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Cazzola M. Matera MG. Novel long-acting bronchodilators for COPD and asthma. Br J Pharmacol. 2008;155:291-29
 Novartis Europharm Ltd. Onbrez^a Breezhaler^a Summary of Product Characteristics.



ONB Ad1 08/12 M⁻

Change by design

n the last editorial we introduced the notion of additive manufacturing (including stereolithography) and 3D printing. We gave an example about its medical use in surgery but its applications may also include medical devices and research.

Imagine the following scenario. A piece of an old X ray machine in a Sudanese hospital has broken down. The parts are no longer available and there are no funds to buy a new equipment. With a 3D printer the broken part can be scanned, repaired virtually and a replacement printed within hours. Whola! Besides, to avoid going through all this trouble, since there is also a Bolivian hospital ten thousand kilometers away who has that same X Ray machine, a replicator can transmit the same data pertaining to the repaired piece to Bolivia so that the hospital will have a spare. Just imagine this ... or rather, simply realise that all this is occurring now, as we talk ... is this not reminiscent of the science fiction series Stargate SG-1?

Other applications include portable small ultrasound scanners. The size, weight and cost of the imaging consoles has obviously shrunk along the years, but the transducer probe which is placed on the body has remained largely unchanged and is now the most costly part of the system. GE has now developed an additive system to print the transducer which is hoped to bring the costs down.

And imagine receiving your 3D printed tailor-made dental crowns or hearing aid shells while you are still at the dentist or ENT specialist!

The use of 3D printing in surgery has also paved the way for more accuracy in complicated operations, with a greater degree of success. For example, if a surgeon needs to remove a tumor from a patient but there is a high probability that a nerve or artery is damaged in the process, a 3D model of the tumor from the patient's CT scans can be created using a 3D printer (indeed, the materials that can be printed range from metals and ceramics to rubber-like substances. Some machines can also combine materials, making an object rigid at one end and soft at the other). The surgeon can then practise on the model before working on the patient. In this way, the surgeon will be able to make the necessary incisions with confidence. The benefit-risk ratio of the operation will thus improve.

Indeed some researchers are already using 3D printers to produce simple living tissues, such as skin, muscle and short stretches of blood vessels. There is a possibility that larger body parts, like kidneys, livers and even hearts, could one day be printed and if the bio-printers can use the patient's own stem cells, the body would be less likely to reject the printed organs after a transplant.

Another important contribution of this application is in the field of nanotechnology. Interestingly, nanotechnology products have been around for more than a decade now. A case in point is Titanium dioxide which is used to manufacture selfcleaning glass in buildings. It basically reacts with sunlight to break down organic dirt. In addition the material is also hydrophilic, attracting rain which washes the residue. However their boom which was heralded like the imminent second coming of Christ by foul-mouthed financial Farizees, never materialised. More than twelve years later this particular sector still remains an exciting research domain but in my opinion, maybe these nanotechnology products have lost some hype due to their prolonged infancy. Now, with the advent of additive manufacturing, the gap between product and manufacturing innovation will hopefully be bridged faster.

Furthermore, it will certainly also influence pharmaceuticals' manufacturing. A joint venture between the Massachusetts Institute of Technology and Novartis has recently been developed, pioneering a continuous manufacturing process for the pharmaceuticals industry, whereby raw materials are put into one end of a machine and tablets come out at the other end. It relies on a combination of chemistry and engineering, speeding up some processes and slowing down others to make them work together. The number of operations involved in producing a particular drug, has been cut from 22 to 13 with the processing time being reduced from 300 hours to 40. Besides, instead of testing each batch of material, each finished tablet is individually monitored to ensure it meets the required specification. In addition since the pilot line described above can fit into a shipping container, it could be moved anywhere. In fact Stephen Sofen, the project's director stated "Instead of a giant, purpose-built plant to supply the global market, you could imagine smaller, regionalised plants."

On the other hand Professor Lee Cronin, chair of Chemistry at Glasgow University, and his team has developed a new 3D printing process to synthesize chemicals. Prof Cronin believes his research could one day lead to lowcost chemical printers at home that would allow patients to print their own prescriptions. Such a scenario would certainly earthquake the healthcare industry as it could drastically bring the cost of care down for patients. As they wrote in the Nature Chemistry Journal, last April, "This would not only place traditionally expensive chemical engineering technology within reach of typical laboratories and small commercial enterprises, but also could revolutionise access to healthcare and the chemical sciences in general in the developing world."

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Date of preparation: April 2012

* Derma Membrane Structure

ISSUE GUIDE



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contents

- 06 Gastrointestinal cancer screening and surveillance programmes: a worldwide perspective Part II
- 10 The use of performance enhancing drugs in sports: Doping
- **Opportunities and announcements**
- Healing & Disease Reversal The Series
- Are we over-investigating our patients?
- Caring beyond the immediate
- The changing face of medicine throughout the ages
- 23 One World, One Home, One Heart -The theme for World Heart Day

COVER:



The fleet of milk floats used by the MMU

The Milk Marketing Undertaking (MMU) was launched in May 1938 following the recommendations of a commission set up in 1931 ' to supply safe and nutritious milk free from pathogenic bacteria and moreover, to encourage an increase in the consumption of fresh milk'. The sale and distribution of pasteurised milk commenced in pint bottles, 1/4 pint penny cartons and 1/2 pint two penny cartons in Valletta, Sliema, Floriana and Hamrun in special electrically driven vans (also known as milk floats). The photo depicts the fleet of milk floats used by the MMU and was taken in late 1930's or early 1940's. The vehicles had several advantages including low sound emissions and cleanliness - surely eco-friendly and futuristic for that period!

Photography: Richard Ellis

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Gastrointestinal cancer screening and surveillance programmes: a worldwide perspective – Part II

JURGEN GERADA

Stomach

Gastric cancer remains one of the most important malignant diseases with significant geographical differences in distribution. Annual mass screening for gastric cancer has been provided in Japan, Chile and Venezuela, aiming at detecting early gastric cancer. Japan introduced this screening programme in the 1960s using barium X-ray studies⁶. Barium X-ray study was regarded as a superior screening test out of four tests that were evaluated and studied, mainly photofluorography, serum pepsinogen levels, endoscopy and H. pylori antibody testing7. Sensitivity ranged between 60-80% and specificity ranged between 80-90%. Those that had an abnormal X-ray were offered upper endoscopy together with treatment. The 5 year survival rates that were achieved, as reported in 2008, were 74-80% in the screened group versus 46-56% in the non-screened group. Despite this programme, 40% of gastric cancers remain undetected and overall mortality was reduced by only 8%. This was mainly due to selection bias as the people who underwent screening were generally healthier than those who did not 6. Moreover, a cohort of 24,000 individuals in Japan, classified into screened and unscreened groups and followed up for 40 months (1992 - 1995), failed to show statistically significant reduction in mortality, once again due to selection bias8.

While gastric cancer screening is not practiced in the US, ASGE suggests carrying out surveillance endoscopy in patients with gastric premalignant conditions. Gastric adenomas have a high malignant potential and should be resected endoscopically or surgically with a surveillance endoscopy 1 year post-resection to assess the excision site, and every 3-5 years thereafter if the stomach is polyp-free. Patients with gastric intestinal metaplasia are not advised to undergo surveillance as there is lack of data in this field. On the other hand, patients with high grade dysplasia of the stomach should be considered for gastrectomy. Lastly, patients with FAP and tylosis should undergo surveillance programmes, while others with HNPCC should be considered for surveillance⁹.

Small Bowel

Tumors of the small bowel are quite rare and for this reason, there is a severe lack of guidelines on their management. To date, there are no screening programmes to detect small bowel tumors in asymptomatic individuals. Sporadic duodenal and ampullary adenomas are usually found incidentally during a routine OGD. These have been described to have malignant potential and ASGE has recommended surveillance postsurgical or endoscopic resection. Surveillance for ampullary neoplasms vary from 1-6 months after the index procedure, followed by a repeat exam every 3-12 months for a period of at least 2 years. High grade dysplastic lesions require more intense monitoring. Formal recommendations regarding surveillance intervals for duodenal adenomas, on the other hand, could not be given due to the limited data available and should be decided on an individual basis. Moreover, data suggest that patients with duodenal or ampullary neoplasms are at a higher risk of colorectal polyps and neoplasia and should be offered screening colonoscopy¹⁰.

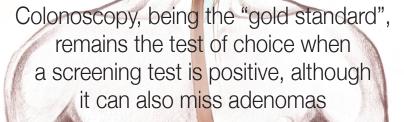
Colon

In 2002, CRC comprised 9.4% of the global cancer burden and its incidence is expected to increase as the world's population is ageing. The risk of CRC increases with age and family history. It is rare below the age of 50 but increases dramatically thereafter. CRC is the only gastrointestinal cancer where screening asymptomatic patients is practiced in many countries, with Malta joining them this October. CRC screening is however complex as there are multiple options and requires patient effort¹¹.

The two most common tests used for this screening are a stool-based test and an endoscopy or radiological-based test. Stool-based tests work on the basis that they detect blood shed by the tumor. The guaiac fecal occult blood test is the most common test used, however it requires dietary restrictions to avoid false positive results. Fecal immunochemical testing, on the other hand, obviates the need for these restrictions. Endoscopy, in the form of flexible sigmoidoscopy, is also widely practiced. This entails examination of the colon up to 60cm, is less timeconsuming than a colonoscopy, avoids sedation, bowel preparation is easier and morbidity is negligible if polypectomy is not required. Therapeutic procedures in the same examination can also be done. The disadvantage is that it misses right-sided lesions. Colonoscopy, being the "gold standard", remains the test of choice when a screening test is positive, although it can also miss adenomas. Alternatively to endoscopy, in countries with limited resources, radiological tests such as DCBE or CT colonography remain a possibility. DCBE, although inferior to colonoscopy, may still detect 50% of large polyps. CT colonography, on the other hand, has high sensitivity and specificity for large polyps but less so for small polyps. Disadvantages include the fact that flat lesions are frequently missed and patients are exposed to ionized radiation¹¹.

Below, we shall see how screening is carried out differently in different countries. In the US, ACG recommends that quality colonoscopy is offered first, starting at age 50, and every 10 year





thereafter. Afro-Americans should start at age 45. Patients who decline colonoscopy should be offered an annual fecal immunochemistry test or a 5-yearly flexible sigmoidoscopy¹². A completely different approach is adopted in UK. Individuals between the ages 60 - 69 are invited for screening every 2 years. FOBTs are sent out by post to their home and thereafter every 2 years until age 69. This is done if the test is negative. Positive tests will then be followed up by a colonoscopy¹³. Scotland has a similar programme to that of the UK, however they have extended the age range from 50 - 74. A positive FOBT will be followed by a colonoscopy, whereas a negative FOBT will be followed up by a repeat FOBT

every 2 years¹⁴. A recent meta-analysis of studies evaluating screening using FOBT estimated mortality reduction to be 15%¹⁵.

Recent data suggests that 5 countries, namely UK, France, Australia, Belgium and Finland now offer national screening programmes, the most common screening modality being FOBT, followed up by endoscopy in positive tests. On the other hand, another 6 countries, namely US, Germany, New Zealand, Portugal, Switzerland and Spain, offer opportunistic screening where a test is offered to asymptomatic individuals who have seeked medical help for other reasons unrelated to CRC ¹⁵.

Patients with moderate or high risk of colorectal cancer

Patients who have a moderate or high risk of developing CRC are thus screened as part of a surveillance programme. Patients with moderate risk include patients with a positive family history of CRC, while patients with high risk include:

- Patients following detection of colorectal adenomas;
- Patients with inflammatory bowel disease;
- Patients following CRC resection;
- Patients with acromegaly;
- Patients with FAP, HNPCC, juvenile polyposis and peutz-jeghers syndrome;
- Patients with ureterosigmoidostomy.

It is worth mentioning some differences between US and UK regarding these programmes in the moderate risk group and the first 2 high risk groups:

Family History of Colorectal Cancer

Guidelines issued by the ACG in 2008 recommend patients with a first-degree relative diagnosed with CRC at age ≥60 years to have screening as the average risk population, i.e. colonoscopy every 10 years, starting age 50. Patients with a first-degree relative diagnosed with CRC or advanced adenomas at age <60 years, or two first-degree relatives with CRC or advanced adenomas, should have a colonoscopy every 5 years starting at age 40, or 10 years younger than the age of diagnosis of the youngest affected relative¹². On the other hand, BSG guidelines, issued in 2010, recommend patients with one affected first-degree relative age <50, to have a single colonoscopy at age 55 and average risk population recommendations thereafter. If the first-degree relative was diagnosed age \geq 50, recommendations are the same as the average risk population¹⁶.

Patients with colorectal adenomas

2010 BSG guidelines risk-stratify such patients into low, intermediate or high risk depending on the number and size of adenomas detected. Surveillance is by means of colonoscopy every 5 years for low risk patients (1-2 adenomas, both <1cm), every 3 years for intermediate risk patients (3-4 small adenomas or at

The Synapse

least one \geq 1cm) and every year for high risk patients (≥5 small adenomas or \geq 3 at least \geq 1cm)¹⁶. ASGE guidelines also stratify such patients in a similar way, the only difference being in the intermediate risk where the number of adenomas can be from 3 – 10¹⁷.

Patients with inflammatory bowel disease

CRC surveillance in this high risk group using colonoscopy and pancolonic dye-spray should start after 10 years of colitic symptoms. Once again, BSG guidelines stratify patients in low, intermediate and high risk depending mainly on disease activity and extent and other risk factors such as FH of CRC or PSC. Low risk patients (no active disease) should repeat colonoscopy every 5 years, intermediate risk patients (mild active disease or FH) every 3 years and high risk patients (moderate/severe active disease or FH or PSC) every year¹⁶. On the other hand, ASGE recommends colonoscopy every one or two years beginning 8 - 10 years after disease onset in patients with extensive colitis. A case-control study showed a reduction in mortality in CRC in patients with ulcerative colitis using such surveillance programme¹⁷.

Liver, biliary tree and pancreas

Surveillance for HCC is widely practiced across the world, however it is still controversial whether such

management is beneficial or not, and which surveillance modality is best to use. In the US, the patients at risk of developing HCC, who are routinely surveilled, are

- Hepatitis B carriers: asian males over 40; asian females over 50; african/north american blacks; family history of HCC;
- All patients with cirrhosis. The rationale for such surveillance is to detect small HCC lesions as

these are amenable to resection or liver transplantation. AASLD, in 2010, recommended screening these patients with just an ultrasound every 6 months. They argue that AFP, having a sensitivity of 66% and a specificity of 82%, is still inadequate as a screening test for HCC18.

In 2009, WGO suggested screening every 6-12 months in some patients, depending on the clinical scenario, whereas in high-risk patients, this should be done every 4-6 months. The test they recommend is an ultrasound, as the AFP still shows an imbalance between sensitivity and specificity. Moreover, combining both tests increased costs and false positive rates19.

On the other hand, BSG in 2003, recommended 6-monthly screening using both AFP and ultrasound to the same at-risk population mentioned above. They emphasized the use of high quality ultrasound with a dedicated

equipment and operator expertise. Despite these recommendations, they also stated that there is not enough data to show long-term improvement in survival with this programme²⁰. Following these guidelines, a new randomized controlled trial, in 2004, carried out in China, comparing surveillance versus no surveillance, showed a reduction in mortality by 37% when 6-monthly surveillance strategy using AFP and ultrasound was applied²¹.

As regards cholangiocarcinomas and pancreatic tumors, as of today, there are no screening programmes in asymptomatic patients.

Conclusion

Screening programmes are challenging and complex to organize. For these to be successful, multiple events have to occur hand-in-hand, starting from patient awareness and primary care physician recommendation, to patient acceptance, financial coverage, risk stratification, screening test, timely diagnosis, timely treatment to appropriate follow-up. If any of these is not of high quality, then screening will fail¹¹. Although the above screening programmes are already reducing mortality, interventions should be aimed at improving uptake of patients and targeting noncompliance, mainly for CRC screening, as this is the most widely practiced¹⁵. S

ADDrevia	luons
AASLD:	American Association for the Study of Live
	Diseases
ACG:	American College of Gastroenterology
AFP:	Alphafetoprotein
ASGE:	American Society for Gastrointestinal
	Endoscopy
BSG:	British Society of Gastroenterology
CRC:	Colorectal cancer
DCBE:	Double contrast barium enema
FAP:	Familial Adenomatous Polyposis
FH:	Family history
FOBT:	Faecal occult blood test
HCC:	Hepatocellular carcinoma
HGD:	High grade dysplasia
HNPCC:	Hereditary non-polyposis colorectal cancer
LGD:	Low grade dysplasia
OGD:	Oesophagogastroduodenoscopy
PSC:	Primary sclerosing cholangitis
WGO:	World Gastroenterology Organization
WHO:	World Health Organisation

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The use of performance enhancing drugs in sports: Doping

Since centuries ago, man has always tried to find ways to improve human performance whilst suffering less in doing so. People who were thought to be the best were preferentially fed better diets and given treatments that were considered to be beneficial to their performance.

Scandinavian mythology states that drinks, probably containing *Amanita muscaria* mushroom, were administered to Norse warriors with the aim of enhancing performance, despite causing the person to verge onto the brink of insanity! In the early 19th century, Dr Albert Schweitzer noted that in Gabon, Africa, the inhabitants were able to ingest leaves or roots and work all day without feeling hunger or thirst, yet still displaying gaiety all throughout.¹

In 1807, Abraham Wood admitted to making use of opium in order to remain awake for 24 hours during the endurance walking race of Britain.² This resulted in race organizers increasing the walking distances to over 500miles, as this increased the number of spectators. Similar endurance events were developed for cyclists, as organizers thought that it is more 'spectacular' to see cyclists reach total exhaustion and fall off their bike, often causing multiple cyclists to fall! This brought more spectators (who paid at the gate), increased the prize winnings and thus provided a great incentive for people to make use of substances in order to try to stay awake to ride these great distances.

However, the dark side soon emerged, when the riders started to suffer from extreme exhaustion and hallucinations. The participants would require weeks to recover, and some never returned to normality. The public started to get outraged at this, calling it brutality.

Strychine was also found to be utilized in the 1904 Olympics and actually thought to be necessary for endurance races, such as the marathon. Thomas Hicks was on the verge of collapsing during the 1904 Olympics marathon, when his trainer, Charles Lucas intervened by injecting him with strychnine, handed him a glass of brandy and set him off running once more. He required a further injection 4km away from the finish, but was still awarded the gold medal.

The father of anabolic steroids in the US is John Ziegler (1917–2000), who after learning that the Russians made use of performance enhancing drugs to be successful, worked with the CIBA pharmaceutical company and developed oral anabolic steroids. This came in the form of methandrostenolone, appearing in the market in 1960. That same year, in the Olympics in Rome, a Danish cyclist Knut Jensen collapsed and died during a 100km cycle race. Amphetamines and a drug called nicotinyl tartrate were found in his system.

In the 1970s, East Germany was intentionally providing its athletes with anabolic steroids. Ages started from 10 years old, and they were given to athletes without divulging what the pills were, just stating that they were 'vitamins'. This resulted in Germany greatly increasing the number of gold medal winners in the Olympics, yet it was rare for an athlete to be banned for doping. It is estimated that 10,000 athletes were involved, many of which still bare the mental and physical scars of their side effects, some of whom are still seeking compensation.

However eventually the ban on anabolic steroids, as well as its testing were enforced. In 1988, Ben Johnson won the 100m sprint event in the Seoul Olympics, yet he then tested positive for steroids. Carl Lewis and Marion Jones had similar stories splashed over the media, and their Olympic titles stripped off them. It appeared that the use of performance enhancing drugs was rampant, without any form of control throughout and many top American athletes, were testing positive for banned substances.

In 1998, the whole Festina team taking part in the cycling Tour de France was disqualified following a find in the team car of a large amount of performance enhancing drugs, including EPO (erythropoietin).

These and other similar reports are alarmingly on the increase in the sporting world.

The use of performance enhancing drugs in sports, also known as doping, is becoming a larger problem in all types of sport. Doping is defined as any substance or drug that, when taken, gives an athlete an unfair advantage relative to a 'clean' athlete. The main aim of doping is to enhance athletic performance.³ The banning of these drugs promotes a more level playing field which is what all sporting organisations seek to achieve.

This led to the formation of the World Anti-Doping Agency (WADA). WADA was established in 1999 as an international independent agency composed and funded equally by the sport movement and governments of the world. Its key activities include scientific research, education, development of antidoping capacities, and monitoring of the World Anti Doping Code.

The main reason for banning performance enhancing drugs is the alleged risk of harming the athlete's health (including the risk of causing death), providing an equal opportunity for all athletes as well as promoting 'clean' sports to the general public. Yet although there seems to be general consensus amongst sports people, as well as the International Olympic Committee (IOC), that the use of performance enhancing drugs is unethical, there is an ongoing controversy on the use of modern sporting equipment and specialised sports suits/garments in that these also enhance athletic performance and may thus be considered as 'technological doping' as they aid performance and give an unfair advantage over fellow athletes.

Going back to the 'conventional' type of doping, the latest form of doping is in the form of blood doping, where athletes make use, or rather abuse, blood transfusion or EPO. EPO is a natural growth hormone that works by stimulating the production of red blood cells to increase their number, hence increasing the oxygen carrying capacity and the VO₂ max, which is positively correlated to success in endurance sports such as long distance swimming, cycling, running, rowing and skiing.

Since the 1990s athletes have abused EPO as it is less easy to detect than blood transfusions, however an official test to detect EPO only started to be carried out in 2002. Although EPO is used for medicinal purposes, athlete abuse can raise the haematocrit up to 70%, making the blood more viscous as a result of this polycythaemia. This strains the heart and can cause heart failure and may result in sudden cardiac death especially whilst the athlete is sleeping.

Athletes who are tested for doping and found to have an unusually high haematocrit level will receive a doping ban. This led athletes to time their EPO use in relation to competition time, in order for their haematocrit to return to a 'within range' level of normal. Dopers and their support crew know how long it takes for the substances to be cleared out of the body, or to remain at exactly the upper border of the legal limits, whilst maintaining their performance enhancing effect. They use this knowledge to their benefit.

Previously athletes were only tested after winning a competition, so this enabled this type of doping to be practiced without getting caught, so the next step was to introduce outof-competition testing. Competitive athletes were to consent to a doping test even out-of-competition periods. This presented other problems, as athletes do not live in one location, or can conveniently be out of town if a doping control person had to request a dope test. This could be done purposely to avoid being caught with doping. However, WADA has initiated the Anti-Doping Administration and Management System (ADAMS), where an athlete must log online and state their location for an hour each day. This will enable doping control officers to test an athlete on any given day. If the athlete is absent, the athlete will be sanctioned.

WADA also issues a list of banned substances, which is revised annually. This can be located on www.wada-ama. org/. This list also contains medications used to treat illnesses. If an athlete requires a medication from the banned list, and there is no other alternative, a therapeutic use exemption must be applied for. A sports medicine doctor or a similar specialist is required to fill in this form along with documentary evidence of the athlete's condition. The athlete will be informed whether or not their medication is accepted for general well-being purposes.

There are also a number of over-the-counter medications, notoriously cough and flu medications, that contain banned substances, such as ephedrine. A doctor may prescribe this legally and the athlete ingests the medication, yet when tested for doping, a positive result is found, resulting in the athlete being sanctioned. The Global Drug Reference Online (www.globaldro. org) is a useful tool for doctors and athletes alike, where they can input the name of the proposed medication and information about whether or not it is a banned substance will be provided. This is also useful to check about food supplements that may contain prohibited substances within them.

The fight against doping is a constant upward battle, yet despite science's advances over time, the 'cheats' are always one step ahead and know how to cover up doping, until anti-doping agencies have time to catch up.

One worrying fact about doping... when a group of elite athletes were asked if they would take a pill that would guarantee them sporting success, yet as a result they would certainly die by the age of 40 years, a staggering more than 60% of athletes replied positively!

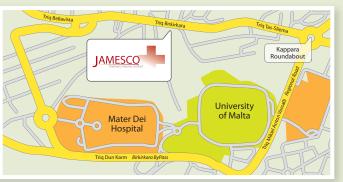
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The Synapse



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The Organising Committee of the VIII Malta Medical School Conference is pleased to announce that this established major triennial event will be held between 29th November and 1st December 2012.

The event will be hosted at The Westin Dragonara Resort, St Julians. Local and overseas speakers of international standing will contribute to this multidisciplinary Conference which showcases recent developments in clinical and scientific research. The Conference comprises the largest assembly of local doctors and ancillary medical and paramedical fields.

Oral presentations and posters on several specialities will be presented, while plenary sessions delivered by invited speakers will focus on cutting edge developments. More details on the Conference including a provisional programme and speciality areas are available on the Conference website: http://www.um.edu.mt/umms/mmsc/

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ALBERT CILIA-VINCENTI

Reversal essesid & gnileeH

This series reviews Dean Ornish's evidence-based claims of healing & disease reversal by dietary and lifestyle changes. He is a California University Professor of Medicine in San Francisco. This instalment discusses anti-inflammatory dietary and lifestyle changes.

Chronic inflammation may be an important underlying factor in a number of chronic diseases, including atherosclerosis, diabetes, arthritis, dementia, autoimmune diseases and many others. Acute inflammation, like stress, may be beneficial and is a normal part of the body's defence system. But if this defence system runs out of control and is chronically activated and systemic, the body mistakes its own tissues for enemy invaders and attacks its own tissues and organs. An endless cycle may be established wherein one part of the body's chemistry is trying to regenerate damaged tissues while another part of its chemistry is tearing them down.

As chronic inflammation starts rebuilding and tearing tissues apart, inflammatory activity escalates, as the immune system is desperately using the only means it knows to protect the body against a foreign invader that isn't foreign at all. Tissues become more inflamed and the cycle starts spinning out of control.

Such chronic inflammation doesn't have the same outward signs of acute inflammation, so

individuals may not realise they have an inflammation problem. A study of an apparently healthy elderly population found that those with the highest levels of C-reactive protein and interleukin-6 (two systemic inflammation markers) were 260% more likely to die during the next 4 years than those with lower levers of these markers.¹ The increase in deaths was due to cardiovascular disease and other causes.² We may feel healthy, but if inflammation is smouldering inside us, we may be in significant trouble.

One way chronic inflammation can be set off is when part of the genetic code controlling inflammation is upregulated. The genes controlling the inflammatory response can be "turned on" by a number of environmental factors, and the inflammatory response won't slow down until these genes are "turned off".

Anti-inflammatory drugs, though often useful for acute problems, interfere with the body's own immune response and may lead to serious side-effects. On the other hand, the benefits of statin cholesterol-lowering drugs may be due as much to their antiinflammatory effects as to their cholesterol-lowering ones. Lowdose aspirin may help reduce myocardial infarction and colon cancer risk for the same reason. A number of dietary and lifestyle factors may play a significant role in initiating and maintaining chronic inflammation.

> These include unhealthy dietary choices, lack

of exercise, obesity, metabolic syndrome, chronic stress, smoking, environmental toxins and pollution, and chronic infections.

In the Harvard Nurses' Health Study, for example, higher intakes of red and processed meats, sweets, desserts and refined grains increased blood inflammatory markers, whereas higher consumption of fruit, vegetables, legumes, fish, poultry and whole grains decreased blood inflammation markers.^{3,4,5,6} Foods low in calories and saturated fats and high in plant sterols, soluble fibre, soy protein, nuts and omega-3 fatty acids also decrease inflammation. Healthy dietary choices, moderate exercise and stress-management techniques decrease risk of chronic inflammation. This is a powerful step towards healing organ systems, losing weight and feeling healthy. Inflammation is at the root of so many different diseases that reducing its impact may have a profound effect on one's life.

Foods that are dense in nutrients have the highest nutritional value. Nutrient density is the amount of nutrients a food contains divided by the number of calories. Foods are nutrient-dense when they have a lot of nutrients and few calories. Many people try to make up in quantity what they don't have in quality. When you eat high-quality delicious foods you don't need as much to feel satisfied as when you gobble down loads of junk food. Ideally, high quality foods are organic and less processed. This might not be possible or affordable for many people, but it's a goal worthwhile striving for.

As explained earlier, smaller portions of good foods are usually more satisfying than larger portions of junk foods, especially if you pay attention to what you're eating For example, the "French paradox" (why they have lower heart disease rate than one would expect from their diet) is often attributed to red wine, but other factors may play a more important role. A meal in France may include some high-fat items, but generally in small portions and usually freshly prepared and savoured with a group of friends in a dinner that may last several hours. The social support and community of these meals also have a protective effect.7 When food is that good, one can have more pleasure and fewer calories.

There is growing awareness that foods often have benefits that are not seen when isolated nutrients in these foods are studied. Researchers found that people who ate a lot of fruits and vegetables were at lower risk for cancer and heart disease. It presumed that this protective effect was due to beta-carotene but, one study involving 22,071 physicians, found no statistically significant benefit from beta-carotene tablets after 12 years.⁸ Another study tested whether beta-carotene protected against skin cancer among 1,621 adults – no benefit was found after 4.5 years of treatment.⁹

A Finnish study, testing the effect of beta-carotene among people with high cancer risk, found an 18% increase in lung cancer among smokers taking the nutrient compared to smokers who did not.¹⁰ A similar US study found a 28% increase in lung cancer among men at high risk of the disease who regularly took beta-carotene.¹¹ A Harvard Medical School placebo-controlled betacarotene randomised trial involving 40,000 women, found the same incidence of heart disease and cancer in both groups,¹² but women smokers who ate 5 or more carrots per week had a substantially lower risk of lung cancer.¹³ Another study showed increasing intake of vitamin E-rich foods reduced Alzheimer's disease risk, but vitamin E supplements were not significantly associated with Alzheimer's disease.¹⁴ Since there are at least 100,000 protective substances in fruits and vegetables and other unrefined foods, it may be that betacarotene is not the right one to study. It is more likely that the interaction among these protective substances, in their natural forms, may be what is most beneficial.

Our bodies have evolved to derive optimal benefits from natural, whole, unrefined foods. Unfortunately although food technology has now extracted certain nutrients from foods and processed or altered them in new ways, we may not always be able to predict their outcomes. \$

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Are we over-investigating our patients?

There has always been controversy about the value of several new (and expensive) methods of investigating disease, particularly cancer. The argument which has been accepted by most physicians has always been that the earlier diagnosis is made, the better the prognosis. We feel much happier when we can remove an obvious cancerous mass, and have relied on the concept of 'disease-free interval' as the benchmark of success.

If advanced diagnostic techniques had no other drawback apart from cost to the community, this argument seemed reasonable enough. However, voices against such a blanket approach have become more strident in recent years.

A recent article in *Scientific American*, the sort of journal laypersons as well as practitioners give credence to, has highlighted the case against this approach.¹ These arguments may be summarised as follows:

- 1. A number of 'cancer diagnostic' tests, including mammography and tests for prostate cancer, the two most common cancers in the western world, have serious effects on patients without saving their lives. As an example, of the 40 million mammograms carried out in the US every year, 138,000 discovered breast cancer, but this diagnosis did not help up to 134,000 (97%) of them. Most of these tumours were either very slow-growing, or would have been detected anyway later on without a deleterious effect, or else they were so aggressive that no treatment would have been of any long-term value. It has been suggested by the U.S. Preventive Services Task Force (2009) that mammograms should be performed at a later stage and less frequently than previously recommended.
- Chest X-rays have come under similar criticism, in that tumours have appeared within a couple of months of the examination. And therefore were not effective in preventing the disease.

 PSA (Prostate Specific Antigen) has now been practically relegated to the assessment of patients with established prostate cancer, and has all but lost its lustre as a screening test for this condition.

It would indeed be a mistake to conclude that such tests are irrelevant. The conclusion to be drawn is that selection of patients for examination should be based on clearly indicated medical conditions, and not used as a blanket screening program.

Related to this is the concept of 'quality of life' as opposed to 'diseasefree interval'. Months of misery endured by patients on radiation or chemotherapy are justified only if the eventual quality of life justifies the procedures.

One could argue that saving even a single life out of thousands screened is



Months of misery endured by patients on radiation or chemotherapy are justified only if the eventual quality of life justifies the procedures a worthwhile exercise. However, against this, one has to keep in mind that a diagnosis of serious disease brings with it, at the very least, a great deal of worry, not to mention physical discomfort from complications of the treatment itself. This is justifiable only if the benefits obtained from early diagnosis render the sideeffects acceptable calculated risks.

If such problems are serious enough for somatic diseases, they are even more pronounced for genetic disorders. There is simply no justification of undertaking complex diagnostic genetic procedures where there is no foreseeable cure, or where available modalities of treatment are not available or allowed in this country. This is becoming more and more relevant in view of the very real possibility that in the near future we are likely to possess extensive knowledge of our own genome with all its blemishes and possible genetic abnormalities. It is well to bear in mind that while all patients have the right to know, they also have the right not to know all the gory details relating to their disease, or tendency to disease.

Dissuading patients from overinvestigating themselves, like overindulging in various medicinals for all sorts of imagined conditions, may be an up-hill battle. Such tests are likely to become more and more easily available, and could very easily lead to misinterpretation and over-treatment. Genetic tests are available on the internet. In Australia, there is currently a move to have nurses perform X-rays. There is much scope and considerable financial incentive for control of medical tests to be taken away from medical supervision. This I believe is a mistake, not because non-medical persons cannot be trained to read an X-ray or perform a genetic test, but primarily because no medical test should be interpreted otherwise than in the milieu of medical practice, where symptoms, signs and ancillary examinations are integrated into one meaningful whole. S

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CARING BEYOND THE IMMEDIATE

t may not be evident to everybody but there are usually numerous people working behind the scenes, anticipating how our health will suffer or benefit and preparing strategic measures to help us deal with what we sometimes may bring upon ourselves. Key to this is what everybody simply calls the Health Promotion Unit, a unit which falls under the Health Promotion & Disease Prevention Directorate (HPDP) and is entrusted to protect and promote health in the Maltese Islands.

Heading a team of 29 employees with several other external primary care professionals working in close collaboration within specific initiatives, Dr Charmaine Gauci has been at the helm directing the whole set-up since 2007. Becoming a medical doctor in 1991, she works today far from the clinical field or rather, within the community with a good ear to the ground, listening to what people



out there really need, and working to achieve the possible in protecting and promoting health.

"I must say that I enjoyed working in clinical practice and after graduating had my stint in various specialities from casualty to gynaecology, paediatrics and so on. However I found myself fascinated with the whole concept of public health, so much so that I proceeded studying and achieved a Master in the topic and then followed up with a PhD in epidemiology. I eventually headed the Unit for the Prevention and Control of Infectious Diseases until the 2007 reform which saw the enmeshment of this unit with the Health Promotion Department giving an emphasis on prevention. It was ideal – both my interests were now under one hat. I applied for the post of Director and was successfully accepted, and have held the post since."

The HPDP is divided into three distinct units which work in tandem. The Infectious Disease Prevention & Control Unit is responsible for the surveillance of prevalent infectious diseases and takes action accordingly. "In summer for instance, one common threat is food-borne illness. When reports are lodged in, even by individuals who experienced foodborne illness after eating certain foods





or after eating in certain establishments, we investigate. We also investigate cases of meningitis and where the cases are related to school children, we check the patients' contacts, visit the school, and doctors talk to parents of peers so that prophylaxis is distributed, to lessen the carriage of this dangerous disease."

Dr Gauci also explains how the HPDP is roped in every time illegal immigrants land in Malta, most especially to screen for tuberculosis which is prevalent in African countries. "It is a fact that immigrants who are infected with TB, will develop acute forms of TB after arriving in a country such as ours with low TB prevalence. Hence upon arrival we screen all immigrants for active TB and treat and isolate as necessary. This will limit the spread of this infectious disease, protecting staff, the general population and the migrant population."

The second unit is the Health Promotion Unit which takes care of observing our lifestyle, its changes and the repercussions of such. One of the current initiatives is to enhance healthy cooking skills based on the Mediterranean diet with a key cooking personality being roped in to create easy-to-prepare recipes that are simple, cheap and effective towards meeting dietary needs. Targeting obesity is a high priority, by supplying helpline services for free nutritional advice, weight management classes, and free aerobics with much of this being successfully done through partnerships with local councils and health centres.

"There are seasonal promotions such as the one during summer to help educate people combat heat effectively. Then there are the ongoing promotions such as the one which encourages our population to quit smoking via educational means, the Quit helpline and smoking cessation classes. All this apart from breast cancer awareness, sun damage awareness, cancer prevention and other initiatives. We work hard to be present where people congregate - at trade fairs, village fairs, banks, schools, hotels. ... employers are our allies within many establishments and their cooperation is fundamental towards reducing sick hours off the job by keeping their employees healthy."

A new unit was also established - the Non-Communicative Disease Prevention & Control Unit which works towards building long-term strategies to prevent illnesses and maintain health. For example, we developed the NCD strategy to target priority diseases such as cardiovascular disease, respiratory disease, arthritis, osteoporosis, mental illness, and dental health via the four biological risk factors ie high blood pressure, cholesterol, diabetes and obesity coupled with a healthy lifestyle approach. Another strategy was the Healthy Weight for Life Strategy, which was launched earlier this year.

"Being constantly one step ahead of what needs to be done means working on evidence-based projects that allow us to analyse and compare with other countries so we obtain the best outcomes. One such project is the healthy cooking campaign which is seeing recipes being filmed on CD and ready for distribution to the public. We need to continue with awareness but need to increasingly work towards behaviour change, which we know does take time."

Dr Gauci is also involved in other things related to her work. Being a senior lecturer at the University of Malta, she tries to pass on her experience to students and currently she is also the president of the Malta Association of Public Health Medicine. Incidentally time is another precious part of her life within her family. Being married and the mother of a teenager means she is constantly juggling things as most women do. However she strongly believes that being a successful woman today is also about finding time to balance out the act. "Many women do everything they can to keep things running smoothly and then forget they have to care for their own wellbeing. As a professional my aim is to help people avoid illness or rather, learn how to maintain good health. Part of the good health recipe is also adopted by myself so I dedicate time to my own relaxation - I walk every day, I swim as often as I can (pools are handy places all year round), go to Zumba classes, and so on ... "

Does she miss her medical practice? "I never practised as a general practitioner but I still take care of my immediate family's medical needs when these arise. I would miss the doctoring had it not been for the fact that my profession allows me plenty of public contact when I go out on the field. Rather than medicate, I listen to people and encourage them to live a healthy lifestyle and take measures to protect them from infectious disease. It's a different way of being a doctor isn't it?" \$

The Synapse



The changing face of medicine

Introduction

The art of medicine is not talked much about these days. Patients figure it out, too, for the art of medicine transcends all else when an anxious individual confronting death or a serious illness looks at us and asks, "What's the best for me?" Our response distinguishes medicine as a timeless noble craft from medicine that's is simply the interpreation of lab results which for the patient means nothing. There has always been a mixture of art and science but over the ages this art/ science ratio has undergone a dramatic change. Using the 20th century retrospectoscope, it would appear that medicine in the past was predominantly art with only a little science thrown in.1

Some five million years ago, anthropologists tell us, Africa witnessed the first ape men. Within three million years, our upright, large-brained ancestor *Homo erectus* evolved, who learned how to make fire, use stone tools, and eventually speak. This omnivore fanned out about a million years ago into Asia and Europe, and a direct line leads, around 150,000 BC, to *Homo sapiens*.²

Our palaeolithic precursors led brief lives. Nevertheless, they escaped the plagues that were to besiege later societies. Infectious diseases (small pox, measles, flu and the like) must have been virtually unknown, since the micro-organisms responsible for them require high population densities to provide reservoirs of susciptibles.² The spread of different pathogens occurred as humans colonised the globe and and they were themselves colonised by pathogens. As it multiplied, the human race moved out of Africa, first into the warm regions of Asia and southern Europe, and then furthur north.²

What we now recognise as medicine is a consequence of

developments in Western society over the past three centuries. In premodern cultures, the family was the main institution coping with sickness. In communities there have always been individuals who acted as healers, using a mixture of physical and magical remedies. Many of these traditional systems of treatment survive today in non-Western cultures throughout the world. The various folk remedies and healing techniques were passed from generation to generation. Illnesses were frequently regarded in magical or religious terms and were attributed to the presence of evil spirits or 'sin'.3

The idea of public health took shape in the early twentieth century. The state began to assume responsibility for improving the conditions in which the population lived. Sanitation and water systems were developed to protect against disease. Before, cholera epidemics used to eradicate a large





throughout the ages

number of people.⁴ In 1854 John Snow, who is considered the father of field epidemiology, found the source of cholera in the contaminated water system of London. Attention was thus devoted to housing as well as working conditions. Regulations were imposed on slaughterhouses and places of food processing. Burials were monitored to ensure that they did not pose a health threat. Medicine became a public domain, not only pertaining to individual illness. Hospitals, prisons, asylums and schools were built and were controlled by specific regulations to safeguard the public wellbeing and prevent disease.

The "scientific method" began in Bologna around 1315 when the first recorded public human dissection was conducted by Mondino de' Luzzi. His *Anatomia mundini* (1316) became the standard text on the subject.² From Bologna the practice quickly spread throughout Italy – though anatomy teaching with a human corpse became routine in England and Germany only after 1550. The emphasis in medicine was changing from philosophy to practical physical science and anatomy, thus anatomy and surgery paved the way for the scientific method. This method as we know it today consists of identifying a problem, postulating a hypothesis, testing the hypothesis by observing and experimenting, and then interpreting the data and drawing a conclusion. This is the basis of modern experimental science and the basis of modern medical science.

With the invention of the stethoscope by Rene Theophile Hyacinthe Laennac (1816), the microscope by Antoni van Leeuwenhoek (1632-1723) and Roentgens' X-rays in 1895, science was becoming more and more important in medicine. Harvey's scientific study of the human circulation (1628), Koch's scientific studies of microbes causing human disease (1872 – 1882), and Curies' studies of radium (1897 – 1904) all were important medical advances based on science.²

During the late 19th and early 20th centuries, Sir William Osler (1849 – 1919) was recognised as one of the greastest medical teachers of all time. He strongly influenced the organisation of the clinic at John Hopkins Hospital in Baltimore and perfected teaching medical students at the patient's bedside. A very famous saying of this great teacher is the following: *"The good physician treats the disease, but the great physician treats the disease, but the great physician treats the patient."* He taught his students the art of medicine utilizing the stetoscope, physical examination, and patient history with *"the patient as his text".*⁴

Understanding the individuality of the sick is part of medicine's art, well chronicled by the Roman educator A. Comelius Celsus in his masterly work

The Synapse 🔶

"The good physician treats the disease, but the great physician treats the patient"

De Medicina, written 2,000 years ago. Celsus teaches that the physician applies a common knowledge while searching in a given patient for unique characteristics that may be at odds with established dogma. He writes, "Nay, even in the same patient, the particular characteristics of a disease are very variable, and those who have been treated for a time in vain by the ordinary remedies have been often restored by contrary ones." Attention to individuality – then and now – makes all the difference in quality care.¹

Health is traditionally equated to the absence of disease. A lack of a fundamental pathology was thought to define one's health as good, whereas biologically driven pathogens and conditions would cause an individual to suffer from poor health and label him as "diseased". However, such a narrow scope on health limited our understanding of what constitues good health, thwarted our treatment efforts, and perhaps more importantly, suppressed prevention measures.

In 1977, American Psychiatrist George Engel introduced the major theory in medicine, the Biopsychosocial (BPS) Model. The model accounted for biological, psychological, and sociological interconnected spectrums, each as systems of the body. In fact, the model accompanied a dramatic shift in focus from disease to health, recognizing that psychosocial factors (e.g. beliefs, relationships, stress) greatly impact recovery the progression of and recuperation from illness and disease.5 The concept of wellness is particularly stressed, where the state of being in good health based on the biopsychosocial model is accompanied by good quality of life and strong relationships. This is in contrast to the traditional, reductionist biomedical model of medicine that suggests that every disease process can be explained by an underlying process or cause (germ theory of disease).

The BPS model underlines the importance of handling the three

systems together. A growing body of empirical literature suggests that patient perceptions of health and threat of disease, as well as barriers in a patient's social or cultural environment, appear to influence the likelihood that a patient will engage in health-promoting or treatment behaviours, such as medication taking, proper diet, and engaging in physical activity.

"Personalised medicine" is today's lingo, spearheaded by increasing research into human genomics and pioneering therapies which seek out and target differences among diseases commonly thought to be the same. In the next ten years the era of bio-engineering will achieve new milestones in areas like miniaturised instruments and the application of stem cell techniques for the production of human tissues. Artificial intelligence components will assist in clinical decision making. Molecular medicine will have a greater impact in diagnosis and screening.

Society is continually changing and the role of doctors in shaping the nature and provision of health care has changed accordingly.⁶ Changing lifestyles, with the associated problems such as obesity, cardiovascular disease and cancer will continue to place more emphasis for health education and health behaviour.⁷ In an article in the *British Medical Journal*, Plamping stated that a doctor's opinion is no longer regarded as sacrosanct and a new dialogue is developing between health care consumers and providers.⁸

We are living in an age where more and more information is available – from a variety of sources – to draw on in making choices about our lives. Individuals are becoming 'health consumers' – adopting an active stance towards their own health and wellbeing. Not only patients are able to make choices about the practitioners to consult, but they are also demanding more involvement in their own care and treatment. The use of the internet has already resulted in a more demanding and knowledgeable patient. This is, first and foremost, a fascinating reflection of transformations occurring within modern societies.⁹

Another challenge is tele-medicine which on a global scale is already a reality. The growing practice of telemedicine puts this technology to work by allowing doctors to consult each other about management of their patients even from thousands of miles away. Computers that make use of artificial intelligence may be used to analyse difficult medical problems and advising physicians on the patient's diagnosis. These new technologies must not detach the physician from the patient. The patient-doctor relation is a fundamental relationship which binds the two together. As an eminent Havard professor, Francis W. Peabody (1881 -1927), so well stated: "The secret of care of the patient, is caring for the patient."

Conclusion

With the patient being the central person there is the danger of invasion of his privacy. This danger to privacy is always a challenge and medicine must deal with ethical and social issues that accompany its progress. Doctors must never lose sight of the fact that they are the guardians of their patients' best interests. Medicine in the future will continue to take different forms but the best interests of the patient will never change and always need to be protected.

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One World, One Home, One Heart the theme for World Heart Day

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orld Heart Day was created in 2000 to inform people around the world that heart disease and stroke are the world's leading cause of death, claiming 17.3 million lives each year. In Malta, ischemic heart disease is the leading cause of death accounting for 21% of all deaths. In 2010, there were 319 male deaths and 328 female deaths, a decrease of 47 male deaths and an increase of 19 female deaths over the previous year.

In partnership with WHO, the World Heart Federation organizes awareness events in more than 100 countries. These events vary from one country to another and include free health checks, organized walks, runs and fitness sessions, public talks, scientific forums, exhibitions, concerts, carnivals and sports tournaments. The World Heart Day takes place on 29 September each year. This year the theme is One World, One Home, One Heart focusing on women and children. Heart disease was traditionally associated with men and older persons. However we are seeing an increasing number of cases of ischaemic heart disease in women. In fact presently, half of deaths worldwide occur in women. One should also bear in mind that since women and mothers are usually the gatekeepers of the family's health, they have a significant influence to this respect. Furthermore, with risk factors being increasingly established during early childhood, this is putting the paediatric population at an increased risk of heart disease when they become adults.

Risk factors for heart disease include hypertension, hypercholesterolaemia and increased glucose levels, smoking, inadequate intake of fruit and vegetables, being or obese and physical inactivity. We know that at least 80% of premature deaths from heart disease and stroke could be avoided if the main risk factors, namely, tobacco, unhealthy diet and physical inactivity, are addressed.

Compared with nonsmokers, smoking is estimated to increase the risk of coronary heart disease by 2 to 4 times. Smoking causes reduced circulation by narrowing the arteries, increases peripheral vascular disease, and causes abdominal aortic aneurysm. Cessation can significantly reduce the risk of suffering from smoking-related diseases. The Health Promotion and **Disease Prevention Directorate offers** a free quitline service on 8007 3333 as well as free smoking cessation classes in health centers to help smokers guit. As a health professional you too can help by following the ABC model (Ask, Brief Advice, Cessation support).

Research has shown that the traditional Mediterranean diet reduces the risk of heart disease. In fact, a recent analysis of more than 1.5 million healthy adults demonstrated that following a Mediterranean diet was associated with a reduced risk of overall cardiovascular mortality.

The Mediterranean diet emphasizes:

- Eating primarily plant-based foods, ٠ such as fruits and vegetables, whole grains, legumes and nuts;
- Replacing butter with healthy fats such as olive oil and canola oil;

- Using herbs and spices instead of salt to flavour foods;
- Limiting red meat to no more than a few times a month;
- Eating fish and poultry at least twice a week.

Regular physical activity, fitness, and exercise are critically important for the health and well-being of people of all ages. Research has demonstrated that all individuals can benefit from regular physical activity, whether they participate in vigorous exercise or some type of moderate healthenhancing physical activity.

World Heart Day raises awareness amongst health professionals and the general public for the urgent need for everyone to take control of his heart health by living a healthy lifestyle with a healthy diet, increased physical activity and staying away from tobacco. Secondary prevention measures targeting risk factors including being overweight, obesity, hypertension, diabetes, high triglycerides and cholesterol and reducing stress couple up with the primary prevention measures. S

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