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# THE HIMALAYAN HEALTH



Respected Doctor/s,

As for the question of whether a doctor should give his cell phone number to his patients or not, I'd say it's an option for the doctor whether he'd give his cell phone number (and which cell phone number). But for the sake of better patient management and doctor-patient relationship, it is preferable to provide. Some studies have shown that patients feel highly satisfied and reassured that they can contact their doctors whenever the need arises. It has even cut down the number of unnecessary trips to the emergency room.

Giving out your personal numbers to patients sometime really becomes a bit of a nuisance. Patients will try to seek consultancy for free but more importantly, irritating at busy time. But if the patient understands the right use of this privilege given by Doctor, can do wonders in improving Doctor-Patient relationship and patient care.

Patient should bear in mind that doctors have every duty to put their patients first but they must understand that doctors can provide this facility only when they are free. Moreover if patient inquire about any problem they should not be rest assured that this is over because whether it is online consultation or telephonic, it has got some limitations.

Now the big question is *who will educate the patients regarding the limitations of this usage- Doctor, attendant or somebody else?*

One thing is guaranteed in the era of electronic gadgets, Doctor and Patient need to understand, feel and hear each other.

But no matter what kind of technology will be used, ethical rules should always be followed. As doctors are duty-bound to take care of their patients, patients do have the duty to take care of their own health by being well-informed and with respectful thought that their "doctors do have personal life also".

Till the next issue.....

Regards,

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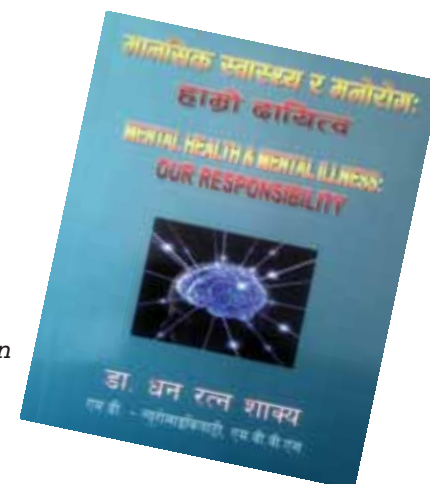
## Book Review

## “MENTAL HEALTH & MENTAL ILLNESS: OUR RESPONSIBILITY”

A book which teaches to bear the responsibility for mental health promotion

**Dr. Robin Maskey, MD**

Assistant Professor, Department of Internal Medicine, BPKIHS



Mental health problems are common worldwide<sup>1</sup> and Nepal is no exception.<sup>2</sup> Many people including illiterate to well read, are less aware about the psychiatric problems; stigma and ignorance hinder the proper management of these problems. Unfortunately, there is a scarcity of mental health service facility, professionals and resources including printed documents e.g. books, manuals and literature on mental health and psychiatry in Nepal.<sup>3</sup> Most of the time, these mentally ill people are either under recognized, not treated or are under the treatment of non-psychiatric clinicians. Limited number of working mental health professionals are bound to be overloaded in providing services to many ill people. So, less attention has been there to furnish medical literature and to prepare local situation based books in this direction. We come across few author writing on mental health and illness in Nepal. Dr. Dhana Ratna Shakya has stood up exceptional in this regard. His book 'Suicide and Mental illness: Our Responsibility' has proved its value.<sup>4</sup> Currently, another book by this author "Mental Health and Mental Illness: Our Responsibility" has come out. In the pretext of scarce resources and books regarding mental health and illness, Dr. Shakya's this book will, I am sure bridge the gap, both for clinicians and lay people.

Dr. Shakya is currently working in the post of Associate professor of Psychiatry in B P Koirala Institute of health sciences, Dharan, Nepal. When even medical professionals hesitate to talk and discuss psychiatric issues, I remember him being referred among colleagues for open and comprehensive dialogue since our residency. Personally, I came to know the author in BPKIHS as my colleague during MD residency since 2003 AD. Besides the fame for his dedication to patient service, teaching and research, I found him always concerned for

adding to medical literature. He has always been inspiring to me as a teacher, friend, and researcher; and off course a tireless writer on mental health issues. I have also gone through various other books on different public health problems (cardiovascular, ear, skin, child health, breast, dental health, hepatitis B) written by him for lay people as client counseling series. His constant concern for common people's health and awareness for that has encouraged also me. We professionals need to share our experience, knowledge and idea with different sectors of society for the improvement of health. And, I am impressed with his ability to express technically complex and complicated facts in simple and comprehensive language.

This book "Mental Health and Mental Illness: Our Responsibility" has been published as a reference book for medical students and non psychiatrist medical professionals and as the tenth of his client counseling series. With about 325 pages, the attractive color cover and 40 chapters, the author has ably covered extensively on mental health and mental illness. The chapters on Nepalese context are additional ones difficult to get in other books. As he is known for, he has written the texts of this book in simple, comprehensive and succinct language.

As an Internist involved in academia, I found this book as a boon for: Under-graduate (UG) students, Post graduate (PG) residents of various medical programs (MBBS, BDS, MD, MS, MSc), nursing (PCL, BSc, MSc) and other health science students (BPh, MPh) including non mental health professionals. Since written in Nepalese language, as the author stated it would be useful to patients, their family and all lay people interested to learn about mental health and mental illness. Besides providing

essential information on the topics, this book well describes the responsibilities of concerned sides and strategies to bear them. Slightly different to his previous books (primarily written for patients and family), this book primarily means to teach medical students and non-psychiatrist medical professionals their responsibility for promotion of mental health and for the management of mental illness. Mental illness is common affecting all corners of society; all are vulnerable to mental illness at some point of their life.<sup>1,2</sup> So, this is the book for all, at least once to read. I strongly believe that this book will help people to prevent, timely recognize, and treat mental illness and to promote mental health. Considering the quality of book and paper, this book is worth paying its price (of only Rs. 350).

At last, I wish him a success in his future endeavors. I hope we will get opportunity to read more and more of other works by Dr. Shakya.

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## Review

## Calcium supplementation, Osteoporosis & Cardiovascular disease

**Christian Meier, Marius E. Kraenzlin**

Division of Endocrinology, Diabetes and Metabolism, University Hospital, Basel, Switzerland

### Summary

Adequate intakes of calcium and vitamin D are essential preventive strategies and essential parts of any therapeutic regimen for osteoporosis. However, calcium supplementation is not without controversy and benefits on skeletal health need to be balanced against potential risks on cardiovascular disease. The published data so far suggest a potential detrimental effect of calcium supplement on cardiovascular health (i.e. myocardial infarction) although further prospective studies are needed to clarify the gradient of risk. Since food sources of calcium produce similar benefits on bone density as supplements and dietary calcium intake does not seem to be related with adverse cardiovascular effects, calcium intake from nutritional sources needs to be enforced. In patients with low calcium intake supplements are warranted aiming for a total calcium intake of 800 to 1000 mg/d together with adequate vitamin D replacement. Nevertheless we should keep in mind that for significant reduction in fracture risk, pharmacological treatment is mandatory in patients at risk of fractures irrespective of calcium and vitamin D supplementation.

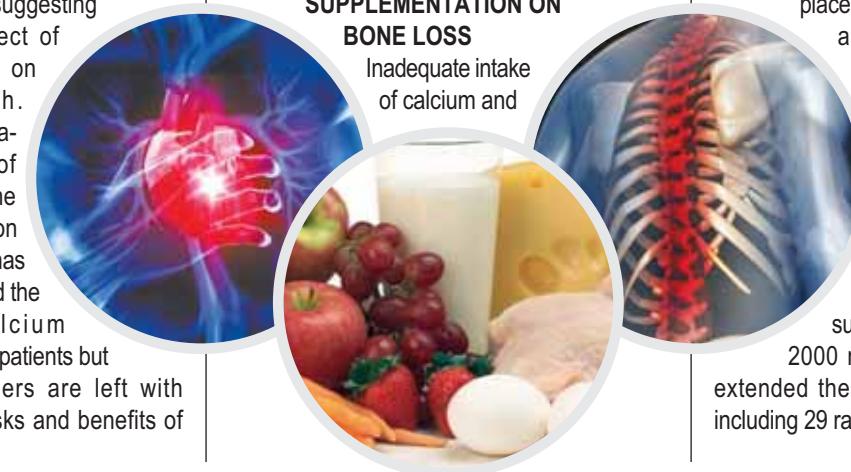
**Key words:** calcium; osteoporosis; fracture; cardiovascular disease; coronary heart disease

### INTRODUCTION

Osteoporosis is a worldwide health issue. It is anticipated that the number of affected individuals, and thereby costs to health care systems, will increase substantially with further aging of the population. Of all the preventive strategies for age-related bone loss and osteoporotic fractures adequate calcium intake is the simplest and least expensive. However, calcium supplementation is not without controversy. In contrast to its effect in maintaining bone mineral density (BMD) in adults its anti-fracture efficacy remains unsettled. Furthermore, controversy has been fuelled after the publication of studies suggesting a potential negative effect of calcium supplementation on cardiovascular health. Specifically, a recent meta-analysis on the effect of calcium supplements on the risk of myocardial infarction and cardiovascular events has questioned the need for and the safety of daily calcium supplementation. Not only patients but also health care providers are left with uncertainties about the risks and benefits of

calcium supplementation. In this review we will briefly summarize the effects of calcium supplementation on the skeletal and cardiovascular system and conclude with practical recommendations for the care of patients at risk for osteoporotic fractures. As several articles recently reviewed the influence of vitamin D on skeletal and non-skeletal endpoints, we will focus largely on the potential benefits and risks of calcium supplementation.

### CALCIUM SUPPLEMENTATION AND SKELETAL HEALTH EFFECTS OF CALCIUM SUPPLEMENTATION ON BONE LOSS



Inadequate intake of calcium and

vitamin D results in reduced calcium absorption with secondary hyperparathyroidism and consecutive bone loss. As bone loss is a strong predictor of fracture calcium supplementation combined with vitamin D has become one of the most widely accepted strategies in primary and secondary prevention of osteoporosis. Several studies have shown the effectiveness of calcium supplementation in slowing or stopping bone loss. In a meta-analysis by Shea et al. the effect of calcium on bone density has been confirmed in postmenopausal women. In this study including 15 trials (1806 patients) the authors found calcium to be more effective than placebo in reducing rates of bone loss after two or more years of treatment, specifically for secondary prevention. Notably, the mean total calcium intake in the calcium trials was mostly above 1000 mg/day (with a dietary calcium intake of 408 to 879 mg/d and additional calcium supplementation between 500 and 2000 mg/d). A recent meta-analysis extended these findings in a larger cohort including 29 randomized trials (63897 patients)

## Case Study

## A Case of Recurrent Infection Caused by a Pancreaticoduodenal Fistula Associated with a Pancreatic Arteriovenous Malformation

Seon-Young Park, Kyoung-Won Yoon, Chang-Hwan Park, Tae-Jin Seo, Hae-Kyung Chung, Ho-Sung Rew, Sung-Beom Cho, Wan-Sik Lee, Hyeun Soo Kim, Sung Kyu Choi, and Jong Sun Rew  
Department of Internal Medicine, Chonnam National University Hospital,  
Chonnam National University Medical School, Gwangju, Korea

### Abstract

Although arteriovenous malformations (AVM) occur frequently in digestive organs, pancreatic AVM is rare. The clinical symptoms of pancreatic AVM are variable and include gastrointestinal bleeding, abdominal pain, jaundice, portal hypertension, pancreatitis, and duodenal ulcer. However, choledochoduodenal or pancreaticoduodenal fistulas complicated with ascending infection and pancreatitis is extremely rare. Herein, we report a case of pancreaticoduodenal fistula associated with a pancreatic AVM that induced recurrent anemia and ascending infection.

**Keywords:** Pancreatic arteriovenous malformation, Pancreaticoduodenal fistula, Infection

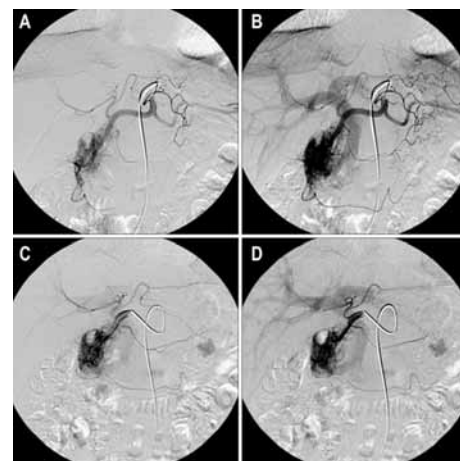
### INTRODUCTION

Arteriovenous malformation (AVM) probably occurs from loss of the regulatory sphincter function of the arteriolarcapillary junction which results in overflow of the arterial blood into the capillaries and venules, producing an arteriovenous shunt. Pancreatic AVM is a rare disease which can be complicated with abdominal pain, gastrointestinal bleeding, portal hypertension, and duodenal ulcer. However, formation of the pancreaticoduodenal fistula by pancreatic AVM is extremely rare. Herein, we report a case of pancreaticoduodenal fistula associated with pancreatic AVM which induced recurrent anemia and ascending infection.

### CASE REPORT

A 58-year-old man was admitted to Chonnam National University Hospital with recurrent fever and epigastric pain for 2 months. Two years ago, the patient visited for exertional dyspnea and he was diagnosed as iron deficiency anemia with pancreatic arteriovenous malformation communicating gastroduodenal artery and pancreaticoduodenal artery with superior mesenteric vein (Fig. 1). Since then he experienced recurrent anemia and he took oral iron preparations occasionally. One month ago, he visited again for fever and epigastric pain. The body temperature was 38.2. Laboratory investigation revealed leukocyte 12,900/mm<sup>3</sup> (neutrophil 79.5%), hemoglobin 14.1 g/dL, platelet 239,000/mm<sup>3</sup>. The blood chemistry were protein 6.1 g/dL, albumin 3.2 g/dL, AST

127 U/L, ALT 96 U/L, alkaline phosphatase 145 U/L, total bilirubin 1.1 mg/dL, gamma glutamyl transpeptidase 190 U/L, amylase 85 U/L, lipase 34 U/L, CRP 9.1 mg/dL, prothrombin time 11.8/92.1/1.05 sec/%/INR.



**Fig. 1**  
Angiography. (A) Common hepatic arteriograms demonstrate an abnormal leash of vessels arising from the gastroduodenal artery. (B) Early venous filling of the superior mesenteric vein and portal vein can be seen. (C) Superior mesenteric arteriograms demonstrate an abnormal leash of vessels arising from the superior pancreaticoduodenal artery. (D) Early venous filling of the superior mesenteric vein and portal vein can be seen.

Despite he underwent thorough examinations including computerized tomography (CT) of chest and abdomen, esophagogastroduodenoscopy and colonoscopy, there was no definitive cause of fever. He recovered after 1 week of antibiotics treatment. He had no history of alcohol ingestion. On admission, the patient appeared acutely ill and he complained tenderness in epigastrium. The body temperature was 36.5. Laboratory investigation revealed leukocyte 9,900/mm<sup>3</sup> (neutrophil 75.5%), hemoglobin 12.2 g/dL, platelet 337,000/mm<sup>3</sup>. The blood chemistry were protein 6.8 g/dL, albumin 3.8 g/dL, AST 16 U/L, ALT 22 U/L, alkaline phosphatase 156 U/L, total bilirubin 0.5 mg/dL, gamma glutamyl transpeptidase 94 U/L, amylase 159 U/L, lipase 34 U/L, CRP 2.0 mg/dL, prothrombin time 11.5/96/1.03 sec/%/INR and the urinary analysis was within normal limit.

The chest X-ray was within normal limit. Abdominal CT showed abnormally dilated vessels which abutted with descending duodenum and communicated with gastroduodenal artery and superior mesenteric vein. The head of pancreas was focally enlarged, soft tissue was infiltrated in the peripancreatic fat plane, and air densities in the main pancreatic duct were detected (Fig. 2). In the suspicion of pancreaticoduodenal fistula, endoscopic retrograde cholangiopancreatography was underwent. A fistula hole was detected in the descending

contd. in pg. 10

## etc

## Positive thinking, life's earning

Imaginations, desire and requirements are infinite. They cannot be placed in certain limits. One being fulfilled, hundreds of them come out. Then being fulfilled, hundreds of them come out. Man becomes active to satisfy one of his desires, but the same moment a number of other desires relating to the above grow by themselves. When he finds himself unable to satisfy those desires by his limited sources, he develops a complex of inferiority; he is disappointed and his way of thinking becomes negative.

Desires have been obsessing the mind even of great scholars, learned sages and saints. Desires perturb even those who have adopted the monastic order. At times it is observed that the non-satisfaction of desires compels one into the monastic order. The desires in their unconscious mind go on making a tussle. Overcoming this situation is possible only when there is a coherence in the way of thinking and the style of working.

God has provided common facilities to all human beings. Man has created a disorder in that provision. These people can be placed in these classes:

**First :** Those in this class take God as a merciless one, who goes on putting in troubles and never the pleaseres. Always perturbed with this opinion such people remain distressed all the time, throughout their lives.

**Second :** The people in this class opine that God has provided both pleaseres and pains which are the invariable parts of life. Being apart from these is not possible. Hence, when in a pleasant state, they feel happy and when in a miserable state, they feel unhappy. They lead their lives with laughters in pleasant state and with tears in miserable state.

**Third :** The ones in the class say how kind God is. We do not deserve this much pleasure and happiness, yet he has kindly provided all this.

The pleasures provided are so large in number that they overflow my bag. With this idea they remain happy always. Facilities are similar, place is common, situations are the same, quantity is equal, but the way of thinking is different. And this way of thinking brings a great variety in the experience of pains and pleasures.

Experience of pleaseres and performance of pious duties can be done only by whose thinking is positive. For such a positive thinking, sweetness is needed in our behavior, activities and speech. A quotation from the Atharva veda: 'Everybody loves them who have sweetness in their behaviour, speech and activities. Only those who are sweet by nature and who know general etiquette can perform pious duties. Your deeds also, therefore, should be like those of great men. Good behaviour is self styled, whether it is for the human beings or for the animals or birds.'

Behaviour speaks of itself. The virtues are judged by that much. How beautiful are these words: 'Man is judged by his virtues, the virtues are judged by his knowledge, the knowledge is judged by his graceful behavior and the graceful behavior is judged by his pleasing nature, trying to keep everyone happy.'

"The medicinal things be sweet, the sky, the waters and the space be sweet, the lord of the land be sweet, and let us also, likewise, be sweet."

'Our behavior with others should be like the behavior which we expect from them.'

It is the behavior which shows how and when animal instinct creeps into human beings and human instinct into animal beings. Let us be optimistic throughout our life, so long as our problems remain to be solved. Success will surely come forth. Barely money dose not solve every problem; alongwith money, will power also is needed.

A millionaire man attended a discourse. At the end of the discourse when he stood up in rush, a pickpocket emptied his pocket. He became sad. The Svamiji asked the reason behind his sadness.

'My pocket has been emptied.'  
'How many rupees have been stolen?'  
'Something between ten and twelve hundred'  
'Why would you, a millionaire, be worrying like this?'

'O lord, I cannot afford a loss; I feel happy with the income, whatever the amount. The loss has loosened my will power and I am now disappointed.'

How dependent has the man become? He has taken the thing as an object which actually is a means. He has started depending upon the thing which should have depended upon him. He desired the things to be his slave and he himself has turned slave to the things. Why and how has this come to be? Just for the way of thinking so far as the positivity of thinking is concerned. We remember this stanza of the national poet 'Dinkar'.

"The trees of iron will grow green, you just of on singing the song of love. This earth will certainly be wet, you just go on shedding tears. Lamentations and cries may fill in the space however densely, skeletons may pile up in heaps, the globe may be paved up with skulls, but the load of the sound of hope will have to be afforded by the breeze. For the living dreams, the way will have to be given by the dead.'

Life brings such moments for man when he loses all the hope at one. Then he must accept the authority of penances:

"Tranquillization of mind, gracefulness, silence, self control and purity of emotion are together called the mental penance."

This way of thinking supports the positivity which is most essential for a progressive life.

## News



## Traffic Pollution May Raise Short-Term Heart Attack Risk

WEDNESDAY, Sept. 21 (HealthDay News) -- Exposure to high levels of traffic-related air pollution appears to temporarily boost the risk for experiencing a heart attack, new British research suggests.

However, the apparent elevation in risk is short-lived, the study team noted, lasting for only one to six hours following exposure and dissipating entirely thereafter.

What's more, air pollution exposure may not bump up overall cardiac risk as much as fast-track it, increasing the chances that an individual already facing a probable heart attack threat will experience it slightly sooner than otherwise.

The finding, published in the Sept. 20 issue of the BMJ, is the work of a team led by Krishnan Bhaskaran, a lecturer in statistical epidemiology in the department of non-communicable diseases epidemiology at the London School of Hygiene and Tropical Medicine.

To assess the potential impact of air pollution on heart health, the investigators analyzed the cases of just over 79,000 patients in England and Wales who experienced a heart attack between 2003 and 2006 in one of 15 different relatively large (London) and small (Cardiff) urban settings.

After noting the hour of each patient's heart attack, the team analyzed relevant time-sensitive regional air pollution data regarding pollutant particles (PM10), carbon monoxide, sulfur dioxide, ozone and nitrogen dioxide levels that had been gleaned from the U.K. National Air Quality Archive. Nitrogen dioxide and PM10, Bhaskaran and colleagues specifically noted, are primarily the product of motor vehicles in urban settings. As such, the team attributed elevations of each to be

an indicator of exposure to traffic-related pollution. After adjusting for various factors such as air temperature, humidity, general flu and viral conditions, holiday occurrences and specific days of the week, the team found that higher ambient levels of both PM10 and nitrogen dioxide did appear to be linked to a short-term rise in the risk of experiencing a heart attack.

But although they looked at heart attack risk for up to 72 hours following air pollution exposure, there appeared to be no increase in risk outside of the one- to six-hour range.

Despite that observation, the team noted in a journal news release that although there may be "limited potential for reducing the overall burden of myocardial infarction through reductions in pollution alone . . . that should not undermine calls for action on air pollution, which has well-established associations with broader health outcomes including overall, respiratory and cardiovascular mortality."

Commenting on the study, Dr. Bertram Pitt, a professor of medicine emeritus at the University of Michigan School of Medicine in Ann Arbor, described the findings as "unsurprising," but "credible."

"There's lots of data that shows that air pollution is a tremendous cardiac risk," he noted. "So if you are part of a vulnerable population and you go out into traffic or something like that and it takes you beyond your threshold you might very well have a heart attack. And once you do, the damage that ensues can go on forever," Pitt explained. "So, the answer is of course to decrease air pollution. Which is, of course, nothing that we haven't heard before. But this is one more indication telling us to do whatever we can do to reduce air pollution exposure," Pitt said. ■

## Quitting Smoking Could Give Memory a Boost

WEDNESDAY, Sept. 21 (HealthDay News) -- In addition to the many known health benefits of quitting smoking, researchers have now discovered another good reason to kick the habit -- it may help improve your everyday memory.

The team at Northumbria University in Newcastle, the United Kingdom, gave memory tests to 27 smokers, 18 former-smokers and 24 never-smokers. The test involved remembering to do assigned tasks at different locations on the university campus.

Smokers remembered only 59% of the tasks, compared with 74% for former-smokers and 81% for never-smokers.

"We already know that giving up smoking has huge health benefits for the body but this study also shows how stopping smoking can have . . . benefits for cognitive [brain] function, too," researcher Tom Heffernan, of the Collaboration for Drug and Alcohol Research Group at Northumbria, said in a university news release. He said this is the first study to examine the effect that quitting smoking has on memory.

"Given that there are up to 10 million smokers in the U.K. and as many as 45 million in the United States, it's important to understand the effects smoking has on everyday cognitive function -- of which prospective memory is an excellent example," Heffernan said. ■

## Abstracts

### Rates of remission/euthymia with **QUETIAPINE MONOTHERAPY** compared with placebo in patients with acute mania

Source - Journal of Affective Disorders, Volume 100, Supplement 1, 2007.  
Terence A. Ketter, Martin Jones, Björn Paulsson

#### OBJECTIVE

To evaluate the effects of quetiapine monotherapy compared with placebo on acute (3-week) and more sustained (12-week) rates of response and remission/euthymia in bipolar disorder patients with acute mania.

#### METHODS

Two similar 12-week multicenter, double-blind, placebo-controlled, parallel-group studies were conducted, with an a priori decision to combine the data and analyze response and remission rates. Response was measured as a decrease of at least 50% in Young Mania Rating Scale (YMRS) scores from baseline to Day 21 and Day 84. Five remission/euthymia criteria were employed to determine efficacy at Day 21 and Day 84: (i) YMRS score = 12; (ii) YMRS score = 12 and Montgomery-Asberg Depression Rating Scale (MADRS) score = 10; (iii) YMRS

score = 12 and MADRS score = 8; (iv) YMRS score = 8; and (v) YMRS score = 8 plus a score = 2 for the YMRS core items of Irritability, Speech, Content, and Disruptive/Aggressive Behavior.

#### RESULTS

Patients treated with quetiapine (n = 208) and placebo (n = 195) had mean YMRS scores at entry of 33.3 ± 6.3 and 33.5 ± 6.7, respectively. Significantly higher response rates were observed with quetiapine compared with placebo, at Days 21 (48.1% versus 31.3%; p < 0.001) and 84 (66.8% versus 40.0%; p < 0.001). At Day 21, remission/euthymia rates with quetiapine monotherapy versus placebo were: 37.5% versus 23.1% (YMRS = 12), 35.6% versus 21.5% (YMRS = 12 + MADRS = 10), 35.1% versus 20.0% (YMRS = 12 + MADRS = 8), 25.0% versus 14.4% (YMRS = 8), and

21.6% versus 14.4% (YMRS = 8 plus core items = 2) (p < 0.01 for all comparisons except YMRS = 8 plus core items = 2: p = 0.06). By Day 84, these had increased to: 65.4% versus 35.9% (YMRS = 12), 60.1% versus 30.8% (YMRS = 12 + MADRS = 10), 58.7% versus 29.7% (YMRS = 12 + MADRS = 8), 60.1% versus 30.3% (YMRS = 8), and 56.7% versus 29.7% (YMRS = 8 plus core items = 2) (p < 0.001 for all comparisons). The average daily dose of quetiapine in responders was 575 mg/day at Day 21 and 598 mg/day at Day 84. Quetiapine was generally well tolerated. Conclusions

Quetiapine was associated with significantly higher response and remission/euthymia rates compared with placebo with most criteria used, in patients with acute mania at the end of both 3 and 12 weeks. ■

Source: Ibrahim Card Med J 2011;1(1):27-32

### A Comparative Study of Efficacy and Adverse Effects Between Alfuzosin and Tamsulosin in the Treatment of Benign Prostatic Hyperplasia

**Background & Objective:** Before the advent of medical therapy for BPH causing lower urinary tract obstructive symptoms (LUTS), the treatment was primarily a surgical one with higher morbidities and inconsistent outcomes. With the advent of alpha-antagonists, the face of BPH treatment took a new look. Currently majority of the medical managements of BPH includes  $\alpha$ -1 adrenoceptor antagonists. Of them tamsulosin and alfuzosin are commonly used with different efficacies and side-effects being claimed. The present study was done to compare the safety and efficacy of tamsulosin and alfuzosin in the treatment LUTS suggestive of BPH.

**Patients & Methods:** The present prospective randomised clinical trial was conducted at the Department of Urology, Chittagong Medical College Hospital to compare the outcomes of tamsulosin and alfuzosin in the treatment of LUTS suggestive of benign hyperplasia of prostate (BPH). A total of 80 subjects selected for the study were randomly assigned to alfuzosin (n = 40) and tamsulosin (n = 40) groups. Alfuzosin 10 mg and tamsulosin 0.4 mg as once-daily doses were given to the patients of respective groups for consecutive 12 weeks with no initial dose titration. Of the 80 patients, 67 patients - 36 in the alfuzosin and 31 in the tamsulosin groups finally completed the treatment as per protocol. The outcome was evaluated at the end of month 1 and 2 in terms of IPSS, Qmax, PVR and complications encountered.

**Result:** The mean ages of alfuzosin and tamsulosin groups were 66.5 and 62.3 years respectively. The mean IPSS, Qmax and PVR at baseline were homogeneously distributed between groups (p = 0.217, p = 0.394, p = 0.174). At the endpoint, IPSS and PVR were significantly less in tamsulosin group than those in alfuzosin group (p = 0.015 and p = 0.038 respectively). The Qmax responded well in both the groups with no significant inter-group difference (p = 0.453). The alfuzosin group had a significantly higher postural hypotension, dizziness, asthenia and GI tract upset compared to the tamsulosin group. However, tachycardia, headache and rhinitis were more common in the tamsulosin group than those in the alfuzosin group. At the endpoint alfuzosin group experienced a significant reduction in blood pressure compared to their baseline figures (p < 0.001). In the tamsulosin group the diastolic blood pressure decreased slightly in the 1st month of treatment, but they again stabilized during 2nd month of treatment, while systolic blood pressure did not experience any change. Both treatment groups exhibited an improvement of Qmax 3 ml/s from baseline. However, improvement of total symptom score in terms of IPSS 25% from baseline was significantly higher in the alfuzosin group (88.9%) than that in the tamsulosin group (48.9%) (p < 0.001).

**Conclusion:** Tamsulosin is a better than alfuzosin for patients with LUTS suggestive of BPH who are normotensive or hypertensive but well-controlled with conventional antihypertensives.

**Key words:** Tamsulosin, alfuzosin, lower urinary tract symptoms & benign prostatic hyperplasia. ■

## Biotech

# Contact LENS

Source - wikipedia

A contact lens (also known simply as contacts for a pair) is a corrective, cosmetic, or therapeutic lens usually placed on the cornea of the eye. Leonardo da Vinci is credited with describing and sketching the first ideas for contact lenses in 1508, but it was more than 300 years later before contact lenses were actually fabricated and worn on the eye.

Rigid ones  
were

contact lenses are less affected by wet weather, do not steam up, and provide a wider field of vision. They are more suitable for a number of sporting activities.



Additionally, ophthalmological conditions such as keratoconus and aniseikonia may not be accurately corrected with glasses.

## HISTORY

In 1888, Adolf Fick was the first to successfully fit contact lenses, which were made from blown glass.

Leonardo Da Vinci is frequently credited with introducing the idea of contact lenses in his 1508 Codex of the eye, Manual D, where he described a method of directly altering corneal power by submerging the eye in a bowl of water. Leonardo, however, did not suggest his idea be used for correcting vision—he was more interested in learning about the mechanisms of accommodation of the eye.

René Descartes proposed another idea in 1636, in which a glass tube filled with liquid is placed in direct contact with the cornea. The protruding end was to be composed of clear glass, shaped to correct vision; however the idea was impracticable, since it would make blinking impossible.

In 1801, while conducting experiments concerning the mechanisms of accommodation, scientist Thomas Young constructed a liquid-filled "eyecup" which could be considered a predecessor to the contact lens. On the eyecup's base, Young fitted a microscope eyepiece.

People choose to wear contact lenses for many reasons, often due to their appearance and practicality. When compared with spectacles,

However, like Leonardo's, Young's device was not intended to correct refraction errors. Sir John Herschel, in a footnote of the 1845 edition of the Encyclopedia Metropolitana, posed two ideas for the visual correction: the first "a spherical capsule of glass filled with animal jelly", and "a mould of the cornea" which could be impressed on "some sort of transparent medium". Though Herschel reportedly never tested these ideas, they were both later advanced by several independent inventors such as Hungarian Dr. Dallos (1929), who perfected a method of making molds from living eyes. This enabled the manufacture of lenses that, for the first time, conformed to the actual shape of the eye.

It was not until 1887 that a German glassblower, F.E. Muller, produced the first eye covering to be seen through and tolerated. In 1887, the German ophthalmologist Adolf Gaston Eugen Fick constructed and fitted the first successful contact lens. While working in Zürich, he described fabricating afocal scleral contact shells, which rested on the less sensitive rim of tissue around the cornea, and experimentally fitting them: initially on rabbits, then on himself, and lastly on a small group of volunteers. These lenses were made from heavy blown glass and were 18–21mm in diameter. Fick filled the empty space between cornea/callosity and glass with a dextrose solution. He published his work, "Contactbrille", in the journal Archiv für Augenheilkunde in March 1888.

Fick's lens was large, unwieldy, and could only be worn for a couple of hours at a time. August Müller in Kiel, Germany, corrected his own severe myopia with a more convenient glass-blown scleral contact lens of his own manufacture in 1888.

Also in 1887, Louis J. Girard invented a similar scleral form of contact lens. Glass-blown scleral lenses remained the only form of contact lens until the 1930s when polymethyl methacrylate (PMMA or Perspex/Plexiglas) was developed,

contd. in pg. 11



## Patients Care

## Why I Give My Cell Phone Number to My Patients

You may gain more rapport without losing sleep.

Winthrop C. Dillaway, MD  
Fam Pract Manag. 2009 Jul-Aug;16(4):24-25.



Nearly five years ago I learned that the cell phone can be a surprisingly powerful tool for family physicians. I had just assumed the role of medical director at a student health center when I saw a medical student with a sexually transmitted infection (STI) that I thought warranted a second opinion. The chairman of the Department of Pediatric and Adolescent Medicine, whom I had not met, was the local expert on STIs. I called him, and he offered to work the patient in right away. An hour later he called me back and said, "I gave your patient an antibiotic and an appointment for next week. I also gave him my cell phone number and told him to call me tomorrow if he is not better, or if he is worried." That physician's availability and accessibility to both me and my patient so impressed and inspired me that I began giving my cell phone number to anxious patients.

### TAKING A CHANCE

I gave out my number tentatively at first, but over time I have become comfortable doing it. I simply write it on a prescription pad or a business card and hand it to the patient as part of the planning at the conclusion of the visit. I make it clear that they have my permission to call anytime after hours if they are worried about their symptoms. Intuitively, physicians do not want to give out their personal phone numbers to patients. We expect that too many patients would be intrusive and inappropriate. I find the opposite; only once or twice a month do I get after-hours phone calls on my cell phone. Only one patient, one time, blatantly abused this privilege. Otherwise, these calls have always been appropriate. My experience has been so positive that I now give out my cell phone number three or four times per day.

### REASSURING THE WORRIED PATIENT

I've found that giving out my cell phone number offers patients as much healing and comfort as any other part of the treatment plan. Most patients come to their office visit worried. Patients need, want and deserve reassurance. Giving my patients direct access to me by phone

sends at least two important messages. It tells them that I am truly a partner in their care. It also demonstrates that I am confident in our treatment plan, as if to say, "I am sure you will be OK, but if you need me, you may call me, even in the middle of the night."

### EMPOWERING THE PHYSICIAN

Sharing a personal phone number with our patients is empowering for us. We want and enjoy rapport with our patients. Enabling them to contact us directly increases our bond and promotes understanding and trust, which is professionally gratifying. We instinctively protect professional boundaries to manage our stress and maintain a healthy work-life balance. While some would think that giving out your cell phone number crosses these boundaries, I have found that it decreases my stress to know that my sick and worried patients can easily reach me if needed. Furthermore, it helps to reduce liability risk. This is why I note in the chart the date and time I give out my cell phone number. I also keep at hand a formatted note pad and use it to jot down conversations that happen after hours. I file these notes in patients' records.

### SKIPPING THE ANSWERING SERVICE

Relying on my cell phone rather than an answering service has been a positive change. Answering services tend to be impersonal and inconsistent because the calls are triaged and the on-call physician may not know the patient's problems and concerns. I do understand that the answering service is a useful buffer for the tired, overworked physician, but the system is not completely reassuring to either the physician or the patient.

### STUDYING HOW PATIENTS RESPOND

A study conducted at the Hospital of the University of Pennsylvania<sup>1</sup> reinforces two findings of my own: First, giving out your cell phone number fosters the patient's perception that the physician is more caring. Second, patients generally demonstrate restraint and respect for its appropriate use. In a conversation

with one of the authors of the study, Kingsley Chin, MD, a surgeon who is now in private practice, I asked if he still gives out his number to patients and if he would recommend this to other physicians. His response was an enthusiastic "yes" to both questions. He, too, emphasized that his patients felt less anxiety knowing that they could call him. He has never had an unnecessary call and says the majority of patients apologize when they call him and express gratitude for the privilege.

### WILL IT WORK FOR YOU?

Each physician's patient population, practice style and personal life is unique, and the decision to give out your cell phone number must be balanced with a number of considerations. There isn't a standard policy for cell phone use for physicians to follow. It will likely work for most physicians and their patients, but for others it won't. For example, I am in the process of changing job assignments and soon will be giving family medicine care to a population of patients with mental illness. A psychiatrist colleague has advised me against giving out my cell phone number to these patients because of boundary and transference problems, a point of view I will strongly consider. For physicians who would like to try this approach but aren't certain that their patients will respond appropriately, I would suggest trying it with one or two patients, then gradually adding more. You can always abandon it if it turns out not to work.

My STI consultant and I agree that it is physicians who have the most to gain from sharing their cell phone numbers with their patients. The reduction in liability risk, improved quality of care and increased rapport with our patients has enhanced our satisfaction with practice.

I hope more physicians will try it, and I invite those who do to send a letter to the editor of FPM to inform others about how it worked for them. ■

contd. from pg. 6

A is needed by the body for many things. It helps the body to produce and maintain healthy membranes, like the synovial membrane found in joints. It's also necessary for the proper function of the immune system.

Why it helps-When vitamin A levels are low, we may wind up with an immune system that is weak, leaving us more susceptible to infection, or one that is overactive, leading to auto-immune disease. Adequate amounts of vitamin A in the diet may help to restore the healthy function of the immune system.

#### Food reach in vitamin A/beta-carotene are-

- sweet potatoes,
- carrots,
- calf liver,
- kale,
- winter squash,
- collard greens,
- chard,
- cantaloupe,
- mustard greens,
- romaine lettuce,
- spinach, parsley,
- cayenne pepper,
- peppermint leaves,
- Brussels sprouts,
- tomatoes, broccoli,
- asparagus, and
- apricots.

6. Zinc- Zinc is an important component of the nutritional package for rheumatoid arthritis. Several studies have shown that people who have rheumatoid arthritis have low blood levels of zinc, often associated with high levels of inflammatory biochemicals in the blood.

Why it helps- Our bodies use zinc, along with copper, to make an inflammation-fighting enzyme called superoxide dismutase. This enzyme is found in inflamed joints, where it

neutralizes free radicals

#### Food reach in Zinc are-

- Oysters
- Toasted Wheat Germ
- Veal Liver
- Sesame Seeds and Tahini (Sesame Butter)
- Low Fat Roast Beef
- Roasted Pumpkin and Squash Seeds
- Dried Watermelon Seeds
- Dark Chocolate and Cocoa Powder
- Lamb (Mutton)
- Peanuts

7. Calcium and Vitamin D- People with rheumatoid arthritis tend to have bone loss as a result of their condition and are at an increased risk of ending up with osteoporosis. This may be a result of the excessive inflammation or it may be a result of certain anti-inflammatory medications. Whatever the cause, research has shown that getting adequate amounts of calcium and vitamin D in the diet can help to prevent or even reverse this bone loss.

Why it helps- Calcium and vitamin D work together as a team to build healthy and strong bones. Increasing your intake of both of these nutrients may protect you from the debilitating long-term consequences of this bone loss.

#### Food reach in Calcium and Vit. D are

- Mustard greens,
- collard greens,
- turnip greens and spinach
- Shrimp and fortified milk ( Vit.D)

#### FOODS TO AVOID

There are many foods to avoid with arthritis, including caffeine, sugar, carbonated beverages, and foods high in saturated fats. Certain foods should be avoided because they can complicate the symptoms of arthritis, causing inflammation of the joints and reduced calcium absorption. Sugar and caffeine are the main culprits for arthritis sufferers.. Gluten and products containing refined flour may also cause

inflammation and pain to occur. Products containing solanine prevent the body from having an immune response to inflammation. The chemical solanine is found in potatoes, peppers, tomatoes, eggplant, and tobacco, and many arthritis sufferers find that a type of allergic reaction to these vegetables will cause his or her arthritis to flare up.

Other people suggest that fatty, red meats and dairy products, such as eggs and milk, are foods to avoid with arthritis. Acidic foods, such as oranges, grapefruit, and grapes should be avoided altogether or intake should be reduced. Vegetable oil and margarine should be used sparingly when preparing meals, and the amount of fried foods consumed should also be limited.

#### GENERAL RECOMMENDATIONS

General dietary recommendations for a person with arthritis include:

- Eat a well-balanced diet. This will help to maintain general good health, and a healthy weight.
- Avoid crash dieting or fasting.
- Increase dietary calcium to reduce the risk of osteoporosis in later life.
- Drink plenty of non-alcoholic fluids.
- Keep your weight within the normal range. Excess bodyweight increases the stress on joints, especially weight-bearing joints such as the knee and hips.

Tips for managing arthritis and diet- If you think a particular food may aggravate your arthritis, it can help to keep a diary of your food intake and symptoms. After a month, you may have some idea about which food could be provoking symptoms. Discuss these results with your doctor.

Don't cut whole food groups from your diet – for example, all dairy products – without talking to your doctor, as you may miss out on important vitamins and minerals. ■

## Clinical Review

J Headache Pain. 2011 August; 12(4): 405–409.

# Migraine & restless legs syndrome: is there an association?

Paul R. Cannon and Andrew J. Larner

Walton Centre for Neurology and Neurosurgery, Lower Lane, Fazakerley, Liverpool, L9 7LJ UK

#### Abstract

Occasional clinical reports have suggested a link between migraine and restless legs syndrome. We undertook a systematic review of the evidence, which supports this association, and consider possible shared pathogenic mechanisms and the implications for current clinical practice.

**Keywords:** Migraine, Restless legs syndrome, Comorbidity, Dopamine, Sleep



#### Introduction

Comorbidity may be defined as the association of two diseases in individuals at a frequency greater than that expected statistically by chance. Migraine may be complicated by the presence of a number of comorbidities (Table 1). These comorbid conditions may augment the perceived severity of migrainous symptoms and/or pose additional challenges for effective patient management. It is therefore essential that any disease co-existing with migraine is identified and managed appropriately.

Table 1  
Recognised comorbidities of migraine  
Stroke  
Subclinical vascular brain lesions  
Coronary artery disease  
Patent foramen ovale  
Affective disorders: depression, anxiety  
Epilepsy  
Fibromyalgia  
Possible comorbid conditions  
Irritable bowel syndrome  
Coeliac disease  
Chronic fatigue syndrome  
Raynaud's phenomenon  
Asthma  
Narcolepsy  
Sleep deprivation

Restless legs syndrome (RLS), also known as Ekbom's syndrome, is a condition characterised by uncomfortable and sometimes painful sensory disturbances in the lower limbs producing an irresistible urge to move in order to relieve the sensation, particularly at rest and at night. RLS was not until recent times considered a possible migraine comorbidity.

Indeed, two recently published texts devoted to RLS reflect the uncertainty: Chaudhuri et al. stated that RLS is seen in increased frequency in migraine cases, whereas Hening et al. did not even mention migraine in their extensive (and contemporaneous) monograph. Since RLS is a potentially treatable condition, it is important to clarify whether it is comorbid with migraine. The availability of validated criteria for the diagnosis of RLS, the IRLSSG criteria, might facilitate study of this question. We therefore undertook a review of the available evidence which addresses this issue, and considered possible mechanisms of pathogenic overlap between migraine and RLS.

Method  
The medical databases Ovid, PubMed and NHS Evidence were searched by combining the key terms, migraine or migrain\$ with restless legs syndrome. Electronic searches were supplemented by hand searching the bibliographies of relevant articles. Both authors read the title and abstract of all studies identified by the electronic searches, and agreed on eligibility of the studies identified, the full text of which was read and critically appraised.  
Results  
From the articles retrieved (Table 2), we identified eight studies deemed eligible for inclusion.

Table 2  
Articles retrieved by search strategy  
Database Results obtained  
Migraine or migrain\$ and restless legs syndrome  
Ovid (Medline) 12  
PubMed 23  
NHS evidence 50

No population-based study of the coincidence of migraine and RLS was identified, but several studies of clinical samples have been reported. Young et al. screened 50 primary headache patients with intractable headache admitted to an outpatient infusion centre using the IRLSSG criteria. They reported that 34% of their patients met RLS criteria, higher than expected considering that the RLS prevalence rate in the general population has traditionally been stated to be between 1 and 10%, although this may be lower in Asian populations. Clearly, this was a small study sample and there was no control group, but the findings have been largely confirmed in subsequent studies.

Rhode et al. performed a case control study on 411 patients with migraine with 411 age- and sex-matched control subjects and found that the former had a statistically significant higher lifetime prevalence of RLS than the control group (17.3 vs. 5.6%,  $p < 0.001$ ). It was also noted that migraine patients with RLS tended to be older than those without RLS, in keeping with the epidemiological finding that RLS incidence typically increases with age. In an observational study, d'Onofrio et al. conducted interviews and neurological examinations in 200 patients affected by primary headaches and in 120 age- and sex-matched controls. They reported an increased RLS prevalence in headache patients compared to control subjects (22.4 vs. 8.3%,  $p = 0.002$ ), with a preponderance in patients who suffered from migraine without aura. Sleep disturbances were more frequent in headache patients with RLS (50.0 vs. 32.7%,  $p < 0.001$ ). Chen et al. compared the prevalence of RLS



## Alternative Therapy

# CHANGING DIET CAN HELP WITH ARTHRITIS

Yogesh Shrestha, ( Pharmacist )

If you suffer from arthritis, you may have heard that a specific diet or certain foods can ease your pain, stiffness, and fatigue. Someday, food may be the medicine of choice for those with arthritis and related inflammatory diseases. For now, here's information that may help you separate the facts from the myths about diet and rheumatoid arthritis

## FOODS THAT MAY HELP INCLUDE

1. Omega 3 fatty acids- Fatty acids are a family of special fats that the body needs but can't make for itself, so you have to get them from food.

Why it helps –Once in the body, they collect in cells, where they help form hormone-like substances, called leukotrienes, that put the brakes on inflammation

### Food reach in omega-3 fatty acids are-

- Cold-water fish such as salmon, tuna, mackerel, and trout.
- Nuts and seeds, beans, soy products, green leafy vegetables, and cooking oils such as canola oil.

2. Vitamin C-Deficiency of vitamin C-rich citrus fruits has been known to produce scurvy since 1753, over 250 years ago. One of the chief symptoms of scurvy is profound joint troubles

Why it helps-vitamin C helps form collagen, the protein "glue" that holds cells together. Collagen is especially important in connective tissue to insure healthy ligaments, cartilage, tendons and the joints themselves

### Food reach in vitamin C are-

- Guavas
- Bell peppers
- Dark leafy greens (Mustard greens, garden cress)
- Broccoli, Cauliflower, Brussels Sprouts
- Papayas
- Oranges and Clementines (Tangerines)
- Strawberries



thus helps to remove toxins. Vitamin E, like the nonsteroidal anti-inflammatory drugs used for arthritis, inhibits the prostaglandins that play a role in pain.

### Food reach in Vitamin are

- Wheat germ oil
- Sunflower oil
- Safflower oil
- Nuts and nut oils, like almonds and hazelnuts
- Green leafy vegetables, like lettuce, spinach, turnip, beet, collard, and dandelion greens
- Tomato products
- Pumpkin
- Sweet potato
- Rockfish
- Mangoes
- Asparagus
- Broccoli
- Papayas
- Avocados

4. Selenium-Selenium is a mineral that helps boost the immune system and fight off infection. It is an antioxidant that reduces molecules called free radicals that can damage healthy cells and is therefore useful in fighting the effects of aging.

Why it helps-The body's immune system naturally makes free radicals that can help destroy invading organisms and damaged tissue, but that can also harm healthy tissue. Selenium, as an antioxidant, may help to relieve symptoms of arthritis by controlling levels of free radicals

### Food reach in Selenium are-

- crimini mushrooms,
- cod,
- shrimp,
- salmon,
- snapper,
- yellowfin tuna,
- calf liver.

5. Vitamin A-Low levels of vitamin A are associated with rheumatoid arthritis. Vitamin

3. Vitamin E-Another antioxidant, Vitamin E may be helpful in both the prevention of and the treatment of (pain relief and increased joint mobility) Osteoarthritis. Vitamin E was tested against a NSAID (diclofenac) and was found to be equally as effective. Vitamin E also has many antioxidant properties.

Why it helps-Vitamin E protects against muscle-wasting and is essential in cellular respiration,

contd. in pg. 16

contd. from pg. 12

majority of RLS patients have sleep complaints. Might the sleep disturbance caused by RLS exacerbate migraine and so explain the link between the two conditions? As previously mentioned, two of the epidemiological studies of migraine and RLS found sleep disturbance to be more evident in headache patients with RLS.

Clinical trials have shown that treating RLS with dopamine agonists can enhance sleep quality. However, there are currently no data which address the issue of whether treating RLS can improve the sleep of migraine patients and thus benefit migraine control, albeit that dopamine agonists may provoke premonitory migraine symptoms. Future studies might include a randomised control trial assessing this aspect of migraine management.

## DISCUSSION

Studies in selected patient groups strongly suggest that RLS is more common in migraine patients than in control populations. However, a population-based study, perhaps the most definitive way to establish concurrence, has yet to be reported. It should be noted that certain conditions found to be comorbid with migraine in clinic-based studies were not confirmed as

such in population-based studies (e.g. hypertension).

There are a number of plausible hypotheses, which might explain a link between migraine and RLS. Of these, some have favoured dopaminergic imbalance. However, the opposing effects of dopaminergic agonists (improve RLS, provoke migraine premonitory symptoms) and antagonists (improve migraine, provoke drug-induced akathisia) in the two conditions would seem to negate any simplistic explanation at the level of neurotransmitter release or receptor sensitivity. Central mechanisms rendering the brain more sensitive to sensory stimuli with impaired habituation might be invoked, but precise mechanisms remain elusive. Hence, other explanations of the RLS-migraine link remain viable, of which sleep disturbance, as a consequence of RLS and as a trigger for migraine, remains an attractive possibility.

Whilst knowledge remains incomplete, what should be the pragmatic response to these data at the clinical interface? For example, should migraine patients attending the headache clinic be screened for RLS? Current (2010) guidelines from the British Association for the Study of

Headache (<http://www.bash.org.uk/>) do not mention RLS, far less advocate screening for it. It would certainly be difficult at this point in time to make a robust case for RLS screening in all headache patients, far less for measuring iron indices in all migraine patients. Nevertheless, it may be deemed good practice for clinicians to be vigilant for RLS symptoms in migraine patients, particularly in those with complaints of sleep disturbance or excessive daytime somnolence. Such screening for RLS might be performed with a single question [33]. However, even if a diagnosis of RLS is made, there is currently no evidence that specific RLS treatment will impact on migraine symptoms, indeed these drugs may cause adverse effects. Nonetheless, the possibility that improved sleep quality following treatment of RLS might be associated with improvement in migraine has some face validity.

Clearly more studies are required at both the basic and clinical level in this area to address the many outstanding questions. Trials in which both migraine and RLS symptoms are evaluated concurrently may help to inform clinical practice.

*Congratulations*




**Dr. Sanju Babu Shrestha**

for successfully completing  
**"Hair Transplantation Training"**  
 from Kyungpook National University Hospital,  
 Daegu, South Korea,  
 for the first time in Nepal.

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*Congratulations*



**Prof. (Dr.) Ashok Kumar Banskota**  
 World of Children Health Award Winner

Expressing our joy & pride in your  
 wonderful vision and work towards  
 changing lives of children with disability !

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Your opinions (Please mark ✓)

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Dr's Pen	Poor <input type="checkbox"/>	Fair <input type="checkbox"/>	Good <input type="checkbox"/>	Excellent <input type="checkbox"/>
Clinical review	Poor <input type="checkbox"/>	Fair <input type="checkbox"/>	Good <input type="checkbox"/>	Excellent <input type="checkbox"/>
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Your views regarding The Himalayan Health (THH)

To,  
The Editor  
The Himalayan Health,  
GPO Box: 12928, Kathmandu

# HUMOURS

## The Automated Doctor

One day, Pete complained to his friend, "My elbow really hurts. I guess I should see a doctor." His friend said, "Don't do that. There's a computer at the drug store that can diagnose anything quicker and cheaper than a doctor. Simply put in a sample of your urine, and the computer will diagnose your problem and tell you what you can do about it. It only costs \$10.00.

Pete figured he had nothing to lose, so he filled a jar with a urine sample and went to the drug store. Finding the computer, he poured in the sample and deposited the \$10.00.

The computer started making some noise and various lights started flashing. After a brief pause, out popped a small slip of paper which read:

You have tennis elbow. Soak your arm in warm water, avoid heavy labor. It will be better in two weeks.

That evening while thinking how amazing this new technology was and how it would change medical science forever, he began to wonder if this could be fooled. He decided to give it a try. He mixed together some tap water, a stool sample from his dog, and urine samples from his wife and daughter. He went back to the drug store, located the computer, poured in the sample and deposited the \$10.00.

The machine again made the usual noises, flashed lights, and printed out the following analysis:

Your tap water is too hard.  
Get a water softener.

Your dog has ringworm.  
Bathe him with anti-fungal shampoo.

Your daughter is using cocaine.  
Put her in a rehabilitation clinic.

Your wife is pregnant . . . twin girls.  
They aren't yours.  
Get a lawyer.

And if you don't stop jerking off, your elbow will never get better.

contd. from pg. 1

reporting that calcium supplementation, alone or in combination with vitamin D, is effective in reducing bone loss at the hip and the spine in women and men aged 50 years or older.

After reaching peak bone mass there is an age-related yearly bone loss in both sexes of about 1%, which is accelerated to 2% for up to 14 years in women around the age of menopause. To keep bone loss to a minimum, increased dietary calcium is needed, or calcium supplementation needs to be added in order to maintain a total daily calcium intake of about 1000 mg.

### EFFECTS OF CALCIUM SUPPLEMENTATION ON FRACTURE RISK

In contrast to the effectiveness of calcium supplementation in slowing bone loss, its influence on fracture risk is still a matter of debate. The controversy is in part attributable to the relatively small number of studies that have addressed fracture endpoints. More importantly, the available trials are heterogeneous with respect to the dose and preparation of calcium used, whether calcium is used as monotherapy or in combination with vitamin D, whether patients were adherent to the supplementation regimen, and lastly due to differences in study populations (e.g. age, gender, magnitude of fracture risk, institutionalised versus community-dwelling). According to various studies which used a combined intervention of calcium and vitamin D, fracture risk was reduced in frail elderly populations. In their meta-analysis including 29 randomized trials, Tang et al. reported that calcium supplementation (alone or in combination with vitamin D) is effective in preventing osteoporotic fracture in elderly women and men. The risk of any fracture was reduced over average treatment duration of 3.5 years (RR 0.88, 95%CI 0.83–0.95). Interestingly, the fracture risk reduction was greatest in individuals who were elderly, lived in institutions, had a low body weight, had a low calcium intake or were at high baseline fracture risk. For calcium-only supplementation, a minimum dose of 1200 mg was needed for favourable treatment effect. In a randomized placebo-controlled trial among healthy community-dwelling older men and women, Bischoff-Ferrari et al. showed that four years of supplementation with 1200 mg calcium alone is associated with a reduction in risk of all fractures and minimal trauma fractures.

After supplementation was stopped the benefit of calcium was lost.

Two concerns need further attention. Firstly, as with other medical interventions that need long-term adherence, compliance has been shown to be poor in some studies limiting the beneficial effect of calcium supplementation on fracture risk. A number of studies show no significant benefit when data were analysed using an intention-to-treat approach, but trends toward benefit in per-protocol analyses. Secondly, reduction in total fracture risk does not necessarily imply that risk for specific fracture types, such as hip fractures are also reduced. Reid et al. reanalysed the Tang meta-analysis considering only hip fractures and found a non-significant relative risk reduction associated with calcium use 0.91 (95%CI 0.80–1.04). Subgroup analyses showed that the relative risk of hip fracture was significantly lower for combined supplementation (calcium plus vitamin D; RR 0.84, 95%CI 0.73–0.97) than that for calcium supplementation alone (RR 1.50, 95%CI 1.06–2.12). Furthermore and in accordance with two other trials, calcium supplementation alone was associated with an increased risk of hip fracture. Meta-analysis of these three studies demonstrates a relative risk of hip fracture of 1.50 (95%CI 1.06–2.12) on calcium supplementation alone. In contrast and according to a recent meta-analysis, nutritional calcium intake (such as milk consumption) was not associated with hip fracture risk in women and men.

These findings suggest that calcium supplementation alone without adequate vitamin D intake is not an appropriate preventive strategy to reduce hip fracture risk. The study by Boonen et al. confirmed that only in

combination with vitamin D may calcium intake reduce the risk of hip and any non-vertebral fractures.

### CALCIUM SUPPLEMENTATION AND CARDIOVASCULAR DISEASE

Based on interventional studies it has generally been proposed that calcium supplements may have favourable effects on the cardiovascular system by its effects on intestinal fat absorption and blood pressure. It was suggested that calcium supplements are binding lipids and bile acids in the gut thereby interfering with fat absorption. A recent meta-analysis of randomized, controlled trials investigating faecal fat excretion in relation to calcium intake (supplements or dairy) confirmed increased fat excretion to an extent that could be relevant for prevention of weight gain. Indeed, observational studies have found that dietary calcium intake is inversely related to body weight and body fat mass. In contrast, however, other studies questioned a beneficial effect of calcium on lipid metabolism. A recent study by Reid et al. found no significant treatment effect of calcium intake on the ratio of HDL to LDL cholesterol nor on weight, fat mass, lean mass, triglycerides, or total, LDL, or HDL cholesterol. More consistent are data on the effect of calcium treatment on blood pressure with demonstration of average decrements of 1 to 2 mm Hg in both systolic and diastolic pressures. In the most recent randomized controlled trial there were downward trends in systolic and diastolic blood pressures within the calcium-supplemented groups, but there were no significant treatment effects over the whole trial period of two years. In a post hoc analysis of those with baseline calcium intake below the median value (<785 mg/d), blood pressures showed borderline treatment effects as compared with placebo;

Table 1: Benefits and risks of calcium supplementation. Treatment effect estimation (NNT/NNH) based on data from published meta-analyses evaluating the effect of calcium supplements on fracture risk and cardiovascular events (treatment duration 4–5 years).

	Calcium group, number events	Control group, number events	NNT / NNH
<b>Benefit?</b>			
Non-vertebral fracture	388/3356	426/3384	NNT 74
Hip fracture	77/2773	52/2801	NNT 109
<b>Harm?</b>			
Myocardial infarction	>166/6116	130/5805	NNH 210
Stroke	212/6116	190/5805	NNH 476

hence calcium supplementation may decrease blood pressure in those with low dietary intakes. The effects of calcium supplementation on blood pressure are probably induced by the natriuretic effect of calcium.

**POTENTIAL NEGATIVE CARDIOVASCULAR EFFECTS OF CALCIUM SUPPLEMENTS**

Whether these modest changes in cardiovascular risk factors ultimately result in improved cardiovascular morbidity and mortality is questioned since recent studies have suggested that calcium supplementation may be harmful and associated with increased vascular events.

In a five year randomized, placebo-controlled trial in 1471 healthy older women (mean age 74 years) Bolland et al. reported increases in rates of cardiovascular events in women allocated to calcium supplements (calcium citrate, 1000 mg). Contrary to the study's hypothesis of benefit, subjects' self-reports of adverse events showed a two-fold excess of myocardial infarction (RR 2.12, 95%CI 1.01-4.47) and a non-significant increase in the risk of stroke (RR 1.37, 95%CI 0.83-2.28). Based on this meta-analysis and its absolute risk estimates a NNH for myocardial infarction of 210 and a NNH for stroke of 476 over five years can be calculated (table 1).

Subsequently the same authors performed a meta-analysis of cardiovascular events in randomized, placebo-controlled studies of calcium supplements (without vitamin D co-administration). Most patients included in the analysis were women (median age of 74.5 years) and their mean dietary calcium at baseline ranged between 400 and 1200 mg/d. It remains unclear to what extent cardiovascular risk factors (e.g. hypertension, diabetes or lipid disorders) were prevalent as these data were not available in most studies included into the meta-analysis. Calcium supplements (calcium citrate or gluconate, 500-2000 mg) significantly increased the risk of myocardial infarction by 31% in five trials involving 8151 participants where individual patient data were available, and by 27% in 11 trials involving 11921 participants where trial level data were available. There were no statistically significant increases in the risk of stroke or death. Both studies have received major attention due to the potential detrimental effect on cardiovascular health,

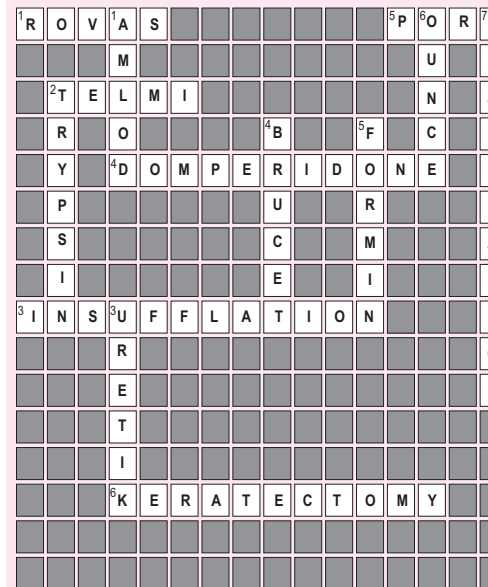
nevertheless major criticism has also been raised. In the first trial the risk of myocardial infarction was no longer significantly increased once the data had undergone a quality control audit using the national database of hospital admissions. The meta-analysis showed a significant increase in myocardial infarction, although none of the studies by itself observed significant results, not even the largest one. Importantly, data on cardiovascular events were collected from self-reports, death certificates and medical records, but were not defined as primary study endpoints. These and other criticisms, such as the fact that no attenuation of mortality has been observed, have been carefully addressed by the authors concluding that calcium supplementation should be used with caution in particular as potential benefits on skeletal health seem limited. In contrast to the findings of Bolland et al., a recently published interventional trial of calcium carbonate showed no negative cardiovascular effect. This study examined atherosclerotic vascular hospitalisation and mortality data from a 5-year randomized controlled trial with a 4.5 year post-trial follow-up. The participants were 1460 women (mean age 75 years) recruited from the general population and randomized to receive 1200 mg calcium carbonate daily or placebo. The intervention group that received calcium supplementation did not have a higher risk of death or first-time hospitalisation from atherosclerotic vascular disease in either the 5-year RCT or during the 9.5 years of observational study. Of note, the results of this study are not directly comparable with the meta-analysis by Bolland et al. as they choose a broad composite endpoint of atherosclerotic vascular disease (including atrial fibrillation and congestive heart failure) without analysis of specific endpoints such as myocardial infarction or stroke.

Whereas these studies examined the effect of calcium monotherapy the question arises whether co-administered calcium and vitamin D affects cardiovascular risk or whether the potential negative effect of calcium on cardiovascular events might be attenuated in combined treatment. There is some evidence that vitamin D might have an independent beneficial effect on mortality. In a randomized, placebo-controlled trial over seven years the Women's Health Initiative reported no adverse effect of calcium and vitamin D (1000 mg

calcium and 400 IU vitamin D daily) on any cardiovascular endpoint. Importantly, 54% of the participants were taking personal (non-protocol) calcium supplements at randomization (total calcium intake, exclusive study medication: app. 1150 mg/d) and 47% were taking personal vitamin D supplements (total vitamin D intake, exclusive study medication: app. 365 IU/d). This study has been reanalysed taking into account the interaction of personal use of calcium supplements. The authors conclude that calcium supplements with or without vitamin D modestly increase the risk of cardiovascular events, especially myocardial infarction (HR 1.22, 95%CI 1.00-1.50), a finding obscured in the WHI calcium/vitamin D study by the widespread use of personal calcium supplements. The risk for myocardial infarction and stroke (HR 1.17, 95%CI 0.95-1.44) were similar to those observed in the meta-analysis by Bolland et al. In women taking personal calcium supplements at randomization, the addition of calcium and vitamin D did not increase cardiovascular risk suggesting that there may not be a dose-response relationship between calcium supplement and the risk of cardiovascular events. The concept that abrupt change in plasma calcium concentration (which results after supplement ingestion) may be responsible for the observed increased cardiovascular risk remains speculative. A meta-analysis by Wang et al. including four prospective studies of healthy persons found no differences in incidence of cardiovascular disease between calcium supplement recipients and non-recipients. Results of secondary analyses in eight randomized trials showed a slight but statistically non-significant risk reduction in cardiovascular disease with vitamin D supplementation at moderate to high doses (app. 1000 IU/d) but not with calcium supplementation, or a combination of vitamin D and calcium supplementation.

To judge whether the observed effect of calcium supplements on cardiovascular endpoints represents a reliable signal which needs further attention one would like to understand possible mechanisms relating calcium supplementation with vascular disease. Although speculative some interesting mechanisms have been discussed in a recent review by Reid et al. Several studies have shown transient increases in serum calcium levels into the borderline hypercalcaemic range following ingestion of

**Answer to THH Crossword 042**



**Across**

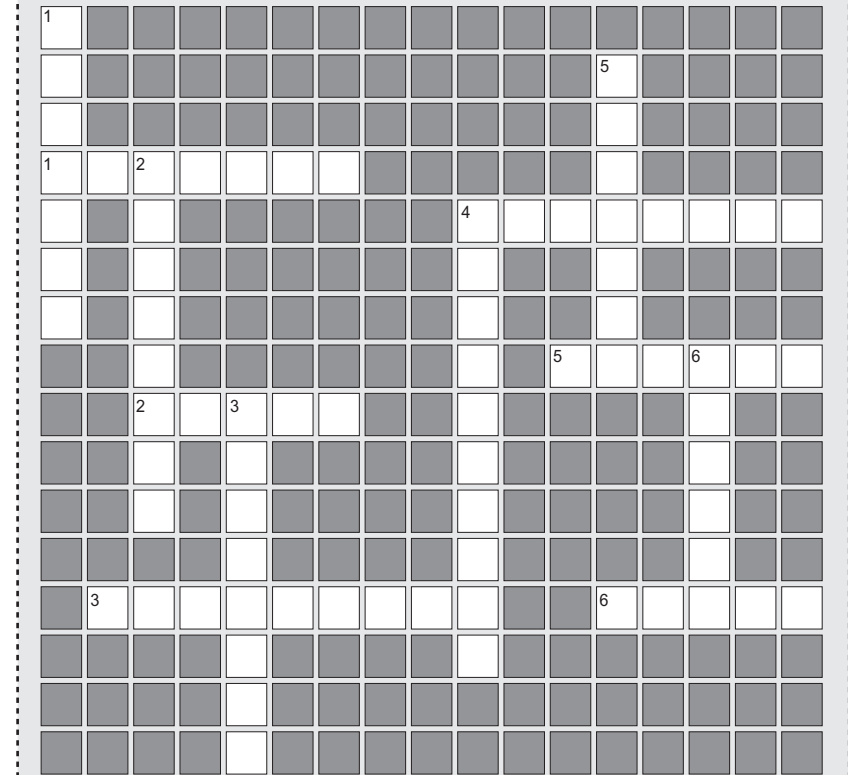
1. The super statin.
2. The gold standard medication.
3. the act of blowing air or powder into a cavity.
4. composition of EMENORM.
5. A minute circular opening on a surface.
6. Evcision of the cornea.

**Down**

1. Only Amlodipine in NEpal haring 3yrs of self life.
2. A digestive enzyme converting protin into amino acid.
3. The diuretic.
4. Still stands high in analgesics.
5. formed in glucose control.
6. Imperial measurement of weight.
7. The act of ejecting semen.

**THE HIMALAYAN HEALTH CROSSWORD 043**

*Win a fabulous prize...*



**Across**

1. Lapen's Amytriptyline.
2. A gold standard medication.
3. The process of teething.
4. An agent which increase the flow of urine.
5. A constricted portin or neck.
6. For the renal and retinal benefits.

**Down**

1. A hormone secreted by the walls of stomach.
2. A form of muscle or plant carbohydrate.
3. A nitrogenous and fatty substance found in nerve tissue.
4. A drug which reduces functional activity of an organ.
5. Relating to uterus.
6. An instrument used to hasten delivery of the fetal head in parturition.

Entries should reach to the editor by 15th Poush 068. In case of more than one correct entry, the winner will be decided by lucky draw.

NMC No.:.....  
 Name : Dr.....  
 Address: .....  
 Signature: ..... Tel: .....  
 Date:.....  
 Submitted by:

Now you can also send your entry by online on [www.npl.com.np](http://www.npl.com.np)

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between different primary headache groups. Headache diagnosis was based partly on physician interview and partly on patient-completed questionnaire, and RLS diagnosis was based on IRLSSG questionnaire confirmed by physician telephone interview. Of the 1,041 headache patients recruited, 772 had migraine, 218 tension-type headaches (TTH), and 51 cluster headaches (CH). There was no control group. The study found that RLS was more common in migraine patients (11.4%) than in TTH (4.6%) and CH (2.0%) ( $p = 0.002$ ). The lower frequency of RLS in this population suggested that an ethnic factor may contribute to RLS prevalence. Frequency of RLS increased with increasing number of migrainous symptoms (linear by linear association,  $p < 0.001$ ).

Migraine patients with RLS had worse scores in six of the seven components of the Pittsburgh Sleep Quality Index (PSQI), a questionnaire used to assess sleep quality in the past month, in which total scores range from 0 to 21 with a score greater

than 5 indicating poor sleep quality. Patients with migraine and RLS were found to be more likely to have a PSQI score greater than 5 compared to the patients with migraine alone (92.0 vs. 78.1%,  $p = 0.002$ ). The study thus indicated that RLS might have a negative impact on sleep quality in migraine patients.

Limitations of these studies include the use of selected populations, use of patient questionnaires which may be subject to recall bias, and the adoption of cross sectional study designs which give only point, rather than lifetime, prevalence.

### PATHOGENESIS

Despite the potential limitations of these four clinical studies, they have consistently found that RLS is more common in migraine patients than in comparator groups. If migraine and RLS are comorbid, rather than simply coincident, are there shared aetiological factors and/or pathogenic mechanisms which might explain the association? A number of possible explanations have been offered for the association of RLS and primary headache, three of which (not mutually exclusive) have attracted most attention: dopaminergic dysfunction and dysfunctional brain iron metabolism; genetic linkage; and sleep disturbance.

### DOPAMINERGIC DYSFUNCTION AND DYSFUNCTIONAL BRAIN IRON METABOLISM

It has been postulated that RLS may be caused by dysfunction in central dopaminergic pathways. The strongest argument in favour of this is the rapid and dramatic improvement in RLS symptoms with dopamine agonist drugs which are now licensed for the treatment of RLS. Animal models have shown that lesions to the A11 dopaminergic nucleus of the dorsal-posterior hypothalamus, the only nucleus providing dopaminergic stimulation to the spinal cord, produces a RLS-like phenotype. Dopamine has also been implicated in migraine pathogenesis: there is evidence for dopamine receptor hypersensitivity in migraine patients. Administration of low doses of dopamine agonists can trigger attacks of premonitory symptoms in migraineurs, including nausea, yawning and food craving. Conversely, dopamine antagonists may be of use in migraine treatment. Of note, when a trial of the dopamine antagonist droperidol was performed in acute migraine, a commonly reported side-effect was "acute drug-induced akathisia", which might possibly have been RLS since the two conditions may be difficult to differentiate clinically. Young et al. also found that headache patients with RLS were at a greatly increased risk of developing drug-induced akathisia when treated with intravenous dopamine receptor blocking agents. Cologno et al. carried out a case control study on 164 patients with primary headache disorders screening each participant for the presence of RLS and premonitory migraine dopaminergic

symptoms (yawning, nausea, somnolence or food craving). Concordant with previous studies, an increased incidence of RLS was found in migraineurs (25.6%). Intriguingly, those with co-existing migraine and RLS reported a higher prevalence of dopaminergic symptoms accompanying their migraine attacks than those without RLS (47.6 vs. 13.1%,  $p < 0.001$ ), adding to the argument that a dopaminergic imbalance could be the pathogenic connection between migraine and RLS.

Iron dysmetabolism is well recognised in RLS, some cases being secondary to iron deficiency, and iron therapy being one approach to treatment of RLS. There may be a link between brain iron and dopamine systems. Iron accumulation has also been documented in the brains of migraine patients.

### GENETIC LINKAGE

Individually, RLS and migraine seem to exhibit a polygenic inheritance pattern, both occurring with increased frequency in those with positive family histories. Currently, at least seven genetic loci have been linked to RLS. In addition, occasional pedigrees in which RLS and migraine appear to co-segregate over several generations have been presented.

Sabayan et al. suggested that it was credible to assume that migraine and RLS may have a joint origin, based in part on a common genetic linkage mapped to chromosome 14q21. This was described in an Italian family with idiopathic autosomal dominant RLS (OMIM %608831); one patient in the pedigree (III.17) had both RLS and migraine. Soragna et al. described a susceptibility locus for migraine without aura (OMIM %607501), also at 14q21, but there was no mention of RLS in affected individuals in this Italian family.

### SLEEP DISTURBANCE

Sleep disorders are observed in a disproportionate number of patients with primary headache disorders. Epidemiological studies indicate that sleep deprivation is one of the most common precipitating factors for migraine attacks. Improving sleep hygiene is often a component of headache management strategies, which alone may resolve or greatly improve headache complaints in some cases. Given that RLS is, by definition, worse at nighttime, it is not surprising that the vast

500 to 1000 mg calcium as a supplement which is in contrast to the intake of calcium from dietary sources. Ingestion of calcium-rich foods has been shown to result in much smaller changes in circulating calcium levels, which might be due to slower intestinal transit as calcium rich foods are usually ingested together with proteins and fat. A systematic review recently showed that dairy food consumption is not associated with a higher risk of coronary heart disease.

In contrast, however, high-normal levels of serum calcium have been related to cardiovascular disease, including carotid artery plaque thickness and abdominal aortic calcification. Direct correlations between serum calcium levels and coronary heart disease or stroke have been observed in postmenopausal women and men as well as in patients with primary hyperparathyroidism. Hence, one could assume that calcium supplements, not taken together with meals, would result in elevations of circulating calcium above the upper normal range. In fact, hypercalcaemia after intake of calcium supplements is transitory lasting for about six hours. Repeated intake of supplements with repeated calcium peaks may therefore translate into increased risk of cardiovascular disease. Other potential mechanisms linking calcium supplements with cardiovascular disease include acceleration of coronary artery calcification, induction of a hypercoagulable state and effects on arterial stiffness with impaired vasodilatation. Practical consequences

A general function of everyday clinical practice is the identification of persons with an increased risk of fractures, the initiation of preventive measures and the institution of a therapeutic intervention appropriate to their individual fracture risk. Nowadays, a case-finding strategy that is designed to investigate people (by DXA) with a clearly increased risk of fracture is recommended. Drug therapy is indicated where there is increased risk of fracture. This applies to patients who have already experienced a fracture, especially a vertebral or hip fracture or patients with an increased absolute 10-year fracture risk (assessed by the "WHO Fracture Risk Assessment Tool" (FRAX®).

Antiresorptive preparations, particularly bisphosphonates, denosumab and selective

oestrogen receptor modulators are primarily used in the therapy of osteoporosis. In this context it is noteworthy that calcium supplementation is only a weak resorption inhibitor which is reflected by the small effect on fracture risk reduction. Hence, while adequate calcium intake should generally be ensured as a preventive strategy additional pharmacological treatment is mandatory in patients with increased fracture risk and treatment to prevent fractures cannot exclusively be based on calcium and vitamin D supplementation (except for the rare case of osteomalacia).

The recently published report of the Institute of Medicine in the USA (IOM) states that 1000–1200 mg of calcium is the estimated average daily requirement for women and men over 50 years with an upper limit (that is likely to pose no risk) of 2000 mg/d. As comprehensively discussed in an editorial by Burckhardt these figures are derived from studies in populations whose bone health was not optimal. Importantly, these studies were not titrated against circulating levels of 25(OH)vitamin D which is crucial considering the role of vitamin D in the regulation of intestinal calcium absorption. It therefore seems reasonable to assume that the recommendations of the IOM may be too high. In clinical practice assessment of an individual's dietary calcium intake is recommended before prescribing additional calcium supplements and calcium supplementation should be restricted to patients with low calcium intake only (<800 mg/d). Dietary calcium intake can be assessed by simplified questionnaires. It has to be acknowledged, however, that this is only a simplified estimate of calcium intake, more precise assessment with thorough quantification should be based on questionnaires such as the Food Frequency Questionnaire (FFQ). Using a semiquantitative questionnaire in daily routine we observed that most patients in our Osteoporosis Clinic generally have sufficient nutritional calcium intake. In a review of 1461 consecutive patients who were referred for osteoporosis assessment a median dietary calcium intake of 1020 mg/d (range, 100–3600 mg/d) was recorded. 73% of patients reported having a daily calcium intake of more than 800 mg. This indicates that routine supplementation of calcium is not warranted in all patients, but patients with inadequate intake need to be

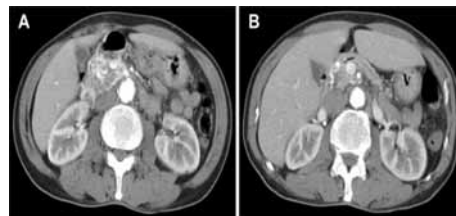
identified and treated aiming for a total daily calcium intake of 800 to 1000 mg.

In a posthoc analysis of the meta-analysis by Bolland et al. suggesting an overall increased cardiovascular risk in patients on calcium supplementation there was an interaction between dietary calcium intake and the risk of myocardial infarction. When the cohort was divided into two groups by baseline dietary calcium intake (above and below the median) there was an interaction between dietary calcium and the risk of myocardial infarction with increased risk in patients with a daily intake above 800 mg. In contrast, risk of myocardial infarction was not elevated in women with an intake below 800 mg ( $p = 0.01$  for interaction). As the risk of cardiovascular events is predominantly observed in studies with higher doses of calcium supplements (1000–2000 mg), lower doses seem to be safe. Practically, this indicates that a total calcium intake of about 800 mg (dietary calcium intake and calcium supplement) would be adequate, as long as optimal vitamin D levels are ascertained. In contrast to the ingestion of calcium-rich foods, calcium supplements taken in the fasting state may result in transient hypercalcaemia (which has been related to cardiovascular disease). In order to prevent relevant hypercalcaemia supplements should be taken after meals and higher doses of supplements are preferably divided into portions of 500 mg.

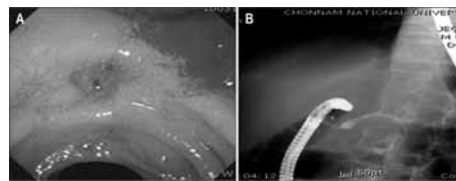
In summary, potential negative effects of calcium supplements need to be balanced against the benefits of treatment. The published data so far suggest a potential detrimental effect of calcium supplement on cardiovascular health (i.e. myocardial infarction) although further prospective studies are needed to clarify the gradient of risk. Since food sources of calcium produce similar benefits on bone density as supplements and dietary calcium intake does not seem to be related to adverse cardiovascular effects, calcium intake from nutritional sources needs to be enforced. In patients with low calcium intake supplements are warranted aiming for a total calcium intake of 800 to 1000 mg/d together with adequate vitamin D replacement. Nevertheless we should keep in mind that for a significant reduction in fracture risk, pharmacological treatment is mandatory in patients at risk of fractures irrespective of calcium and vitamin D supplementation. ■

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duodenum proximal to minor papilla. When the radiopaque dye was injected through the fistula, the dilated pancreatic duct was visualized (Fig. 3) and the cholangiogram via ampulla of Vater was normal. Review of the past abdominal CT films revealed air densities in the main pancreatic duct also.



**Fig. 2**  
Abdominal computerized tomogram. (A) Abnormally dilated, conglomerated vascular structures in the pancreatic head abutting the descending duodenum are seen. (B) The pancreatic parenchyma is atrophied except at the pancreatic head, and there are air pockets in the dilated pancreatic duct.



**Fig. 3**  
Endoscopic retrograde cholangiopancreatography. (A) The mucosa of the duodenum and of the fistula located at the descending duodenum proximal to the minor papilla are edematous and easily friable. Around the fistula tract, bleeding telangiectasias can be seen. (B) When the radiocontrast dye is injected through the fistula, the dilated pancreatic duct is visualized.

On hospital day 5, he complained abdominal pain and the body temperature was 39.5. The leukocyte was 12,900/mm<sup>3</sup> (neutrophil 91.7%) and *Citrobacter freundii* was cultured from peripheral blood. On hospital day 8, the fever and abdominal pain was relieved with antibiotics. We recommended surgical therapy for the prevention of portal hypertension and recurrent ascending infection. But, he refused surgery and other conservative treatment including angiographic embolization or transjugular intrahepatic portosystemic shunt. And after that, he was lost to follow-up.

## DISCUSSION

Although AVM can be occurred frequently in digestive organ such as cecum, ascending colon, jejunum, and ileum, pancreatic AVM is rare and reported first by Halpern et al. Doppler ultrasonography and CT can be helpful, angiography has played the most important role in the diagnosis and planning the therapy of pancreatic AVM. The angiographic findings of pancreatic AVM include 1) dilated and tortuous feeding arteries, 2) racemose intrapancreatic vascular network followed by a transient dense pancreatic strain, 3) early venous filling into the portal vein, and 4) early disappearance of the pancreatic strain. The vessels most commonly affected by a pancreatic AVM are the splenic artery (42%), gastroduodenal artery (22%), and small pancreatic arteries (25%).

The clinical symptoms of pancreatic AVM were variable including gastrointestinal bleeding, abdominal pain, jaundice, portal hypertension, pancreatitis, and duodenal ulcer. Gastrointestinal bleeding can be occurred by following mechanisms, first, direct intestinal bleeding from intestinal mucosa, second, bleeding from pancreatic duct, and third, bleeding from esophagogastric varices associated with portal hypertension. In the present case, although there was no evidence of massive gastrointestinal bleeding, chronic occult blood loss might have occurred from telangiectasia associated with pancreatic AVM. Duodenal ulcer or duodenitis appears to be associated with regional ischemia caused by the diseased mucosa. Recurrent inflammation of duodenum and pancreas might have induced the fistula tract between pancreatic duct and duodenum. However, choledochoduodenal or pancreaticoduodenal fistula associated with pancreatic AVM is extremely rare, and according to the English literature, only 2 cases have been reported and so far, there was no report about recurrent ascending infection caused by pancreaticoduodenal fistula associated with pancreatic AVM. *Citrobacter freundii* is gram negative enteric bacilli which can be found in human intestine and infects urinary and biliary tract. In the present case, there was no evidence of infection focus other than pancreaticoduodenal fistula. Invasion of *Citrobacter freundii* via pancreaticoduodenal fistula might have induced pancreatitis and bacteremia. In the present case, the patient's pancreatic parenchyma was atrophied and the

pancreatic duct was dilated. Chronic ischemia caused by pancreatic AVM could induce chronic pancreatitis and chronic pancreatitis was acutely exacerbated at each time of ascending infection by pancreaticoduodenal fistula. It is known that pancreatitis associated with pancreatic AVM can be occurred by bleeding from AVM into the pancreatic duct and ischemia of the pancreas. Ascending infection via pancreaticoduodenal fistula should be considered as a cause of pancreatitis.

Complete cure is achieved by total resection of the affected organ, or at least the involved portion. Once after portal hypertension developed, it cannot be corrected even after surgical resection, so early diagnosis and proper treatment is important. In case of inoperable conditions, transcatheter arterial embolization, radiation therapy, and transjugular intrahepatic portosystemic shunt seems to be the alternative treatment for complications of pancreatic AVM. In summary, pancreatic AVM is a rare disease, but can induce life threatening complications. Herein, we report a case of pancreaticoduodenal fistula associated with pancreatic AVM which induced recurrent anemia and ascending infection. ■

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allowing plastic scleral lenses to be manufactured for the first time. In 1936, optometrist William Feinbloom introduced plastic lenses, making them lighter and more convenient. These lenses were a combination of glass and plastic.

In 1949, the first "corneal" lenses were developed. These were much smaller than the original scleral lenses, as they sat only on the cornea rather than across all of the visible ocular surface, and could be worn up to sixteen hours per day. PMMA corneal lenses became the first contact lenses to have mass appeal through the 1960s, as lens designs became more sophisticated with improving manufacturing (lathe) technology.

Early corneal lenses in the 1950s and 1960s were relatively expensive and fragile, resulting in the development of a market for contact lens insurance. Replacement Lens Insurance, Inc. (now known as RLI Corp.) phased out its original flagship product in 1994 after contacts became more affordable and easier to replace. One important disadvantage of PMMA lenses is that no oxygen is transmitted through the lens to the conjunctiva and cornea, which can cause a number of adverse clinical effects. By the end of the 1970s, and through the 1980s and 1990s, a range of oxygen-permeable but rigid materials were developed to overcome this problem. Chemist Norman Gaylord played a prominent role in the development of these newer, permeable contact lenses. Collectively, these polymers are referred to as "rigid gas

permeable" or "RGP" materials or lenses. Although all the above lens types—sclerals, PMMA lenses and RGPs—could be correctly referred to as being "hard" or "rigid", the term hard is now used to refer to the original PMMA lenses which are still occasionally fitted and worn, whereas rigid is a generic term which can be used for all these lens types. That is, hard lenses (PMMA lenses) are a sub-set of rigid lenses. Occasionally, the term "gas permeable" is used to describe RGP lenses, but this is potentially misleading, as soft lenses are also gas permeable in that they allow oxygen to move through the lens to the ocular surface. The principal breakthrough in soft lenses was made by the Czech chemists Otto Wichterle and Drahoslav Lim who published their work "Hydrophilic gels for biological use" in the journal *Nature* in 1959.[16] This led to the launch of the first soft (hydrogel) lenses in some countries in the 1960s and the first approval of the "Softlens" material by the United States Food and Drug Administration (FDA) in 1971. These lenses were soon prescribed more often than rigid lenses, mainly due to the immediate comfort of soft lenses; by comparison, rigid lenses require a period of adaptation before full comfort is achieved. The polymers from which soft lenses are manufactured improved over the next 25 years, primarily in terms of increasing the oxygen permeability by varying the ingredients. In 1972, British optometrist Rishi Agarwal was the first to suggest disposable soft contact lenses.

In 1998, an important development was the launch of the first silicone hydrogels onto the market by CIBA VISION in Mexico. These new materials encapsulated the benefits of silicone—which has extremely high oxygen permeability—with the comfort and clinical performance of the conventional hydrogels which had been used for the previous 30 years. These lenses were initially advocated primarily for extended (overnight) wear although more recently, daily (no overnight) wear silicone hydrogels have been launched.

In a slightly modified molecule, a polar group is added without changing the structure of the silicone hydrogel. This is referred to as the Tanaka monomer because it was invented and patented by Kyoichi Tanaka of Menicon Co. of Japan in 1979. Second-generation silicone hydrogels, such as galyfilcon A (Acuvue Advance, Vistakon) and senofilcon A (Acuvue Oasys, Vistakon), use the Tanaka monomer. Vistakon improved the Tanaka monomer even further and added other molecules, which serve as an internal wetting agent.

Comfilcon A (Biofinity, CooperVision) was the first third-generation polymer. The patent claims that the material uses two siloxy macromers of different sizes that, when used in combination, produce very high oxygen permeability (for a given water content). Enfilcon A (Avaira, CooperVision) is another third-generation material that's naturally wettable. The enfilcon A material is 46% water. ■

# BETASOL-N

Betamethasone Na phosphate 0.1% w/v + Neomycin sulphate 0.5% w/v

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