvulsive therapy (ECT) is also the most effective treatment to treat and cure depression. But this procedure is conducted under general anaesthesia in which small electric currents are passed through the brain causing a short seizure. This technique caused a lot of stigmas as well. Therefore, the doctors and scientists were exploring alternative technique to only stimulate one part of the brain without a generalised seizure.

Transcranial magnetic stimulation (TMS) is the right technique to stimulate only one part of the brain without a generalised seizure. A research team of Dr Anish Mitra at Stanford University in the United States reported the mechanism how severe depression could cause an abnormal brain signal and how magnetic stimulation can reset the abnormal flow of signal. Powerful magnetic stimulation can restore the normal directional flow of brain signal in the patients with depression and quickly relieve patients.

The abnormal neural activity in patients with depression can be used as a valuable biomarker for developing further treatment system. Before conducting treatment, the doctors should identify the biomarker in individual patient separately by using imaging, and then determine in which part of the brain they should perform transcranial magnetic stimulation.

Ref: Euronews, 2023. Scientists pinpoint how depression causes brain signals to go haywire - and how they can be rerouted. Updated: 26/05/2023, Url: https://www.euronews.com/next/2023/05/26/scientists-pinpoint-how-depression-causes-brain-signals-to-go-haywire-and-how-they-can-be-.

High Blood Pressure, Health Problems and Medications

Suffering from high blood pressure for long time may cause different health problems, such as heart disease, stroke, loss of eyesight, chronic kidney disease, and other blood vessel diseases. There are three different stages of high blood pressure. Doctors may recommend the patients to follow healthy lifestyle choices and/or medications depending on their blood pressure conditions. There are several types of medicines for treatment of high blood pressure, which include *ACE inhibitors*, *ARBs*, *Calcium channel blockers*, *Diuretics*, and *Beta blockers*. Some blood pressure medicines, which are not used as often, are *Alpha-blockers, Centrally acting drugs, Vasodilators* and *Renin inhibitors.* Some common side effects of blood pressure medicines are Cough, Diarrhea or constipation, Dizziness, Erection problems, feeling nervous, feeling tired, Headache, Nausea or vomiting, Skin rash, and Weight loss or gain. The following lifestyle changes are recommended to lower high blood pressure: Reducing salt consumption, eating a low-fat/balanced diet, exercise, reducing drinking alcohol, maintaining healthy weight, uptake of less caffeine, and stopping smoking.

Suffering from high blood pressure for long time may cause different health problems, such as heart disease, stroke, loss of eyesight, chronic kidney disease, and other blood vessel diseases. Therefore, it is very important to treat the high blood pressure and keep it under control for healthy life.

At the beginning, doctors recommend the patients to follow healthy lifestyle choices to control high blood pressure if it works and they monitor the blood pressure level. The patients have elevated blood pressure if their blood pressure reading is 120/80 to 129/80 mm Hg. Doctors may recommend the patients to change their lifestyle choices to lower blood pressure level down to the normal range. At this beginning stage, doctors rarely prescribe medicines. However, doctors may recommend medicines to control high blood pressure if lifestyle changes can't lower the high blood pressure to the safe level.

Treatments for high blood pressure:

High blood pressure reading can be grouped in two stages.

Stage 1:

Blood pressure is equal to or higher than 130/80, but lower than 140/90 mm Hg. Doctors may recommend medicines to treat high blood pressure. But if the patients have other diseases or risk factors, their doctors may recommend them both medicines and lifestyle changes at the same time.

Stage 2

Blood pressure is equal to or higher than 140/90 mm Hg. The doctors will most likely recommend that the patients take medicines and recommend lifestyle changes.

High risk patients

Doctor will recommend the patient to measure and monitor their blood pressure regularly before making a final diagnosis of either elevated blood pressure or high blood pressure. If some patients have a higher risk for heart disease, diabetes, heart problems, or a history of a stroke, doctors may prescribe medicines even at lower blood pressure reading below 130/80.

Medicines for high blood pressures

Generally, doctors recommend the patients to take only a single drug at first, but they can recommend two drugs if the patients have stage 2 high blood pressure. There are several types of medicines for treatment of high blood pressure. Doctors will decide which medicine is right for the patient. Sometimes, doctors may recommend the patient to take more than one type of medicine. Different pharmaceutical companies manufacture these medicines under their own brand names. Different types of medicines are listed and described below. Each type of blood pressure medicine is manufactured and marketized under different brand and generic names.

ACE inhibitors

Angiotensin-converting enzyme inhibitors are called ACE inhibitors. They are a type of medicines that prevent enzymes to produce angiotensin II in your body. Angiotensin II narrows blood vessels, which can cause high blood pressure and forces the heart to work harder. Furthermore, Angiotensin II also releases hormones increasing blood pressure. Therefore, ACE inhibitors helps relax your blood vessels, which lowers your blood pressure.

Common examples are enalapril, lisinopril, perindopril and ramipril.

ACE inhibitors may show the most common side effect of a persistent dry cough. They may demonstrate other possible side effects of headaches, dizziness and a rash.

Angiotensin II receptor blockers (ARBs)

Angiotensin II receptor blockers are called ARBs. Angiotensin II receptor blockers reduce the action of angiotensin II in your body, which helps relax your blood vessels and lowers your blood pressure. Therefore, ARBs work in a similar way to ACE inhibitors.

The doctors often recommended ARBs if ACE inhibitors cause troublesome side effects.

Common examples are candesartan, irbesartan, losartan, valsartan and olmesartan.

Uptake of these medications can show the possible side effects of dizziness, headaches, and cold or flu-like symptoms.

Calcium channel blockers

Calcium channel blockers reduce blood pressure by widening your blood vessels. Calcium channel blockers relax blood vessels by reducing calcium entering cells in the wall of the blood vessels.

Common examples are amlodipine, felodipine and nifedipine. Other medicines, such as diltiazem and verapamil, are also available.

Possible side effects include headaches, swollen ankles and constipation. Drinking grapefruit juice along with taking some calcium channel blockers can increase your risk of side effects.

Diuretics

They are, sometimes, called water pills. Diuretics remove excess water and salt from the body through your pee. They help your kidneys remove some salt (sodium) from your body. As a result, your blood vessels don't have to hold as much fluid and your blood pressure goes down.

They're often used instead of calcium channel blockers if calcium channel blockers cause troublesome side effects, or if you have signs of heart failure.

Common examples are indapamide and bendroflumethiazide.

Possible side effects include dizziness when standing up, increased thirst, needing to go to the toilet frequently, and a rash. You might also get low potassium and low sodium after long-term use. You'll have regular blood tests to check for this.

Beta blockers

Beta-blockers can reduce blood pressure by making the heart beat at a slower rate and with less force. They used to be a popular treatment for high blood pressure, but now tend to be used only when other treatments have not worked. Beta blockers are considered less effective than other blood pressure medicines.

Common examples are atenolol and bisoprolol.

Possible side effects include dizziness, headaches, tiredness, and cold hands and feet.

Following blood pressure medicines are not used as often:

Alpha-blockers help relax your blood vessels, which lowers your blood pressure.

Centrally acting drugs signal your brain and nervous system to relax your blood vessels.

Vasodilators signal the muscles in the walls of blood vessels to relax.

Renin inhibitors act by reducing the amount of angiotensin precursors thereby relaxing your blood vessels.

Some common side effects of blood pressure medicines

All blood pressure medicines have side effects. But most of these effects are mild and may go away over time. The side effects include

- Cough,
- Diarrhea or constipation,
- Dizziness or lightheadedness,
- Erection problems,
- Feeling nervous,
- Feeling tired, weak, drowsy, or a lack of energy,
- Headache,
- Nausea or vomiting,
- Skin rash,
- Weight loss or gain without trying

Lifestyle changes

Lifestyle changes can reduce high blood pressure. Some of these changes may take shorter time, while others may take longer time to lower blood pressure. The following lifestyle changes are recommended to lower high blood pressure:

* Reduce salt consumption to less than 6g a day (about a teaspoonful).

* Eat a low-fat, balanced diet including plenty of fresh fruit and vegetables.

* Exercise: Take regular exercise and be active.

* Reduce drinking alcohol.

* Maintain healthy weight and lose wight if you are overweight.

* Uptake less caffeine from drinking coffee, tea and cola.

* Stop smoking.

If you adopt and practise lifestyle changes early, you may avoid taking medicines. Therefore, from today, you should take initiative to change your lifestyle whether you are taking medicine or not to control your elevated or high blood pressure.

Reviewed by Dr Md Anawar Hossain

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Source: MedlinePlus, 2023. High blood pressure medications. URL: https://medlineplus.gov/ency/article/007484.htm

Source: NHS, 2023. Treatment-High blood pressure (hypertension). URL: https://www.nhs.uk/conditions/high-blood-pressure-hypertension/treatment/. Accessed on 06/05/2023.

Neural Mechanisms of General Anesthesia

General anesthesia, which is administered to surgical patients during operation, shares the similar numerous neurophysiologic traits with the process of natural sleep

The neural mechanisms underlying sleep–wake and general anesthesia can help to understand their interactions and how anesthetics cause reversible loss of consciousness. Pharmacotherapies, especially those which involve the neural substrates associated with sleep–wake and general anesthesia regulations, can play a significant role for clinical practice in general anesthesia and sleep medicine.

Nowadays, different advanced medical techniques have been developed that can study specific brain regions and neural circuits regulating sleep–wake brain states and general anesthesia. These study results have advanced our understanding and demonstrate that sleep–wake brain states and general anesthesia show similar neurophysiologic traits.

Reference

Wei-Wei Bao, Shan Jiang, Wei-Min Qu, Wen-Xian Li, Chang-Hong Miao and Zhi-Li Huang, Understanding the Neural Mechanisms of General Anesthesia from Interaction with Sleep–Wake State: A Decade of Discovery. Pharmacological Reviews May 2023, 75 (3) 532-553.

Diabetes, Types of Diabetes, Risk factors, Prevention and Management, Symptoms and Treatment by Medications

Diabetes is a chronic health condition that controls sugar level in your blood. Suffering from diabetes for long time may cause different serious health problems, such as heart disease, vision loss, kidney disease, etc. There are three main types of diabetes, such as type 1, type 2 and gestational diabetes. Lifestyle change can help people to prevent developing type 2 diabetes and reverse it. Different types and classes of medications are used by the patients with type 2 diabetes to lower blood sugar level. Some commonly used medicines are Metformin, DPP-4 inhibitors, GLP-1 and dual GLP-1/GIP receptor agonists and SGLT2 Inhibitors.

What is Diabetes?

Diabetes is a chronic (long-lasting) health condition that controls sugar level in your blood after eating foods. Foods, we eat and drink, are converted into sugar (glucose) and released into bloodstream. Our pancreas releases insulin when our blood sugar levels become high and insulin helps blood sugar enter the body's cells for use as energy.

If people have diabetes, their body doesn't produce enough insulin or if produced, it is not used as well as it should be. Cells may stop responding to insulin. Therefore, blood sugar levels become very high in bloodstream. After long time, this health condition can lead to different serious health problems, such as heart disease, vision loss, kidney disease, etc.

Types of Diabetes

There are three main types of diabetes: type 1, type 2 and gestational diabetes (diabetes while pregnant).

What is Type 1 Diabetes?

An autoimmune reaction (the body attacks itself by mistake) causes type 1 diabetes. This reaction prevents your body to produce insulin. About 5-10% of the diabetic people have type 1 diabetes. The children, teens, and young adults are usually diagnosed with type 1 diabetes. There is no treatment or method to cure it or prevent it, but the people with type 1 diabetes require to take insulin every day to survive.

Type 2 Diabetes

Your body doesn't produce enough insulin or can not use insulin well. As a result, blood sugar level becomes higher than normal levels. It develops over many years. About 90-95% of people with diabetes have type 2.

Gestational Diabetes

Some women get diabetes when they are pregnant although they never had diabetes before pregnancy. It is called gestational diabetes. After the birth of baby, gestational diabetes normally goes away, but mother may get type 2 diabetes later in life. Baby could be at higher health risk. They may have obesity as a child or teen and develop type 2 diabetes later in life. Therefore, gestational diabetes is strictly controlled during pregnancy before the birth of baby.

Prediabetes

Prediabetes condition is the primary state of the body before developing type 2 diabetes. People with prediabetes condition have blood sugar levels higher than normal, but it is not high enough for a type 2 diabetes diagnosis.

Risk:

Prediabetes increases the risk of type 2 diabetes, heart disease, and stroke.

Prevention of prediabetes

Lifestyle change can help people to prevent developing type 2 diabetes and reverse it.

Risk Factors of Diabetes

Different types of diabetes have different risk factors (Ref.: CDC, 2023).

Type 1 Diabetes

Although the risk factors for type 1 diabetes are not very clear, but the

following factors are presumed to be responsible:

- **Family history**: Having a parent, brother, or sister with type 1 diabetes.
- **Age**: You can get type 1 diabetes at any age, but it usually develops in children, teens, or young adults.

Type 2 Diabetes

Risk factors for type 2 diabetes are as below (Ref.: CDC, 2023):

- Prediabetes.
- Overweight.
- Age of 45 years or older.
- Family history of type 2 diabetes.
- Are physically active less than 3 times a week.
- Have ever had gestational diabetes (diabetes during pregnancy) or given birth to a baby who weighed over 9 pounds.
- If you have non-alcoholic fatty liver disease, you may also be at risk for type 2 diabetes.

Risk Factors of Gestational Diabetes (Ref.: CDC, 2023):

- Had gestational diabetes during a previous pregnancy.
- Have given birth to a baby who weighed over 9 pounds.
- Are overweight.
- Are more than 25 years old.
- Have a family history of type 2 diabetes.
- Have a hormone disorder called polycystic ovary syndrome (PCOS).
- Are an African American, Hispanic or Latino, American Indian, Alaska Native, Native Hawaiian, or Pacific Islander person.

Prevention of Gestational Diabetes

Women can prevent gestational diabetes before they become pregnant by changing their lifestyle options. Most important lifestyle changes are as below:

- Losing weight if you're overweight,
- Eating a healthy diet,
- Practising regular physical activity.

How to Prevent or Manage Diabetes

Diabetes can't be cured permanently, but it can be managed by following some lifestyles choices and medications as below:

- Losing weight,
- Eating healthy food,
- Being active/Physical activity,
- Taking medicine as prescribed.

Symptoms of Diabetes

If you have any of the following symptoms, you must consult with doctor, and get your blood sugar tested to confirm your diabetes or prediabetes conditions:

- Frequent urination, often at night
- Very thirsty
- Weight loss without trying

- Getting very hungry
- Having blurry vision
- Having numb or tingling hands or feet
- Feeling very tired
- Having very dry skin
- Having sores that heal slowly
- Having more infections than usual

Symptoms of Type 1 Diabetes

- People with type 1 diabetes may also have nausea, vomiting, or stomach pains.
- Symptoms can develop in just a few weeks or months and can be severe.

Symptoms of Type 2 Diabetes

- It often takes several years to develop type 2 diabetes symptoms.
- Sometimes, symptoms of some people are not noticeable at all.
- It is difficult to notice symptoms for some people.
- Therefore, it is better to understand the risk factors for type 2 diabetes.
- Consult your doctor if you notice any symptoms.

Symptoms of Gestational Diabetes

- Gestational Diabetes normally doesn't show any symptoms.
- Doctor test you for gestational diabetes between 24 and 28 weeks of pregnancy.
- You must change lifestyle options to prevent gestational diabetes, protect your health and your baby's health.

Treatment of Type 2 Diabetes by Medications

Different types and classes of medications are available in the pharmacies that are used by people with diabetes to lower blood sugar. These medications work in different ways, but their main goals are to lower blood glucose/sugar level. Some of them are taken orally, while others are injected. Besides insulin, there are some medications widely used by diabetics. We will discuss some of the more commonly used medicines as below:

- Metformin
- DPP-4 inhibitors
- GLP-1 and dual GLP-1/GIP receptor agonists
- SGLT2 Inhibitors

Metformin

Metformin (Glucophage) is a well-known medication for type-2 diabetes patients and it is called a biguanide medication. It mainly decreases the amount of glucose produced by the liver leading to lowering of blood glucose levels. Metformin makes muscle tissue more sensitive to insulin and also helps lower blood glucose levels. Therefore, glucose becomes available for energy production. Metformin is widely taken by many people with type-2 diabetes and even by people with prediabetes. It is prescribed as a first-line therapy to manage type 2 diabetes.

Side effects

Although metformin may have a side effect like diarrhea, however,

consumption of this drug with food may improve it.

Limitations

Metformin does not help weight loss. Sometimes, metformin may not be sufficient for some people as time goes on. This medication is not fully effective for some people or some people can't manage type-2 diabetes by taking only metformin.

Combination therapy

The people, taking metformin, may need additional medication for their diabetes management. They can take additional oral or injectable medications in addition to metformin. The drugs of different groups act in different ways to lower blood glucose levels. Therefore, the medications from different groups may be used together for individual diabetes management. This is called as combination therapy which is, sometimes, more effective for diabetes management and reduce the diabetes-related complications, such as heart disease or chronic kidney disease. However, you should still continue your diet management and physical activity. Monitor the blood glucose levels after taking the combination therapy. Your healthcare provider will prescribe you the combination of medicines that work best for you and your lifestyle, and provide you the ease of diabetes management.

DPP-4 Inhibitors

DPP-4 inhibitors are the useful medications for the diabetic people, which help improve A1C (a measure of average blood glucose levels over 2-3 months), but they don't cause hypoglycemia (low blood glucose). The main function of this medication is to prevent the breakdown of naturally occurring hormones in the body, GLP-1 and GIP, which reduce blood glucose levels in the body. But these hormones are broken down very quickly. DPP-4 inhibitors interfere in the process of breaking down the GLP-1 and GIP, and therefore, these hormones remain active in the body for longer time, and help reduce blood glucose levels only when they are elevated. The diabetic people taking DPP-4 inhibitors do not have the possibility of getting weight gain, and they can nicely tolerate these medications.

DPP-4 inhibitors currently available in the market are as below:

- Alogliptin (Nesina)
- Linagliptin (Tradjenta)
- Saxagliptin (Onglyza)
- Sitagliptin (Januvia)

GLP-1 and Dual GLP-1/GIP Receptor Agonists

GLP-1 medications lower the blood glucose levels by the following mechanisms. They increase insulin production, decrease glucagon release, keep food in stomach longer than normal time and reduce the feeling of hunger. Thus, these medications keep the blood sugar level under control and provide the benefit of weight loss.

The medications GLP-1 and dual GLP-1/GIP receptor agonists are very beneficial for the blood glucose management of the type-2 diabetic patients. These medications demonstrate almost similar effects to

the GLP-1 and GIP produced in the body, but these drugs are resistant to being broken down by the DPP-4 enzyme. Some of these drugs are useful to prevent heart disease.

All of the medications are used as injections except semaglutide (Rybelsus), which is taken orally once daily. It is an oral formulation of semaglutide. Tirzepatide (Mounjaro) is a dual GLP-1/GIP receptor agonist currently available on the market. The list of all drugs is as below:

- Dulaglutide (Trulicity)
- Exenatide (Byetta)
- Exenatide extended-release (Bydureon)
- Liraglutide (Victoza)
- Lixisenatide (Adlyxin)
- Injectable semaglutide (Ozempic)
- Tirzepatide (Mounjaro)

Side effects

The people taking these medications may experience some most common side effects, such as nausea and vomiting when they start taking these medications or increase the dose of medications. But these side effects normally go away after the consumers take time to adjust to the medications. The patients need to consult with the doctors who can balance the benefits and side effects of these medications.

SGLT2 Inhibitors

SGLT2 inhibitors is a new class of drugs that help to increase elimination of blood sugar into the urine by working on the kidneys. Sodium-glucose co-transporter 2 (SGLT2) works in the kidney to reabsorb glucose. SGLT2 inhibitors prevent this action and help to eliminate excess glucose in the urine. People can reduce blood glucose level by increasing the amount of glucose excreted in the urine. These medications are recommended for the people with type-2 diabetes who have high A1C levels. These drugs also help to reduce blood pressure (small decrease) and gain some weight loss.

The Food and Drug Administration (FDA) has approved the following SGLT2 inhibitors to treat type 2 diabetes:

- Bexagliflozin (Brenzavvy),
- Canagliflozin (Invokana),
- Dapagliflozin (Farxiga),
- Empagliflozin (Jardiance),
- Ertugliflozin (Steglatro)

Other benefits

SGLT2 inhibitors can benefit the people to reduce the heart disease, kidney disease, and heart failure. Therefore, the healthcare providers prescribe these medications for the people with type 2 diabetes who also have heart or kidney problems.

Side effects

The most common side effects observed in the people taking these drugs are genital yeast infections due to increased glucose levels in the urine. There is potential of some other side effects, such as urinary tract infections, constipation, and flu-like symptoms.

Reviewed by Dr Md Anawar Hossain

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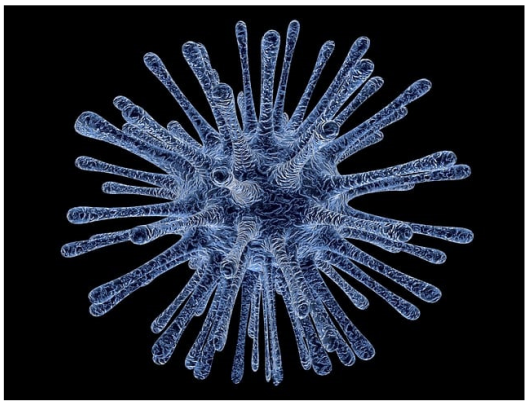
Endocrineweb, 2023. URL: https://www.endocrineweb.com/conditions/type-2-diabetes/insulin-alternatives. Accessed on 16/05/2023.

Outbreak of Marburg Virus Disease in Equatorial Guinea

An outbreak of Marburg virus disease (MVD) occurred in Equatorial Guinea in January 2023. The Ministry of Health and Social Welfare of Equatorial Guinea declared this outbreak on 13 February 2023 after they reported some suspected viral haemorrhagic fever deaths and a positive case in February 2023.



What is Marburg virus disease (MVD)

Marburg virus disease (MVD) is a rare disease. It causes severe hemorrhagic fever and affects both humans and some specific animals. The viral hemorrhagic fever is a very serious disease that may cause death of life. It affects and damages many organ systems of the body including the overall cardiovascular system. This disease also reduces the body's ability to function on its own. It damages the walls of tiny blood vessels causing bleeding, or hemorrhaging. The infection by Marburg virus or Ravn virus, both within genus *Marburgvirus*,

causes this disease. Marburg viruses are zoonotic (or animal-borne) RNA viruses (CDC, 2023). There are no well-established cure or vaccines for all types of diseases.

Co-operation by WHO and Other International Organizations

EDCARN (the Emerging Diseases Clinical Assessment and Response Network) deployed six clinical experts to support the Ministry of Health and mitigate the Marburg virus disease outbreak in Equatorial Guinea. The Global Outbreak and Response Network (GOARN) recruited the clinical experts of different specialty, such as infectious diseases, critical care, and paediatrics. A 20-bed treatment centre and ambulance referral system were established in Bata district of Equatorial Guinea, because this district was the most affected area by Marburg virus disease (MVD).

Reference

Source: WHO, Marburg virus disease outbreak in Equatorial Guinea, 8 June 2023 Departmental news. URL: https://www.who.int/news/item/08-06-2023-marburg-virus-disease-outbreak-in-equatorial-guinea

Source: CDC (Centers for Disease Control and Prevention), National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of High-Consequence Pathogens and Pathology (DHCPP), Viral Special Pathogens Branch (VSPB), Last Reviewed: April 19, 2023. Url: https://www.cdc.gov/vhf/marburg/about.html

Prostate Enlargement

The prostate grows and gets larger as a man ages. Prostate enlargement causes problems when it is large enough. Generally, the size of prostate is equal to that of a walnut or golf ball in adult men, but it can grow to be as large as an orange.

What is Benign Prostatic Hyperplasia (BPH)?

Benign prostatic hyperplasia (BPH) is defined as the prostate enlargement. The prostate grows and gets larger as a man ages. Prostate enlargement causes problems when it is large enough. Generally, the size of prostate is equal to that of a walnut or golf ball in adult men, but it can grow to be as large as an orange.

Enlargement of prostate gland causes following problems:

- It can squeeze the urethra,
- Bladder wall becomes thicker,
- Bladder may weaken over time and can't empty urine fully,
- Urine then remains in the bladder,
- Result in lower urinary tract symptoms,
- Immediately consult your doctor if you can't pass urine at all or if you have renal failure.

Common signs and symptoms

- The severity of symptoms varies from men to men depending on the severity of their individual prostate gland enlargement. Therefore, please consult your doctor if you feel you have the following symptoms, because the symptoms tend to gradually worsen over time.
- The prostate enlargement can bother or block the bladder,
- Frequent urination is a common symptom,
- Urination might occur every 1 to 2 hours, mainly at night,
- Men can't empty the urine and feels that the bladder is still full and needs urination,
- Feeling the urgent need to urinate,
- Need to stop and start several times when passing urine,
- Frequency of urination at night, more than two times,
- Difficulty in passing urine at the beginning,

Severe cases:

- Inability to urinate when benign prostatic hyperplasia becomes severe,
- Infection in urinary tract and leading to bladder damage,
- Blood in the urine,
- Causing kidney damage.

Is it cancer: Benign Prostatic Hyperplasia (BPH)?

- No, it is not cancer,
- It is benign,
- But BPH and cancer can happen at the same time,
- Treatment can help to relieve symptoms,
- BPH is common and found in about half of all men between ages 51 and 60,
- Up to 90% of men over age 80 have it.

Causes of Benign Prostatic Hyperplasia (BPH)

Benign prostatic hyperplasia mainly occurs in older men. Although the causes are not clear, hormone changes are thought to play a role in benign prostatic hyperplasia. Hormones from the testis may be the main factor to trigger prostate cell growth.

Risk factors for benign prostatic hyperplasia (BPH)

There are many risk factors for benign prostatic hyperplasia. Men who are at a higher risk include:

- Age: men over the age of 50 are at a risk of BPH as it rises with age,
- Family history,
- Overweight or obesity increases the risk of BPH,
- Too much body fat may increase hormone levels and other factors in the blood, and stimulate the growth of prostate cells,
- Exercise can lower your risk of BPH,
- Men who don't do exercise and stay active,
- Men at high risk who have metabolic syndrome, diabetes, high blood pressure and eat diet low in fruit, vegetables and legumes,

- Some men with erectile dysfunction (ED).

Prevention of BPH

- There is no sure way to prevent BPH. But following lifestyle can help to prevent benign prostatic hyperplasia.
- Losing weight,
- Eating a well-balanced diet, rich in fruits and vegetables,
- Staying active also helps control weight and hormone levels.

Diagnosis

- Consult your doctor if you have possible symptoms of benign prostatic hyperplasia. But immediately consult your doctor if you see that you have following symptoms:
- Blood in your urine,
- Pain or burning while passing urine,
- Inability to urinate.

Treatment

There are many options for treating BPH. You and your doctor will decide together which treatment is right for you. Mild cases may need no treatment at all. In some cases, minimally invasive procedures (surgery without anesthesia) are good choices. And sometimes, a combination of treatments works best. The main types of treatments for BPH are:
Active Surveillance
Prescription Drugs
Less Invasive Surgery
More Invasive Surgery

Reviewed by Dr Md Anawar Hossain

Pharmaceutical Section

Strategies to Preserve the Efficacy of Antibiotics and Avoid Superbugs

The irrational and random use of antibiotics can create superbugs. Therefore, for the decades, WHO (World Health Organization) has been advising the government and people of every country for the rational use of antibiotics to preserve the efficacy of antibiotics for future generations.

Dr Hanan Balkhy, Assistant Director-General of WHO, Division of Antimicrobial resistance explained the risks and reasons behind these risks if people practise the irrational use of antibiotics. People use these antibiotics to kill bacteria causing disease to humans. But these bacteria also try to survive and adopt different strategies to escape the effect of the antibiotics. Therefore, it is very vital to preserve the efficacy of antibiotics. Otherwise, these antibiotics will not protect us even from common injuries. Dr Hanan Balkhy indicated three points to follow when taking antibiotics.

1. Take antibiotics only when your doctor or health care providers prescribe it for you.
2. Complete the antibiotic course based on the advice provided by your doctor. If you do not complete the course, bacteria will develop mechanisms to become irresponsive to these antibiotics.
3. You must not share your antibiotic with family or friends because physician or health care provider should prescribe it for the person based on specific signs and symptoms. Some certain viral infections really do not require antibiotics.

Dr Hanan Balkhy reported that WHO is working with three other critical organizations, such as animal health, environmental health and agriculture to identify the best hygiene methods to avoid exposure to infection.

Reviewed by Dr Md Anawar Hossain

Source: WHO, 2023. URL: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/media-resources/science-in-5/episode-99-three-things-to-keep-in-mind-when-taking-antibiotics.

Artificial Sweeteners May Be More Dangerous for Health

People avoid sugars due to the fear of weight gain and some other health related problems. They take artificial sweeteners instead of sugar. But according to the World Health Organization (WHO), artificial sweeteners may not help people to lose weight in the long-run, but they have some dangerous health effects. Artificial sweeteners may increase the risk of diabetes, heart disease and death. People consume some common artificial sweeteners or sugar substitutes such as stevia, aspartame and sucralose.

WHO conducted a systematic review of the available evidence. The summary of review indicates that the uptake of non-sugar sweeteners doesn't provide any long-term benefit to lower the body fat in adults and children. But the long-term use of these non-sugar sweeteners may augment the risk of type 2 diabetes, cardiovascular diseases, and mortality in adults.

Dr Francesco Branca, WHO director for nutrition and food safety, also emphasized that the consumption of artificial sweeteners instead of sugar doesn't provide benefit of weight loss in the long-term. Therefore, he recommended the uptake of food with naturally occurring sugars, like fruit, or unsweetened food and beverages. He said that artificial sweeteners are not essential dietary factors and have no nutritional value.

Source: WHO, 2023.

Biologically Active Excipients Need Clinical Investigation

Dr Md Anawar Hossain

The use of biologically active excipients may have potential implications for clinical consideration. The safety risk of excipients should be assessed considering their type and variability. Excipient complexity has been identified in 230 biological formulations.

What are excipients used in medicine?

Pharmaceutical formulation of a drug product consists of the active pharmaceutical ingredient (API) and excipients. The excipients are called inactive ingredients. According to the U.S. Food and Drug Administration (FDA), the excipients are "any component of a drug product other than an active ingredient". Most of the drugs (pill, liquid or injectable) contain a relatively small amount of their active pharmaceutical ingredient by mass, while the rest of composition includes inert ingredients or excipients, such as preservatives, dyes, antimicrobials and other compounds. These supposedly inert ingredient may potentially be biologically active causing unanticipated side effects, according to a preliminary new study by researchers from the UC San Francisco School of Pharmacy and the Novartis Institutes for BioMedical Research (NIBR). Their new study

was published online in Science, July 23, 2020 (Weiler, 2020).

- They systematically screened 3,296 excipients contained in the inactive ingredient database, and identified 38 excipient molecules that interact with 134 important human enzymes and receptors.
- Their study did not look for actual effects on human patients.
- They only intended to flag molecules with the potential to pose negative health effects.
- It needs to be further studied to understand how they might contribute to side effects of drugs in which they are found.

Why are excipients used in medicine?

Excipients are used in medicine to increase

- Product shelf stability and preservation,
- Maintaining tonicity,
- Facilitating drug delivery,
- Ensuring the development of the most efficacious medicine,
- Avoiding immunogenic or other side effects,
- Delivering medicine safely and effectively,
- Distinguishing pills by color.

Problems in use of excipients

The use of these additive materials may have potential implications for clinical consideration. The safety risk of excipients should be assessed considering their type and variability (Ionova and Wilson, 2020).

- Excipient termed as inactive" ingredients are not as inert as the name suggests.
- Excipient complexity has been identified in 230 biological formulations.
- Excipient-related adverse effects have been identified.
- Most commonly occurring excipients are water, sodium chloride, polysorbate 80, sucrose, and mannitol.
- Many formulations don't demonstrate the concentration of the most commonly occurring inactive ingredients.
- Literature survey reported some case reports of excipient-related adverse events.
- These cases included injection site reactions, anaphylaxis, hyperglycemia, and acute renal failure.
- The use of appropriate excipient in medicine is significant because about 92.8% of oral medicines contain at least one potential allergen in its formulation.

- Inactive ingredients in parenterally administered medicines have been associated with increased sensation of pain at the injection site.
- Some inactive ingredients have been identified as the potential factors impacting immunogenicity of biologics.
- These ingredients can exert adverse effects on sensitive and intolerant people, particularly on vulnerable pediatric and elderly people, who have serious and life-threatening diseases and they need treatment with unstable biological medicines.

Biologic drug product

- The formulation development of biological drug products has some difficulties due to their complexity and fragility (Ionova and Wilson, 2020).
- First, stability and preservation present a significant challenge as the API of a biologic is more unstable than in small molecule drugs.
- Protein-based therapeutics have a potential to cause an immunogenic response leading to adverse events that are often not discovered until after the medicine is on the market.
- Most of these medicines must be developed in a liquid form for compatibility with subcutaneous, intramuscular, or intravenous administration.

Present and future of biologics

- The biologics are the fastest growing drug products in spite of the challenges in formulation development,
- The development of biosimilar formulations is expanding rapidly due to the anticipated patent expirations of many biologics,
- The U.S. FDA defines a biosimilar as a “biological product that is highly similar to the reference product notwithstanding minor differences in clinically inactive components and that has no clinically meaningful differences in terms of safety, purity or potency from an existing FDA-approved reference product”.

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Benefits, Current Status and Challenges of Deuterium in Drug Discovery

Deuteration process has significant potential in the discovery of new drugs. But there are some challenges in this process as well.

Substitution of one or more hydrogen atoms with its heavy isotope deuterium (D), which is called deuteration, provides additional neutron to a molecule. Although it seems to be a subtle change, this structural modification, may improve the pharmacokinetic properties, efficacy and safety of drugs compared with the non-deuterated counterparts. The structural modification by incorporating deuterium into molecule and development of new drugs started since early 1960s, but the progress was slow. However, in the last two decades, deuteration process has been increasingly used to improve the pharmacokinetic characteristics of marketed drugs. In 2017, FDA approved the first deuterated drug, such as deutetrabenazine. Deuteration is used not only to improve the marketed drugs, but also to discover novel drugs. The FDA approved the pioneering de novo deuterated drug deucravacitinib in 2022.

Opportunities and challenges for deuteration

Deuteration provides the molecule with bond stability and doesn't change steric hindrance or electronic properties. Deuterium might represent a safer bioisostere compared with fluorine, because fluorinated drugs may produce harmful species for both human health and the environment (e.g., fluoride or fluoroacetate). Deuterium atoms have impact on absorption, distribution, metabolism, excretion and toxicity (ADMET) parameters.

Although the deuteration process has significant potential in the discovery of new drugs, it has some challenges as well. Deuteration technique is challenging, because this reaction needs a rate-limiting bond cleavage step. There are some other reasons which causes the drug failure of some deuterated analogues.

Reference

Di Martino, R.M.C., Maxwell, B.D., Pirali, T. 2023. Deuterium in drug discovery: progress, opportunities and challenges. Nat Rev Drug Discov (2023).

Pharmacovigilance for Quality Investigation of Marketed Medicines

Reviewed by Dr Md Anawar Hossain

Drug is an essential material people have to buy and take it frequently in their life whenever they become sick. It is an important part of life. Drug quality and safety is a prime issue, because it is related to safety of the human life. Any deterioration in drug quality may cause the adverse effects to human body and eventually may cause death. Therefore, continuous monitoring and investigation of marketed medicines is a high priority issue in the pharmaceutical and healthcare sectors. Pharmacovigilance plays a momentous role in drug quality investigation.

Deterioration in quality of marketed medicines may originate from the different processes and issues of drug manufacturing and distribution to the markets. Pharmacovigilance is a part of pharmaceutical and healthcare sciences which can survey, monitor and assess any quality-related adverse effects reported by the drug consumers.

Accordingly, it can suggest some preventive strategies to rectify the defects in the manufacturing and distribution processes, and thus reduce the risk of deterioration in drug quality (Sardella et al., 2021). Pharmacovigilance follows some rigorous processes or steps to perform this job, which includes collection, detection, assessment, monitoring, and prevention of adverse reactions with pharmaceutical products.

In the first decade when a new drug is marketed after getting authorisation from the drug authority, drug safety is surveyed and monitored. Therefore, the information related to adverse reactions of medicines is gathered and assessed to identify any safety issues from its use. This information can be collected and assessed by the drug authority and drug sponsors which will help the manufacturer to modify the quality control, manufacturing and distribution processes.

Some medicines are already on the market for long time. Therefore, their safety information is already well-

known to the authority and manufacturers. However, any safety risk can be generated anytime if the manufacturers do not follow the adequate quality control, appropriate manufacturing processes and distribution systems. As for example, the older medicines, such as generic drugs, can also generate new risks due to the result of inadequate control of their quality process, manufacturing and distribution systems (Sardella et al., 2021). Therefore, the manufacturers should follow the complete integrated manufacturing process for quality control, manufacturing process and distribution systems.

Pharmacovigilance can check the following processes to ensure the product safety and efficacy:

- The manufacturers are following the standard processes, and procedures and quality defects are detected during the manufacturing, proper distribution systems and use of medicinal products,
- Pharmacovigilance can assess (1) product quality complaints; (2) out-of-trend stability studies; (3) cross-contaminations; (4) regulatory actions against manufacturers following inspections; (5) temperature excursions outside the labelling storage conditions during distribution; (6) counterfeit/falsified products detected in the supply channel.
- Pharmacovigilance data can identify manufacturing, distribution or counterfeiting issues.
- Voluntary reporting systems can be running which can help to identify sub-standard/ spurious/falsely labelled/falsified/counterfeit medical products.

How are drug safety hazards created?

- Drug safety hazards have been identified from product quality defects.
- Product contamination has been detected from raw materials.
- Pharmacovigilance has identified drug safety hazards from manufacturing issues.

Reference

Sardella M, Belcher G, Lungu C, Ignoni T, Camisa M, Stenver D I, Porcelli P, D'Antuono M, Castiglione N G, Adams A, Furlan G, Grisoni I et al., 2021. Monitoring the manufacturing and quality of medicines: a fundamental task of pharmacovigilance. Therapeutic Advances in Drug Safety, Vol. 12: 1–17.