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P.O.Box 35034 Amman 11180 Jordan.

Telefax (+962) 6 5671146 or 5671147

medlab@go.com.jo

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Editor: Yahia F. Dajani, F.R.C.Path.

**EDITORIAL****PROVOKED AND UNPROVOKED VENOUS THROMBOEMBOLISM**

Venous thromboembolism may be provoked after a period of inactivity, such as prolonged bed rest or several days after an operation, especially long procedure with deep anesthesia. Such event can often be prevented by anti-coagulation that should be continued for 3 months.

Venous thromboembolism may develop when unprovoked, with a high risk of recurrence reaching 40% at 5 years. Warfarin is over 90% efficient, but carries a risk of major bleed in 1 to 2% of such patients per year.<sup>1</sup> Besides, warfarin interacts with many foods and drinks and requires, at least initially, frequent monitoring.

For prolonged anticoagulation in unprovoked venous thromboembolism, preventing recurrence was weighed against risk of bleeding, using two new oral anticoagulants, namely, dabigatran and apixaban, whose performance was reported in 3 trials involving warfarin and placebo as well.<sup>2, 3</sup> Dabigatran and apixaban are direct inhibitors to thrombin and factor Xa, respectively. In one double-blind trial, 150mg twice daily dabigatran was compared with warfarin to establish an INR of 2-3. In a second trial, same dose of dabigatran was compared to placebo for a period of 6 months. In a third trial, apixaban at 2.5mg or 5mg daily was compared with placebo for a period of 6 months. Dabigatran showed less major bleeds than warfarin, while both showed greater efficacy than placebo in preventing recurrence of thromboembolism. For apixaban, rates of recurrent thromboembolism were similar for the two doses used, while bleeding rates did not differ from that with placebo.

For short term anticoagulation, use of dabigatran or apixaban has not been approved. However, a third new anticoagulant, namely, rivaroxaban became approved for use on short term basis in both Europe and America. Rivaroxaban is more effective than placebo in preventing recurrence but stands greater risk of bleeding. On the other hand, 100mg daily aspirin has been shown in two trials to reduce risk of recurrence by about one-third with no increased risk of bleeding against placebo. But aspirin is less effective than new agents in preventing recurrence.

Briefly, where does the above argument lead us to? New agents offer less bleeds and similar rates to warfarin in preventing recurrence. Extended studies are required to compare new agents with both warfarin and aspirin. Moreover, relation of acute coronary thrombosis event to dabigatran as compared to warfarin<sup>1</sup> should be viewed with caution. For prolonged anticoagulation, approved therapies, so far, include only warfarin, aspirin and rivaroxaban. Dabigatran and apixaban have not yet been, but may later be, approved. Low to moderate risk patients may be given aspirin or warfarin while high risk patients may benefit better from warfarin or rivaroxaban than an only 32% reduced risk of recurrence achieved by aspirin. Risk-benefit decision may be outweighed in individual cases where other disorders co-exist. More information on new agents needs to be clarified before their unqualified usage in venous thromboembolism.

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**The Editor****CORONARY ARTERY DISEASE AND THE GUT****NABIL ABUL RUB, M.D., M.R.C.P.**

Gastroenterologist and hepatologist nabil\_aburub@hotmail.com

Strong relation is suspected between coronary artery disease and small intestine.

Both traditional Chinese and holistic medicine have considered heart and small intestine to be closely related. According to Chinese theory, main branch from heart meridian extends down to small intestinal meridian. A meridian is defined as the channel along which electro-magnetic energy is carried from one specific organ to another.<sup>1</sup> Accordingly, small intestine is complementary to heart, as much as gall bladder is complimentary to liver.

In this article, five proposals will be forwarded, backed by scientific data published in recent years.

Firstly, the fauces (mouth) can be inflicted with ulcerative and inflammatory conditions such as peri-odontitis which have been incriminated by some as adverse effects in the causation of coronary thrombosis.<sup>2</sup> Certain bacterial species harbor both gums and atherosclerotic plaques in the coronary arteries.

Secondly, *H pylori* are gram negative bacteria that colonize gastric mucus found in about 50% of the general population. Infection during childhood is suspected. At low levels, *H pylori* can cause chronic inflammation resulting in gastritis, peptic ulceration and gastric neoplasia. Presence of *H pylori* is associated with greater prevalence of coronary artery disease. A recent study on 1122 survivors of heart attack in men and women aged 30-49 years reported significant association of *H pylori* with coronary artery disease as an independent factor.<sup>3</sup> In other words, patients with acute myocardial infarction had higher prevalence of *H pylori* infection and sero-positivity than in a control population.

Thirdly, some bacterial species that live in small intestine, of *Fermicutes* family, appear to contribute to obesity and metabolic syndrome. Such bacteria flourish with high intake of fat, sugar and alcohol. These bacteria are very efficient at digesting and absorbing those compounds which encourage development of obesity, insulin resistance and the metabolic syndrome. Those bacteria secrete lipo-polysaccharidases causing inflammation that can reach coronary vessels. Recently, inflammation has attracted attention as an important factor in the genesis of coronary thrombosis. Gut bacteria have become implicated in capturing nutritional and stored energy from host for contribution to metabolic syndrome.<sup>4</sup>

Fourthly, ileo-cecal valve dysfunction may cause health problems, such as atrial fibrillation, chest pain and low back ache. By theory alone, if bacteria transfer from colon to small intestine by benefit of an incompetent ileo-cecal valve, such bacteria can overgrow to cause low grade chronic

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## Heart and Gut

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inflammation and may transmit it to the coronaries.

Fifth, a strong relationship has been suggested between gut flora and metabolism of lecithin. Such discovery has been recently made with good evidence forwarded to support it. Lethicin is a lipid prevalent in animal products such as egg yolk, soya beans and many commercially packed foods. A study of 1900 patients at the Cleveland Clinic, by Stanley Hazen *et al* on gut flora metabolism of phosphoryl-choline suggested that it promoted cardiovascular disease.<sup>5</sup> By-products of lecithin produced by gut flora, namely, choline, TMAO (triethylamine-N-oxide) and betaine, could be associated with coronary artery clogging. It followed that those who consumed high animal fat intake in their food were pre-disposed to coronary heart disease irrespective of cholesterol status of the individual. It also opened a strong debate on supporting effect of diet and intestinal bacterial profile on development of coronary thrombosis. Lethicin by-products were found to be ten-fold stronger predictor of heart disease than cholesterol. A more recent study suggested that bacteria in the gut may also play a role in the risk of heart disease through breakdown of wildly consumed L-Carnitine.<sup>6</sup> Gut bacteria can metabolize L-Carnitine to TMAO which in turn can cause atherosclerosis. L-Carnitine is naturally found in red meat and is also supplied as dietary supplement. Diet high in L-Carnitine, to which meat eaters are exposed, have gut microbes that are more prone to form TMAO, while vegetarians and vegans do not produce significant amounts of TMAO. Therefore, bacteria lying in our guts can interact adversely with certain dietary patterns or drugs on the long term. Soya beans, as a nutrient, can be innocuous if fermented, such as in Miso soap, Natto and Tamara Soy sauce. Natto, in particular, is very popular in Japan and provides a rich source for Vitamin K2. It is worth realizing that Vitamin D supplement without Vitamin K2 can be hazardous and may cause precipitation of calcium in coronaries and kidneys. But if Vitamin K2 is added to Vitamin D therapy, a shift of calcium will result in its deposition onto bone instead of the coronaries or kidneys, thus preventing osteoporosis. Osteocalcin plays a supportive role in preventing deposition of calcium in arteries.<sup>7,8</sup>

In conclusion, diet and intestinal bugs can exert great influence on the risk of developing coronary artery disease. Bacterial flora may play a pivotal part in this sequence. Quoting words of Professor Ropeloff in 1930: 'Man is only what his microbes make him'.<sup>9</sup>

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## LETTER TO THE EDITOR

### KEEP AWAY FROM RED MEAT

Subhi K. Zabaneh, M.B.Ch.B (Bristol), F.R.C.S. (London)

*drsubhi.zabaneh@gmail.com*

Now, we can state that "Red meat and its by-products pose a serious threat to life".

The following questions arise here:

1. Why is red meat and its by-products harmful?
2. How does red meat and its by-products increase health risks?
3. Does most processed red meat link to earlier death?

Currently, mounting evidence raises an alarm against red meat consumption in our diet. Several studies have shown that regular red meat consumption damages the heart.

Stanley Hazen from the Cleveland Clinic in USA stated "though cholesterol and saturated fat content in lean red meat is not that high, something else contributes to increased cardiovascular risk". It was discovered that gut bacteria can eat "Carnitine" found in red meat, which is broken down in gas form to be converted in the liver to a chemical called TMAO (trimethylamine N-oxide).<sup>1</sup>

It has been shown that TMAO, the red meat chemical which has been previously ignored, significantly influences cholesterol metabolism, and is strongly linked to the building up of fatty deposits in blood vessels leading to heart disease and death. Vegetarians have fewer gut bacteria than red meat eaters, posing less risk of carnitine.

In view of these recent findings, red meat eaters are advised to look for alternative sources of protein if they regularly eat red or processed red meat.

Another caution worth observing on taking or prescribing supplements of Carnitine, Lecithin, or Choline to delay onset of cognitive deterioration: it is not worth the risk!

Recent research at Harvard Medical School suggests that a diet high in red meat shortens life expectancy, in a study of more than 120,000 people with increased risk of death from cancer and heart disease.<sup>2</sup> On March 7, 2013: a study of 500,000 people across Europe, found that processed meat as in sausages, ham, bacon or other meat: increases risk of early death or dying young from cardiovascular disease and cancer.<sup>3</sup>

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## MEDICAL PERSONALITY



Cairo 1956



Amman 2013

### ZAID MOHAMMAD HAMZEH AL-SMADI

**M.B., B. Ch. (Cairo), D.L.O. (London)**

*Clinic: 1st. Circle Jabal Amman, next to Malhas Hospital.  
Email: zaidhamzeh@orange.jo*

Born May 25<sup>th</sup> 1932 in the City of Salt, at a time when it was a major municipality in Jordan. Time of my birth, May 25<sup>th</sup>, coincided with Independence Day for Jordan. As a child, I had believed all the country celebrated my birthday each year! My family came from Ajloun but had originated from Lubia, a village near Tiberius, Palestine which Zionist invaders had demolished completely after occupying it in 1948. My mother, of Turkish roots, had been born in Damascus and married my father in the days of United Syria, namely, before representatives of Britain and France; Sykes and Picot, conspired in 1916 to divide Syria into four different countries, namely, Syria, Lebanon, Jordan and Palestine.

My school years were spent in Irbid, Karak, Madaba and Amman respectively, moving every time with my family. In Irbid, we first resided in the old western quarter then moved to the new east sector of the city. At the age of 5 years, my father took me to enter the only public school there. The principal Omar Shalabi hesitated, but on seeing me reading the first elementary book, he immediately admitted me to the first elementary class, with pupils Adnan Abu Ghanima, Shams Eldine Jum'a and Hani Mraish among others, with Hasan Hashisho as a teacher to remember. Second elementary was spent in Karak, where my father became Director of Finance. On transfer to Madaba, I joined the only school that taught up to Grade 5. In Madaba we stayed only 3 months, after which we moved to live in Amman where I enrolled in the 3<sup>rd</sup> elementary class in Asbalia School located opposite the Roman Amphitheater and headed by Bakr Sudqi from Al-Maghreb. Next year I moved to Abdalia School, located at the bottom of the road leading to the first circle in Jabal Amman. The School Master was Yousef Jayyousi; also it only taught to 5<sup>th</sup> grade, so did the only other third school in Amman at the time, namely, Al-Hashimiya School in Jabal Al-Waibdeh. There was one secondary school in Amman at the time, namely 'Al-Tajheez' which taught up to a level of two years before the High School Certificate (Matriculation). For completing the last two secondary school years, you had to go to Al-Salt Secondary School. However, when our turn came to transfer, our school, 'Al-Tajheez' added the last two years which enabled us to complete our secondary education in Amman instead of Al-Salt. My memories there take me to my teachers in Arabic Mahmoud Saif Eldine Al-Irani and Naser Eldine Al-Asad. Here is a fact that would not be over looked. Most of the teachers at that time came from Palestine, Syria, Lebanon, Hejaz & Egypt. I passed the Matriculation Examination in 1948, at the time of the Palestinians' exodus, forced out of their own homes to the bewilderment of neighboring countries.

In the summer of 1948, I took an Arab Airways plane, colored red, and flew to Cairo for my university education. I was accepted in the Scientific Stream of Saeediya School in Cairo. At the end of that year I passed the Egyptian 'Tawjihi' Examination, after which I was admitted to medical school in Fouad the First University, Cairo. My years of medical school were full of political upheavals consequent upon a changing political system. During that period of time, I was active in the Jordanian Students' Society in Cairo. I graduated M.B., Ch.B. in December 1955. Name of the university in post monarchy period was changed to Cairo University. I did my internship in Bulaq Hospital, where the year spent there was most instructive.

I returned to Amman as a licensed medical practitioner late 1956 and was appointed in the Ministry of Health, working first in outpatient clinics, then moving to government hospitals, from Maternity Hospital on Salt Road, to Ashrafia (now Al-Bashir) Hospital where I assisted Dr Ghaleb Qussous, famous surgeon of his time. I was then transferred to Al-Hilal Hospital, then to Internal Medicine Hospital with the late Dr Zuhair Malhas, after that to Children's Hospital with the late Dr Hasan Pharoan, eventually ending up in the ENT (Ear, Nose and Throat) Hospital in Jabal Al-Waibdeh. There, the late Dr Subhi Hamada encouraged me to take up ENT for a lifetime career. Throughout my employment in the government I practiced part-time as a family doctor, first in my own house then in my clinic on Rida Street. In the meantime, Dr Subhi Hamada persuaded me to assist him operating in his private practice, which he did in Malhas Hospital. There, I met Rehab, daughter of Dr Qasem Malhas, founder of the hospital.

We got married in April 1959. With our limited money we preferred a honey moon in Europe to an expensive wedding party in Amman. We first flew to Beirut, took the boat to Alexandria, then to Athens and on to Venice. From there, we took the train and roamed around Trieste, Vienna, Zurich, Geneva, Rome, Naples, then took the boat to Capri and last to Brindisi. We went back through the same route where we detoured to Cyprus, Beirut and then to Amman in May 1959. While in Beirut, being a leftist, I was advised by a friend, Ali Khasawneh, not to leave for Amman since conditions there were adverse to political activists like myself. However, on return home authorities did not hamper me. In 1960, my first child Ziad was born, named after my late brother who was a pilot in the R.J.A.F. and died in his plane crash back in December 1956. My colleague and close friend, late Dr. Camiran Nabil, training in Ophthalmology, persuaded me to visit the British Council in Amman and apply for a scholarship in ENT.

The application was accepted. In the summer of 1961. I prepared for my excursion to Britain. My wife was expecting and went to stay at her parents' during my absence together with our child Ziad. I succeeded in the ENT Diploma Examination, which was only held by two other

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## Medical Personality

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Jordanians before me, namely Abdel Salam Majali and Mohammad Najjar of the Royal Army Medical Corps. I could not pursue to obtain further specialization, especially that Subhi Hamada had resigned from the Ministry of Health leaving his post vacant. I became the only ENT specialist in the Ministry of Health, steering with great enthusiasm the ENT Hospital as director. But unexpected development took place. On 29 July 1962, a revolt took place in Yemen against Imam Al-Badr. My younger brother Sahel was Commander of the Royal Air Force. He was ordered to stage an attack against the Egyptian army who had rallied support to the new regime in Yemen. All of us were betaken on November 12<sup>th</sup> 1962 by the news of brother Sahel defecting to Cairo in his military plane. On 17<sup>th</sup> of November, 1962, five days after the defection, I was arrested together with my two brothers Zuhair and Hazem and detained in Abdali prison cells. I was interrogated at depth, suspected of being a communist. The whole action did not seem logical to anybody around us. Our arrest lasted whole 19 days. Afterward, I went back and resumed my work as Director of the ENT Hospital. At the same time, I was working part time in my private clinic. In 1965, the Ministry of Health enforced all its medical employees to work full time, forbidding private practice. Because of that, I resigned, along with 90% of the specialists in the Ministry of Health, to devote all my time to private practice.

As for extra-curricular activities, I decided then not to delve into politics but involve myself in professional issues, such as the JMA (Jordan Medical Association), to which I was twice elected member of Council during the period 1965 to 1968. I often wrote in 'Al-Samma'a' magazine from 1965, shouldering this circular in its early days with its founder the late Dr Bashir Bustami. In my new book that will appear soon with my articles in Al-Samma'a, one may easily find out that the magazine was completely different from today's one! In 1968, I took part in the foundation of Jordan Medical Journal. During my tenure on the JMA Council, the 1967 aggression by Israel took place, with occupation of West Bank of Jordan besides Sinai in Egypt and Golan Heights in Syria. Together with other professional associations including dentists, engineers and lawyers we formed a Joint Forum of Professionals, to which I was elected as Secretary. The Forum became recognized by government and nongovernmental bodies. It was represented, for example, by two members in the then formed 'Save Al-Quds Committee'. The Forum soon was converted to the 'National Forum' with Sulaiman Nabulsi as Head. While serving on the 'Save Al-Quds Committee', I had to visit several capitals in search of political support, such as Beirut, Baghdad, Sofia (Bulgaria) & Rome. But political turmoil in Jordan and entry of 'Fidayeen' into the scene brought to an end the role of the National Forum. In 1970, an internal conflict erupted between them and the armed forces that led to direct confrontation in Black September, during which time I was in Beirut. Along with other Jordanian and Palestinian physicians we managed to send to Amman food and medicines on Alia Airways through the help of its then Director General Ali Ghandour. That coincided with the time Jamal Abdel Nasser of Egypt died.

As member of 'Save Al-Quds Committee' I was part of a delegation that visited Damascus late 1970 on the inauguration of Hafeth Al-Assad as President of Syria. In April 1971 I was an invitee to the National Palestinian Assembly in Cairo chaired by Yasser Arafat & under patronage of Anwar Sadat, President of Egypt. Those activities did not deter me from resorting to other professional and scientific ones. In 1973, I participated in foundation of 'Jordan Surgeons' Society', the first specialists' society in Jordan Medical Association, starting with 44 members. In 1981, ENT Surgeons Society was established in the Jordan Medical Association, of which I was a founding member. In February 1976, 'Al-Shaab' daily newspaper was launched and my shares were not meant for financial reasons; on the opposite, I found a free stage to write a weekly article charge free. My writings related to social and community issues. Unfortunately, as a result of criticizing political figures, the newspaper was closed down in May 1977, not to be allowed to see the light again. In subsequent years, I commenced writing my weekly column in Al-Rai Daily newspaper and continued to do so until now. I got involved in serving the Deaf Society. In 1976, Dr Hassan Badran and I started a school for the deaf on a site between Amman and Zerka, with support by Ministry of Social Affairs. After death of Queen Alia in 1979, I was commissioned to establish a project to care for the deaf and mute. This took me to Italy and America. In 1984, I was elected President of Princess Haya Cultural Center in Amman, serving until 1987. The idea was good though the real value was limited. In April 1985, I was appointed Minister of Health under the prime minister Zaid Al-Refai. This post provided me with an opportunity to initiate 'Health Centers' in remote areas all over the country. I stayed in this position for about 4 years, culminating in my resignation on December 19<sup>th</sup> 1988 owing to my refusal to accept

amalgamating Ministry of Health, Military and Teaching Hospitals in the country under one establishment named 'Jordanian Medical Establishment', a project that antagonized the principles of the Primary Health Care as laid down by the WHO. It did not take long for my fears to come true. Overspending, bad management and upset of all workers in the different sectors led to the demise of this ill fated establishment and ended up with its cancellation by Parliament in 1990. I had worked during my tenure as Minister of Health on changing teaching medicine from English to Arabic, our native language. A decision was finally taken in Damascus on December 7<sup>th</sup> 1988 by Arab Ministers of Health and Arab Ministers of Higher Education to this effect, but the file was shelved there and then until this day! On another theme, as Minister of Health, I had been elected as President of WHO (World Health Organization) for the year 1986-87. It was a great experience.

One week after my resignation as minister, I resumed work in my clinic after 4 years absence!

In 1991, we all grieved the ferocious attack on the Iraqi people. However, my political activities were brief and concentrated on the weekly article in Al-Rai paper and reflected by topics like 'Health System in Jordan', Family Planning', Primary Health Care in Jordan' just to name a few lecture titles given to universities and research centers. In 2005 and for six months I produced and presented a weekly program on Jordan TV entitled 'The Political Saloon'. In June 2009, I represented Jordan at the UNESCO in Geneva, attending as member of the Inter-governmental Committee of the Convention for Protection and Promotion of Diversity of Cultural Expression. Again, that was an invaluable experience. In August 2009, I was elected President of the National Jordanian Antismoking Society for 2 years. I have been a great believer in this campaign since I quit smoking in 1971.

My first book entitled "Between Medicine and Politics/Memoirs" came out in March 2010 with a second edition in Feb 2011. Currently, my second book entitled "Between Medicine and Journalism" is in the stage of proof reading.

As to my family, I live with my wife Rehab now. Our children: Ziad is MBA in aviation management from Emory Riddle University, Florida works for a private company in Amman. Manal was the first qualified audiologist in Jordan in 1987 with B.A. & two Master degrees from USA. In 2007 she got her Ph D & converted to teaching at New Mexico State University, USA. Zeena the youngest got her degree in advertisement design; she lives and works in Panama. With five grand Children, Tarek and Faisal at the university, Lulu and Zaid at high school and Omar at the kindergarten!

Finally, a piece of advice to younger generation that as I remember very well, was delivered by Mr. Ghaleb Sunna'a, one of my teachers, at the farewell party held on the occasion of finishing the high school in 1948: "You ought to adhere to a noble principle in your life". And a word to new doctors: Try to keep in mind that medical service is not a commodity.



Sky line overlooking Dead Sea and Jordan Valley

The opinions and conclusions in the Bulletin are those of the authors and do not necessarily represent the views of the publisher.