Ten Commandments of the 2018 ESC/ESH HTN Guidelines on Hypertension in Adults

Updates on

Dr’s Pen
Renal tubular acidosis & hypokalemic paralysis as a clinical presentation of primary Sjögren’s syndrome
Sedhain A, et al, Case reports in Nephrology 2018
Respected Doctor/s,

We must admit that with the emerging new technology, relevant research and treatments that can improve quality of life of people with diabetes & hypertension, the field of cardiac care & diabetes care is rapidly changing. For the same, in this issue we have highlighted recent commandments of ESC/ESH 2018 guidelines on Hypertension along with recent updates on Standards of Medical Care in Diabetes 2018. We have also enlightened the hopes that are founded on recent discoveries that suggest biological ageing may be entirely preventable and treatable. Advances in medicine over the last two centuries have taught us that we have the power to defeat the diseases that affect us.

Talking about case reports, we have incorporated findings of Dr. Arun Sedhain & team on ‘Renal tubular acidosis & hypokalemic paralysis as a clinical presentation of primary Sjogren’s syndrome’, an autoimmune disease characterized by dryness of the mouth and eyes. On the other hand, Probiotics had always been on the headline in the media lately, for which we have provided an evidence-based review on its clinical use to aware which ones are specifically good for us, and which ones are good for certain purposes or certain benefits.

Moreover, a new study published in the journal JAMA Medical News & Perspective, reports a link between depression and dementia. Its authors suggest their findings may help to inform future dementia research, as CDC data claimed that Alzheimer’s disease and other dementias will impose double the current burden by the year 2060.

We believe that this issue will be informative and as NPL always paced together with the Medical Fraternity for better health of Nepalese, in this issue we have highlighted the recent CSR of NPL Social Welfare Organization in Sunakothi community to find and resolve major health problems of geriatric population.

Working together for healthier Nepal.

Regards,
Phr. Sangam Shakya
Ten Commandments of the 2018 ESC/ESH HTN Guidelines on Hypertension in Adults

A first look at the new European Guidelines for the treatment of high blood pressure (BP) was presented at the European Society of Hypertension meeting in Barcelona on 9 June 2018. These long-awaited guidelines have been jointly developed by clinicians representing the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). The guidelines provide recommendations for doctors across Europe to diagnose hypertension, evaluate risk, when and how to treat hypertension and reduce risk, with both lifestyle advice and medications. The development of the guidelines was led by Prof. Bryan Williams (ESC Chairperson), London UK and Prof. Giuseppe Mancia (ESH Chairperson), Milan, Italy, as lead authors.

1. Definition of hypertension:
Hypertension is defined as a persistent elevation in office systolic BP ≥140 and/or diastolic BP ≥90 mmHg, which is equivalent to a 24h ambulatory BP monitoring (ABPM) average of ≥130/80 mmHg or a home BP monitoring (HBPM) average ≥135/85 mmHg.

2. Screening and diagnosis of hypertension:
Screening programmes should be established to ensure that office BP is measured in all adults, at least every 5 years and more frequently in people with a high normal BP.

When hypertension is suspected the diagnosis of hypertension should be confirmed either by repeated office BP measurements, over a number of visits, or by ‘out of office’ BP measurement using 24h ABPM or HBPM.

3. When to consider drug treatment of hypertension:
Adults with Grade 1 hypertension (office BP 140-159/90-99) aged up 80 years, should receive drug treatment if their BP is not controlled after a period of lifestyle intervention alone. For high-risk patients with Grade 1 hypertension, or patients with higher grades of hypertension (e.g. Grade 2 hypertension; ≥160/100 mmHg), drug treatment should be initiated alongside lifestyle interventions.

4. Special considerations in frail and older patients:
For people over the age of 80 years, who have not yet received treatment for their BP, BP treatment should be considered when office systolic BP is ≥160 mmHg. Frailty, dependency and expectations of treatment benefit will influence the decision treat people aged >80 years, on an individual patient basis, but these patients should not be denied treatment, or have treatment withdrawn simply on the basis of age.

5. How low should BP be lowered?
‘A target range’ for treated BP has been introduced. Office systolic BP should be lowered to <140 mmHg in all treated patients, including independent older patients who can tolerate treatment. The aim should be to target systolic BP to 130 mmHg for most patients, if tolerated. Even lower office systolic BP levels (<130 mmHg) should be considered in patients aged <65 years but not in patients aged 65 years or more. Similar BP targets are recommended for patients with diabetes. Systolic BP should not be targeted to below 120 mmHg because the balance of benefit vs. harm becomes concerning at these levels of treated systolic BP. Office diastolic BP should be lowered to <80 mmHg.

6. Treatment of hypertension: lifestyle interventions are important:
The treatment of hypertension involves lifestyle interventions and drug therapy. Lifestyle interventions are important because they can delay the need for drug treatment or complement the BP lowering effect of drug treatment. Moreover, lifestyle interventions such as sodium restriction, alcohol moderation, healthy eating, regular exercise, weight control, and smoking cessation, all have health benefits beyond their impact on BP.

7. Start treatment in most patients with two drugs, not one:
Monotherapy is usually inadequate
therapy for most people with hypertension, especially now that the BP treatment targets for many patients, are lower than in previous guidelines. Initial therapy with a combination of two drugs should now be considered usual care for hypertension. The only exception would be in a limited number of patients with a lower baseline BP close to their recommended target, who might achieve that target with a single drug, or in some frail old or very old patients, in whom more gentle reduction of BP may be desirable.

8. A single pill strategy to treat hypertension:
Poor adherence to BP-lowering medication is directly related to the number of pills and is a major factor contributing to poor BP control rates. Single pill combination therapy is now the preferred strategy for initial two-drug combination treatment of hypertension and for three drug combination therapy when required. This will control the BP in most patients with a single pill and should improve BP control rates.

9. A simplified drug treatment algorithm:
A combination of an ACE inhibitor or ARB with a CCB or thiazide / thiazide - like diuretic is the preferred initial therapy for most patients. For those requiring three drugs, a combination of an ACE-inhibitor or ARB with a CCB and a thiazide/thiazide-like diuretic should be used. Beta blockers should be used when there is a specific indication for their use, e.g. angina, post myocardial infarction, heart failure with reduced ejection fraction, or when heart rate control is required.

10. Managing cardiovascular disease risk in hypertensive patients—going beyond BP:
Hypertensive patients frequently have concomitant cardiovascular risk factors. Statin therapy should be more commonly used in hypertensive patients with established cardiovascular disease or moderate-to-high cardiovascular disease risk according to the SCORE system. Benefit from statin therapy has also been observed in hypertensive patients at the border between low and moderate risk. Antiplatelet therapy, especially low dose aspirin is also indicated for secondary prevention in hypertensive patients but is not recommended for primary prevention, i.e. in patients without cardiovascular disease.
Updates to the Standards of Medical Care in Diabetes-2018

The American Diabetes Association’s (ADA’s) Standards of Medical Care in Diabetes (Standards of Care) provide the latest in comprehensive, evidence-based recommendations for the diagnosis and treatment of children and adults with type 1, type 2, or gestational diabetes mellitus; strategies to improve the prevention or delay of type 2 diabetes; and therapeutic approaches that reduce complications and positively affect health outcomes. New in 2018, the ADA is updating and revising the online version of the Standards of Care throughout the year with annotations for new evidence or regulatory changes that merit immediate incorporation.

Revised Hypoglycemia Definition

(Sections 6 and 14): The December 2017 issue of Diabetes Care featured a consensus report from the ADA and others in the diabetes community on clinically meaningful outcome measures beyond A1C for type 1 diabetes, which categorized hypoglycemia into three levels. The ADA has updated Section 6 Glycemic Targets and Section 14 Diabetes Care in the Hospital of the 2018 Standards of Care to align with the hypoglycemia definitions in the consensus report and thereby minimize confusion for practitioners. The following updates were approved on 10 March 2018 and added to the living Standards of Care on 11 April 2018.

Table 6.3 (p. S61)
Table 6.3 has been updated to align with the recently published Consensus Report titled: “Standardizing Clinically Meaningful Outcome Measures Beyond HbA1c for Type 1 Diabetes: A Consensus Report of the American Association of Clinical Endocrinologists, the American Association of Diabetes Educators, the American Diabetes Association, the Endocrine Society, JDRF International, The Leona M. and Harry B. Helmsley Charitable Trust, the Pediatric Endocrine Society, and the T1D Exchange”. The consensus report categorized hypoglycemia into 3 levels as outlined in the following table:

<table>
<thead>
<tr>
<th>LEVEL</th>
<th>GLYCEMIC CRITERIA/DESCRIPTION</th>
</tr>
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<tbody>
<tr>
<td>Level 1</td>
<td>Glucose &lt;70 mg/dL (3.9 mmol/L) and glucose ≥54 mg/dL (3.0 mmol/L)</td>
</tr>
<tr>
<td>Level 2</td>
<td>Glucose ≥54 mg/dL (3.0 mmol/L)</td>
</tr>
<tr>
<td>Level 3</td>
<td>A severe event characterized by altered mental and/or physical status requiring assistance</td>
</tr>
</tbody>
</table>

“Glucagon should be prescribed for all individuals at increased risk of clinically significant hypoglycemia, defined as blood glucose <54 mg/dL (3.0 mmol/L), so it is available should it be needed. Caregivers, school personnel, or family members of these individuals should know where it is and when and how to administer it. Glucagon administration is not limited to health care professionals. E” (p. S61)

For alignment with the annotation to Table 6.3, the above recommendation has been updated to state the following:

“Insulin-treated patients with hypoglycemia unawareness or an episode of clinically significant hypoglycemia should be advised to raise their glycemic targets to strictly avoid hypoglycemia for at least several weeks in order to partially reverse hypoglycemia unawareness and reduce risk of future episodes. A” (p. S61)
“Insulin-treated patients with hypoglycemia unawareness or an episode of level 2 (<54 mg/dL [3.0 mmol/L]) hypoglycemia should be advised to raise their glycemic targets to strictly avoid hypoglycemia for at least several weeks in order to partially reverse hypoglycemic unawareness and reduce risk of future episodes.”

Recommendations from the International Hypoglycemia Study Group regarding the classification of hypoglycemia in clinical trials are outlined in Table 6.3. Of note, this classification scheme considers a blood glucose <54 mg/dL (3.0 mmol/L) detected by SMBG, CGM (for at least 20 min), or laboratory measurement of plasma glucose as sufficiently low to indicate clinically significant hypoglycemia that should be included in reports of clinical trials of glucose lowering drugs for the treatment of diabetes. However, a hypoglycemia alert value of ≤70 mg/dL (3.9 mmol/L) can be important for therapeutic dose adjustment of glucose-lowering drugs in clinical care and is often related to symptomatic hypoglycemia. Severe hypoglycemia is defined as severe cognitive impairment requiring assistance from another person for recovery.” (p. S61)

For alignment with the annotation to Table 6.3, the section of text above has been updated to state the following:

“Recommendations regarding the classification of hypoglycemia are outlined in Table 6.3. Level 1 hypoglycemia is defined as a measurable glucose concentration <70 mg/dL (3.9 mmol/L) but ≥54 mg/dL (3.0 mmol/L). A blood glucose concentration of 70 mg/dL has been recognized as a threshold for neuroendocrine responses to falling glucose in people without diabetes. Because many people with diabetes demonstrate impaired counterregulatory responses to hypoglycemia and/or experience hypoglycemia unawareness, a measured glucose level <70 mg/dL (3.9 mmol/L) is considered clinically important, independent of the severity of acute hypoglycemic symptoms. Level 2 hypoglycemia (defined as a blood glucose concentration <54 mg/dL [3.0 mmol/L]) is the threshold at which neuroglycopenic symptoms begin to occur and requires immediate action to resolve the hypoglycemic unawareness or an episode of a clinically significant event. Lastly, level 3 hypoglycemia is defined as a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery.”

“The hypoglycemia alert value in hospitalized patients is defined as blood glucose ≤70 mg/dL (3.9 mmol/L) and clinically significant hypoglycemia as glucose values <54 mg/dL (3.0 mmol/L). Severe hypoglycemia is defined as that associated with severe cognitive impairment regardless of blood glucose level.” (p. S145)

For alignment with the annotation to Table 6.3, the section of text above has been updated to state the following:

“Level 1 hypoglycemia in hospitalized patients is defined as a measurable glucose concentration <70 mg/dL (3.9 mmol/L) but 54 mg/dL (3.0 mmol/L). Level 2 hypoglycemia (defined as a blood glucose concentration <54 mg/dL [3.0 mmol/L]) is the threshold at which neuroglycopenic symptoms begin to occur and requires immediate action to resolve the hypoglycemic event. Lastly, level 3 hypoglycemia is defined as a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery.”

New FDA-Approved Drugs
(Section 8): In December 2017, the U.S. Food and Drug Administration (FDA) approved the GLP-1 receptor agonist semaglutide and the SGLT2 inhibitor ertugliflozin as adjuncts to diet and exercise to improve glycemic control in adults with type 2 diabetes. These medications have the potential to impact patient care and have therefore been added to Section 8 - Pharmacologic Approaches to Glycemic Treatment. The following updates were approved on 10 March 2018 and added to the living Standards of Care on 11 April 2018.

Table 8.2 (p. S79)
The following note has been added to Table 8.2.

“In December 2017, the U.S. Food and Drug Administration approved the SGLT2 inhibitor ertugliflozin as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes.”

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The following note has been added to Table 8.2.

“In December 2017, the U.S. FDA approved the GLP-1 receptor agonist semaglutide as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes.”

Standards of Medical Care in Diabetes—2018 Abridged for Primary Care Providers
The online version of the Standards of Medical Care in Diabetes—2018 Abridged for Primary Care Providers, published in Clinical Diabetes at https://doi.org/10.2337/cd17-0119, has been updated to include the annotations outlined above.

www.npl.com.np
Abstract

Diabetes prevalence shows a continuous increasing trend in South Asia. Although well-established treatment modalities exist for type 2 diabetes mellitus (T2DM) management, they are limited by their side effect profile. Sodium-glucose co-transporter 2 inhibitors (SGLT2i) with their novel insulin-independent renal action provide improved glycemic control, supplemented by reduction in weight and blood pressure, and cardiovascular safety. Based on the clinical outcomes with SGLT2i in patients with T2DM, treatment strategies that make a "good clinical sense" are desirable. Considering the peculiar lifestyle, body types, dietary patterns (long duration religious fasts), and the hot climate of the South Asian population, a unanimous decision was taken to design specific, customized guidelines for T2DM treatment strategies in these regions. The panel met for a discussion three times so as to get a consensus for the guidelines, and only unanimous consensus was included. After careful consideration of the quality and strength of the available evidence, the executive summary of this consensus statement was developed based on the American Association of Clinical Endocrinologists/American College of Endocrinology protocol.

KEYWORDS:
Canagliflozin; South Asia; dapagliflozin; diabetes mellitus; empagliflozin; glycosuria; hyperglycemia; sodium–glucose co-transporter 2

Safe and pragmatic use of sodium-glucose co-transporter 2 inhibitors in type 2 diabetes mellitus: South Asian Federation of Endocrine Societies consensus statement.

Kalra S1, Ghosh S2, Aamir AH3, Ahmed MT4, Amin MF5, Bajaj S6, Baruah MP7, Bulugahapitiya U7, Das AK8, Giri M9, Gunatilake S7, Mahar SA10, Pathan MF7, Qureshi NK11, Raza SA12, Sahay R13, Shakya S14, Shreshta D15, Somasundaram N16, Sumanatilleke M17, Unnikrishnan AG18, Wijesinghe AM16.

Source: Indian J Endocrinol Metab. 2017 Jan-Feb;21(1):210-230.
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Environmental toxic metal contaminants and risk of cardiovascular disease: systematic review and meta-analysis.

Chowdhury R1, Ramond A1, O’Keeffe LM2,3, Shahzad S1, Kunutsor SK4,5,6, Muka T7, Gregson J8, Willeit P1,9, Warnakula S1, Khan H10, Chowdhury S1, Gobin R11, Franco OH7, Di Angelantonio E1,12,13.

Abstract

OBJECTIVE:
To conduct a systematic review and meta-analysis of epidemiological studies investigating the association of arsenic, lead, cadmium, mercury, and copper with cardiovascular disease.

DESIGN:
Systematic review and meta-analysis.

REVIEW METHODS:
Studies reporting risk estimates for total cardiovascular disease, coronary heart disease, and stroke for levels of arsenic, lead, cadmium, mercury, or copper were included. Two investigators independently extracted information on study characteristics and outcomes in accordance with PRISMA and MOOSE guidelines. Relative risks were standardised to a common scale and pooled across studies for each marker using random effects meta-analysis.

RESULTS:
The review identified 37 unique studies comprising 348,259 non-overlapping participants, with 13,033 coronary heart disease, 4,205 stroke, and 15,274 cardiovascular disease outcomes in aggregate. Comparing top versus bottom thirds of baseline levels, pooled relative risks for arsenic and lead were 1.30 (95% confidence interval 1.04 to 1.63) and 1.43 (1.16 to 1.76) for cardiovascular disease, 1.23 (1.04 to 1.45) and 1.85 (1.27 to 2.69) for coronary heart disease, and 1.15 (0.92 to 1.43) and 1.63 (1.14 to 2.34) for stroke. Relative risks for cadmium and copper were 1.33 (1.09 to 1.64) and 1.81 (1.05 to 3.11) for cardiovascular disease, 1.29 (0.98 to 1.71) and 2.22 (1.31 to 3.74) for coronary heart disease, and 1.72 (1.29 to 2.28) and 1.29 (0.77 to 2.17) for stroke. Mercury had no distinctive association with cardiovascular outcomes. There was a linear dose-response relation for arsenic, lead, and cadmium with cardiovascular disease outcomes.

CONCLUSION:
Exposure to arsenic, lead, cadmium, and copper is associated with an increased risk of cardiovascular disease and coronary heart disease. Mercury is not associated with cardiovascular risk. These findings reinforce the importance of environmental toxic metals in cardiovascular risk, beyond the roles of conventional behavioural risk factors.
The list of diseases humankind has managed to defeat is impressive – polio, typhoid, measles, tetanus, yellow fever, smallpox, diphtheria and chicken pox have been almost completely eliminated in many parts of the world. Vaccines and powerful drugs have allowed our species to fight back against the bacteria, parasites and viruses that threaten to kill us. But throughout history, humans have suffered from a condition that they have never been able to escape – ageing. As we get older, our cells stop working as well and can break down, leading to conditions like cancer, heart disease, arthritis and Alzheimer’s disease. Together, ageing-related diseases are responsible for 100,000 deaths per day and billions are spent around the world trying to slow their steady march on our bodies. Some researchers, however, believe we may be thinking about these conditions in the wrong way. They say we should start treating ageing itself as a disease – one that can be prevented and treated. In a recent episode of the BBC Tomorrow’s World podcast, my fellow presenter Ellie Cosgrave and I spoke to some of those who are investigating ways to slow and even halt the ageing process.

Their hopes are founded on recent discoveries that suggest biological ageing may be entirely preventable and treatable. From a biological perspective, the body ages at different rates according to genetic and environmental factors. Tiny errors build up in our DNA and our cells begin developing faults that can accumulate into tissue damage. The extent of these changes over time can mean the difference between a healthy old age or one spent housebound and afflicted by chronic diseases.
The hopes are founded on recent discoveries that suggest biological ageing may be entirely preventable and treatable.

The scientists who hope to do this sit on the fringes of the mainstream medical landscape. But there are now a number of research centres around the world that have made identifying ways of preventing biological ageing a priority. Studies in animals have shown that it is indeed possible to dramatically extend the lifespan of certain species, giving hope that it could also be possible in humans.

One common diabetes drug, metformin, was able to extend the lifespan of rodents. In the early 1990s, Cynthia Kenyon, now vice president of ageing research at Calico Labs, the Google-backed anti-ageing research company, demonstrated that roundworms could live six weeks instead of their natural three just by changing a single letter of their genetic code.

In our Tomorrow’s World podcast episode about ageing, one of the leading figures in human longevity research, Aubrey De Grey, tells us how similar increases in lifespan could be achieved in humans. De Grey is the chief science officer at the Strategies for Engineered Negligible Senescence (Sens) Research Foundation, a California-based regenerative medicine research foundation focused on extending the healthy human lifespan. He explains their goal is to develop a suite of therapies for middle-aged and older people that will leave them physically and mentally equivalent to someone under the age of 30. “Of course, without wiping their memories,” he adds.

De Grey says they want “to fix the things we don’t like about the changes that happen between the age of 30 and the age of 70”. There are seven biological factors De Grey argues are predominantly responsible for cellular damage that accompanies ageing and underlies ageing-related diseases.

“We want to fix the things we don’t like about the changes that happen between the age of 30 and the age of 70” – Aubrey De Grey

These include when cells in a tissue are not renewed quickly enough; when cells replicate uncontrollably as occurs in cancer; when cells don’t die when they should, which is another problem in cancer; damage to the DNA of the tiny power plants found in cells, known as mitochondria; the accumulation of waste products inside the cell; waste products that build up outside cells; and the stiffening of the lattice structure outside of cells, called the extra-cellular matrix, which allows tissues to stretch and bend. De Grey and his team at the Sens Research Foundation say they have identified ways for each of these problems to be combatted with therapies they’re developing.

“The fix for the first (problem) of having too few cells is stem cell therapy,” says De Grey. This provides tissue with a fresh supply of young cells to replace those that die during ageing. Other issues, such as when cells don’t die when they are supposed to, may require more complex solutions.

“In principle, we could use gene targeting to introduce suicide genes – genes which the cells will express that will make proteins that will simply kill the cell,” says De Grey. The trick here, however, will be engineering the genes in such a way that they will only express the lethal protein if the cell’s growth patterns are doing more bad than good. De Grey doesn’t think that it will be possible stop ageing altogether with these types of approaches, but they may give patients an extra 30 years or so of life. He envisages a future where “rejuvenation technologies” can be administered to old people in order to revert their cells to what they were like when they were in their youth, buying them extra time. The idea is that someone who is treated at the age of 60 will be biologically reverted to 30. But because the therapies are not permanent fixes, their cells will end up becoming 60 years old again in another 30 years time.

By then De Grey hopes the therapies could be reapplied as “version 2.0” to revert the same individuals once again to become younger in their cells. As a result, that person’s cells wouldn’t become 60 again until they’re about 150 years old. But, there needs to be some caution when dealing with claims like this. There is no experimental evidence to show that our bodies would respond to this sort of “software update”. Much like computers, with too many updates our bodies could grind to a halt. We culturally accept ageing as unavoidable and so attempts to halt the damage it causes are often dismissed as quack science.

But De Grey believes this kind of thinking, something he calls “the pro-ageing trance”, is holding back the advance of anti-ageing technologies. The problem, he says, is that we culturally accept ageing as unavoidable and so attempts to halt the damage it causes are often dismissed as quack science.

And he is not alone in believing ageing-related diseases can be solved. George Church, a geneticist at Harvard Medical School, told us that while some of his colleagues argue many age-related diseases are so complex that they simply can’t be treated, he finds such thinking to be incorrect.

“If you can control both the
environment and the genetics, you can get people that live youthful healthy lives for exceptionally much longer than others,” says Church. “In industrialised nations, most of the diseases are due to age-related diseases and I think those too can be handled.”

Among the prominent approaches to increasing longevity is a gruesome-sounding procedure that is commonly known as “vampire therapy”. Dementia patients who were given transfusions of blood plasma from younger donors aged between 18 and 30 years old showed signs of improvement in a recent trial. Patient’s with early-onset Alzheimer’s disease regained the ability to bathe or dress themselves, or to do other tasks such as housework. While this trial is still ongoing, one US start-up called Ambrosia is already offering older customers the chance to receive transfusions of blood from donors aged between 16 and 25 years old for $8,000 (£5,985) per treatment. The company says that these transfusions can boost the performance of older people’s lethargic cells, and also claims to have improved the condition of an early-onset Alzheimer’s patient as well as have turned the hair of a 60-something-year-old patient darker. Their research, however, has yet to be published in any peer-reviewed journals and has been criticised for not accounting for the placebo effect. But there are some studies in animals that suggest there may be a biological basis for the effects these treatments are having. In 2013, a study by researchers at the Harvard Stem Cell Institute showed the muscle strength of mice could be improved by a growth factor found in young blood called GDF11, though the findings could not be replicated. BBC Future has previously explored some of the other approaches in animals that could lead to a longer life. Meanwhile, others say the key to longevity is as simple as cutting the amount of calories you consume in a day. But what about actually “curing” death? There have long been proposals to do this by cryogenically freezing a person’s brain or body immediately after death so they can be revived at a later date when technology has advanced sufficiently. A number of companies even offer the opportunity for wealthy clients to preserve their bodies in this way, such the Alcor Life Extension Foundation. However, to date, none of their clients have ever been resurrected from their icy storage units.

Others, such as Ray Kurzweil, theorist of the Singularity and lead engineer at Google have espoused “mind uploading” as a way to achieve (at least digital) immortality. It's easy to conflate these outlandish ideas, which seem more based in science fiction than reality, with the lab-based work De Grey and others in longevity research are doing. But regardless of how it is achieved, extending human lifespans by decades or even hundreds of years will present us with some difficult social realities. As BBC Future has explored before, there could be major societal impacts if we all start living longer. There are some that fear greater longevity could lead to swelling populations and raise doubts that our planet could support such numbers. De Grey himself says he is often asked about whether the technologies he is working on could be abused by wealthy tyrants to give them extended lifespans, while others ask whether we will simply be bored by lives that can be continuously extended.

He has little time for such questions and believes that other technologies – such as artificial meat, desalination, solar energy and other renewables – will increase the carrying capacity of the planet, allowing more people to live longer lives. But this rationale suffers from a dependence on uncertain techno-fixes that may not alleviate suffering in an equally distributed manner.

Yet, if concerns like these had paralysed the early pioneers of vaccination and antibiotics, it is unlikely many of us today could expect to live much beyond the age of 40-years-old. Advances in medicine over the last two centuries have taught us that we have the power to defeat the diseases that afflict us. Perhaps if we apply ourselves, then we can beat ageing too.
Case Study

At the Root: Cutaneous Langerhans Cell Histiocytosis

Roberto Maglie, MD, Margherita Vannucchi, MD, Quintarelli, MD, Marzia Caproni, MD, PhD, Daniela Massi, MD, PhD, Emiliano Antiga, MD, PhD Section of Dermatology, Department of Surgery and Translational Medicine, University of Florence, Italy.; Division of Pathological Anatomy, Department of Surgery and Translational Medicine, University of Florence, Italy.

PRESENTATION
Hair loss is of deep concern to patients, mainly because of its effect on appearance. On rare occasions, however, areas of balding can signal malignancy. A 33-year-old woman was referred to our dermatology clinic because of a 15-year history of scalp eruption accompanied by intense itching and progressive hair loss. Previously, she was diagnosed with seborrheic dermatitis associated with female androgenic alopecia. She was treated with topical steroids for numerous years without improvement, except for transient relief of itching. Five years prior to her referral to our clinic, she underwent surgery for an in situ melanoma of the leg. Otherwise, her past medical history was unremarkable.

ASSESSMENT
Physical examination revealed moderate hair thinning of the frontoparietal scalp, a finding in line with the diagnosis of female androgenic alopecia (Figure 1). Numerous follicular-based, erythematous, scaling papules with overlying yellow to brown crusts were noted on the parietotemporal and vertex areas of the patient's scalp, where hair thinning was striking. The interfollicular skin appeared atrophic, as a result of the prolonged steroid applications, but was without erythema or scaling. Areas of scarring alopecia were absent (Figures 2A and B). The rest of the examination was unremarkable. Laboratory investigations, including a complete blood count, a full hormonal and metabolic panel, antinuclear antibody levels, and the erythrocyte sedimentation rate, showed no abnormalities.

The diagnosis of seborrheic dermatitis was questioned because the condition manifests with erythema and desquamation of the scalp and involves both perifollicular and interfollicular skin. At the same time, the patient's hair loss in the parietotemporal and vertex regions could not be explained by her previous diagnosis of androgenic alopecia, which commonly spares those areas in females.

Thus, a 4-mm punch biopsy was taken from a papular lesion. Histopathology showed dermoepidermal detachment and a dermal infiltrate composed of what appeared to be Langerhans cells, clusters and sheets of large ovoid cells with abundant eosinophilic cytoplasm, and a reniform nucleus. This accumulation of cells tended to have a periadnexal distribution, leading to follicular atrophy, and the accumulation of cells was mixed with numerous lymphocytes, plasma cells, neutrophils, and eosinophils.

Immunohistochemical analysis produced reactions with antibodies against CD1a and S100 protein, confirming the presence of Langerhans cells (Figures 3A-F). Immunohistochemical analysis to detect the BRAF V600E mutation in lesional tissue was negative. Molecular analysis through mass spectrometry base sequencing (Sequenom Laboratories, San Diego, CA) confirmed the absence of the BRAF V600E mutation.

DIAGNOSIS
Based on the combined clinical, histologic, and molecular findings, a diagnosis of Langerhans cell histiocytosis was made. To stage the disease, a total-body computed tomography scan and positron emission tomography were performed. No internal organ involvement was seen.

Langerhans cell histiocytosis is a malignant histiocytic disorder, affecting 1-2 adults and 5-9 children per million.

Clinical variants, ranging from self-healing to life threatening, are characterized by the proliferation of myeloid precursors of dendritic cells with ultrastructural and immunophenotypic features of epidermal Langerhans cells.2 In adults, skin-limited forms are rare; most patients with cutaneous involvement display localized disease in internal organs.3 Currently, cutaneous manifestations occur in nearly 40% of patients.

Cutaneous Langerhans cell histiocytosis preferentially localizes to cutaneous areas where there is a
high production of sebum areas where seborrheic dermatitis typically occurs and flexures. Widespread eruptions or the involvement of genitalia and mucous membranes are also common. The clinical presentation frequently overlaps with that of benign inflammatory diseases, including intertrigo, seborrheic dermatitis, prurigo nodularis, or infections. As a result, diagnosis may be significantly delayed, as the clinical findings generally do not suggest Langerhans cell histiocytosis. Rather, Langerhans cell histiocytosis is most commonly suspected when cutaneous lesions fail to improve with local treatments.

Our patient experienced an unusual presentation. Although there have been reports of Langerhans cell histiocytosis confined to the scalp, including cases with folliculocentric infiltrates, all patients retained normal hair growth. Her diagnosis of androgenic alopecia, which frequently coexists with severe seborrheic dermatitis, represented a major diagnostic pitfall, as it obscured the true cause of hair.

**MANAGEMENT**

Treatment of Langerhans cell histiocytosis has to be based regions, Langerhans cell histiocytosis infiltrated the hair follicles.

Regardless of the organ involved, the diagnosis of Langerhans cell histiocytosis should be considered in patients with unexplained hair loss.
Histiocytosis needs to be confirmed by histopathologic and immune histochemical analyses, and eventually by detecting Birbeck granules through electronic microscopy. In our patient’s case, pathologic histiocytes were positive for the Langerhans cell antigens CD1a and S100 protein, allowing us to exclude other histiocytic or macrophage-dendritic cell neoplasms.

More than 50% of patients with Langerhans cell histiocytosis harbor the BRAF V600E hotspot mutation. Additional mutations have been found in other mitogen activated protein kinase genes, highlighting the pivotal role of that type of oncogenic signaling in a subset of patients. The clinical heterogeneity of Langerhans cell histiocytosis is likely to depend on several elements, including the patient’s specific mitogen-activated protein kinase gene mutation and the manner in which that gene influences the differentiation of the dendritic cell precursor.

Neither immunohistochemistry nor molecular analysis identified the BRAF V600E mutation in our patient. It is possible to speculate that a yet-unknown clonal event occurred in a mature Langerhans cell precursor that was committed to the scalp skin and hair follicles, explaining the absence of systemic disease or additional cutaneous localizations and the indolent clinical course of the patient’s illness.

Treatment of Langerhans cell histiocytosis has to be based on the extent of the patient’s disease and the expected outcome. Adult patients with multisystem disease are candidates for chemotherapy, usually vinblastine-containing regimens. For those harboring the BRAF V600E mutation, the BRAF kinase inhibitor vemurafenib has shown excellent results, but relapse is invariably observed upon treatment discontinuation. Even with treatment, adult Langerhans cell histiocytosis is associated with long-term morbidity and an overall mortality rate of 3%.

Patients with skin-limited disease may benefit from less aggressive approaches. Treatment with oral methotrexate, 6-mercaptopurine topical corticosteroids, topical nitrogen mustard (mechlorethamine), or oral thalidomide has been effective.

Although Langerhans cell histiocytosis limited to the skin generally has a better outcome than multisystemic forms, patients with cutaneous disease may develop systemic involvement; they also have a higher risk of secondary hematologic malignancies, mostly Hodgkin lymphoma. Therefore, it is important to have multidisciplinary follow-up by general practitioners, hematologists, radiologists, and dermatologists. An informal recommendation is to conduct laboratory testing every 6 months, including a complete blood count, a full hormonal and metabolic panel, lactate dehydrogenase and beta-2 microglobulin levels, ultrasonography of the abdomen, and a chest x-ray.

Our patient was prescribed oral methotrexate, and treatment is ongoing. She has had moderate improvement of her symptoms. Her Langerhans cell histiocytosis, initially misdiagnosed as seborrheic dermatitis, was associated with progressive alopecia. Fortunately, no life-threatening complications occurred despite the extended delay in a correct diagnosis. Her disease remains confined to the skin. Clinicians should remember to include Langerhans cell histiocytosis in the differential diagnosis when a patient has inflammation-like skin eruptions that are unexpectedly resistant to classic treatments.
Interest in modifying the gut flora by consuming foods or microbes that may improve overall health dates back to the early 1900s, when it was theorized that certain milks and yogurts may provide a health benefit to the populations consuming them.

The mechanisms of action of probiotics in various diseases are not completely understood, but several hypotheses have been proposed. One theory is that the gut microbiome influences visceral hypersensitivity and pain and that Lactobacillus-induced expression of mu-opioid and cannabinoid receptors in the intestinal epithelium may be able to mediate pain in a manner similar to that of opiates. Another proposed mechanism is modulation of the immune system, and several studies have found that probiotics or their products suppress inflammatory cytokines and stimulate protective cytokines, mostly in models of inflammatory bowel disease (IBD). Finally, probiotics may promote integrity of the intestinal epithelium, protecting intestinal epithelial tight junctions and barrier function, and may create biofilms that secrete factors that can inhibit pathogen invasion.

As understanding of the gut microbiota and the complex interactions involved in inflammation, gut permeability, and dysbiosis advances, the use of probiotics is appealing to clinicians and patients alike. However, while enthusiasm has skyrocketed—particularly in the world of nutritional supplements—scant data support the use of probiotics; the gastrointestinal diseases for which they have benefits and the species that confer these benefits remain unclear, resulting in confusion among both clinicians and consumers. This article provides recommendations for the selection of a probiotic regimen where evidence appears strong and discussion of certain areas where more research is needed before more conclusive recommendations can be made.

**Evidence Search**

The methods used for finding the recommendations involved searching via PubMed, OVID, and the Cochrane Review Library for the terms “probiotics,” “indications,” “dosing,” “pouchitis,” “infectious diarrhea,” “antibiotic-associated diarrhea,” “constipation,” “irritable bowel syndrome,” “hepatic encephalopathy,” “ulcerative colitis,” “Crohn’s disease,” and “Clostridium.” Results were further narrowed into randomized controlled trials, meta-analyses, and review articles in which information about specific strains and dosing could be found. Recommendations were selected based on the relative robustness of the relevant data.

**Pouchitis**

The diagnostic indication in which the data are the strongest is pouchitis. In severe ulcerative colitis (UC) and familial adenomatous polyposis for which a total colectomy is required, the appropriate procedure is a proctocolectomy with ileal pouch-anal anastomosis. The most frequent...
long-term complication of this surgical correction is acute or chronic inflammation of the S- or J-shaped ileal pouch. Symptoms of pouchitis include abdominal pain, fever, hematochezia, urgency, and increased stool frequency. Pouchitis patients have distinct microbial patterns likely due to fecal stasis and colonic metaplasia from the original ileal mucosa, creating an inflammatory milieu associated with bacterial species such as Bacteroidaceae and Clostridiaceae species. Enterococcaceae may have a role in maintaining immunologic homeostasis in the mucosa. The use of probiotics has been found to be most effective in randomized, placebo-controlled trials in both primary and secondary prophylaxis, particularly with the use of VSL#3 (Alfasigma)—a probiotic containing *Bifidobacterium breve*, *B. longum*, *B. infantis*, *Lactobacillus acidophilus*, *L. plantarum*, *L. paracasei*, *L. brevis*, *B. longum*, *B. infantis*, *Lactobacillus*, and *Streptococcus thermophiles*.

Primary prophylaxis has been studied at a dose of 3 g per day for 12 months. Secondary prophylaxis of relapsing pouchitis has been studied at a dose of 6 g per day from 9 months to 1 year. Although antibiotics remain the drug of choice for periods of inflammation, high-dose VSL#3 at a dose of 2 sachets twice daily (3,600 billion bacteria per day) for 4 weeks has been found to be effective for the treatment of mild pouchitis (between 7 and 12 on the Pouchitis Disease Activity Index).

**Infectious Diarrhea**

Infectious diarrhea is another well-studied indication warranting the use of probiotics, but most data are in the pediatric population. A Cochrane Review found that all included studies reported a reduced stool frequency by day 2 and shortened duration of diarrhea by around 25 hours in patients who received probiotics. Probiotics were not associated with any adverse effects (AEs). The most common organism evaluated is the *L. casei* strain GG, which has been used in 13 studies at a dose of 6×10⁹ colony forming units (CFU) twice a day for 5 days.

**Traveler’s Diarrhea**

The use of probiotics also has been studied for prevention of traveler’s diarrhea. Specifically, *Lactobacillus GG* has been shown to be effective because it is acid and bile resistant, adheres to ileal cells, and produces an antimicrobial substance. In a double-blind, placebo-controlled study from Finland, *Lactobacillus GG* was used to prevent traveler’s diarrhea, with protection rates of 1.8% to 39.5%. Another study found that taking *Lactobacillus GG* powder in capsules at a dose of 2×10⁹ bacteria starting 2 days before departure and continuing throughout the trip reduced the risk for diarrhea from 7.4% per day to 3.9% per day.

**Antibiotic-Associated Diarrhea**

A form of infectious diarrhea related to the use of antibiotics is caused by *Clostridium difficile* and is referred to as *Clostridium difficile*-associated diarrhea (CDAD). It is a commonly encountered infection that probiotics have been proven to prevent. The mechanism of action includes alteration of intestinal flora, antimicrobial activity, intestinal barrier protection, and immunomodulation. A systematic review of probiotic use to prevent *C. difficile* infection in hospitalized patients found that probiotics reduced the risk for CDAD by more than 50% when they were taken within 2 days of the first antibiotic dose, with no evident increase in AEs.

There are 2 recommended probiotic regimens. The first is *L. acidophilus* at a dose of 25×10⁹ CFU per day for 2 days, followed by 50×10⁹ CFU per day for the duration of the antibiotic course. Alternatively, *L. casei* can be used at a dose of 19×10⁹ CFU per day with *L. bulgaris* 1.9×10⁹ CFU per day and *S. thermophiles* 19×10⁹ CFU per day, started within 48 hours of initiating antibiotic therapy and continuing until 7 days after cessation of antibiotic therapy. There is insufficient evidence to recommend probiotics alone as treatment for active CDAD, but they may be used as adjunctive therapy to antibiotics in non-severe recurrent disease if no significant comorbidities are present.

**Helicobacter pylori Infection**

Another antibiotic-associated indication for probiotics is in patients undergoing therapy to eradicate *Helicobacter pylori*. In an updated, evidence-based international consensus, experts concluded that probiotics are helpful as adjuvant therapy to prevent or reduce the duration or intensity of associated diarrhea in patients receiving *H. pylori* treatment. In a randomized, placebo-controlled study, patients taking a standard *H. pylori* regimen supplemented with probiotics reported a lower incidence of AEs, including diarrhea, and overall treatment tolerability was improved. The probiotic was given during and for 7 days after *H. pylori* therapy; patients received one of several effective regimens, including *Lactobacillus GG* (Giflorex, Errekappa Euroterapici) administered twice daily, *Saccharomyces boulardii* (Codex, SmithKline Beecham) given twice daily, and a combination of *Lactobacillus* and *Bifidobacteria* administered twice daily.

**Constipation**

Using probiotics in patients who have non-severe chronic constipation and do not have irritable bowel syndrome (IBS)
also has been studied. A randomized, double-blind, placebo-controlled study showed that a probiotic beverage containing *L. casei* Shirota at a dose of 6.5×10⁹ CFU or 65 mL per day for 4 weeks resulted in a significant improvement in both stool frequency and consistency starting in the second week of intervention. Another randomized controlled trial found that *E. coli* Nissle 1917 at a dose of 25×10⁹ CFU for 8 weeks increased stool frequency.

**Irritable Bowel Syndrome**

In IBS, the data are limited largely by methodological shortcomings, but they are more promising for the diarrhea variant (IBS-D). Controlled trials have shown that *B. infantis* 35624 at a dose of 1×10⁸ CFU per day for 4 weeks can improve abdominal pain, bloating, bowel dysfunction, incomplete evacuation, straining, and the passage of gas. One capsule of *B. bifidum* MIMBb75 dosed at 1×10⁹ CFU over 4 weeks effectively alleviates global IBS and improves IBS symptoms simultaneously with a subjectively reported improvement in quality of life. Studies examining a number of Lactobacillus species, including *L. salivarius* UCC4331, *L. plantarum* DSM9843, *L. plantarum* LPO1, and *L. plantarum* 299V, as well as *B. bifidum* MIMBb75, *B. breve* BR, and VSL#3 also have shown an improvement in patient-reported symptoms, including flatulence and bloating, but have shown no overall effect on stool quality or frequency.

**Hepatic Encephalopathy**

In various forms of chronic liver disease, the liver—secondary to damage and diverted blood flow—loses the ability to clear ammonia from the body. The increasing levels of ammonia lead to a reversible encephalopathy known as hepatic encephalopathy. Treatment is aimed at either increasing the excretion of or decreasing the production of ammonia. Lactulose, a prebiotic, works via ion trapping coupled with a potent laxative effect. Rifaximin (Xifaxan, Salix) works by decreasing the population of urease-producing bacteria. Probiotics are theorized to work by making the gut environment more favorable for non-urease-producing bacterial species or modifying the pH of the gut lumen, thereby decreasing the production of ammonia and preventing or reversing hepatic encephalopathy.

A randomized controlled trial has shown that a dose of 3 capsules per day containing 112.5 billion viable lyophilized bacteria per capsule, each containing 4 strains of *Lactobacillus* (*L. casei*, *L. plantarum*, *L. acidophilus*, and *L. delbrueckii*) *subsp bulgaricus*), 3 strains of *Bifidobacterium* (*B. longum*, *B. breve*, and *B. infantis*), and 1 strain of *Streptococcus salivarius* (*subsp thermophilus*) was more effective than no treatment for secondary prophylaxis of clinical hepatic encephalopathy, and was as effective as standard lactulose therapy. Overall, however, no mortality benefit has been identified to support the use of probiotics alone in the treatment of hepatic encephalopathy.

**Ulcerative Colitis**

Alterations in gut microbiota have been shown to play a role in the pathogenesis of Crohn’s disease (CD) and UC. As with many of the other indications discussed, strong evidence is lacking in IBD because of small sample sizes, variations in probiotic regimens, or variations in dosing. However, in 2 randomized controlled trials, *E. coli* Nissle 1917 given at a dose of 200 mg per day (2.5-25×10⁹ viable bacteria per capsule) for 12 months was found to be at least as effective as mesalamine in the prevention of relapse of UC during symptom-free periods in patients followed over 1 year. Furthermore, there were no significant differences between mesalamine and *E. coli* Nissle 1917 in safety and tolerability measures in UC patients.

**Crohn’s Disease**

In CD, the data, again, are minimal and overall show either no significant difference between any studied probiotic strain alone and placebo or, less optimistically, show worse outcomes compared with standard medical therapies. A small randomized controlled trial has shown that a dose of 2×10¹¹ CFU of freeze-dried viable *B. longum* in a gelatin capsule, and a sachet containing 6 g of Synergy I (Orafti, Tienen) given twice daily for 6 months, resulted in an improvement in both endoscopic and histologic scoring of CD compared with placebo alone. This intervention, however, did not lead to improvement in patient-reported symptoms. At the time of this writing, there were no data recommending the use of probiotics alone in the maintenance or induction of remission in CD.

**Cautions and Considerations**

It is imperative that clinicians consider and discuss contraindications and risks when recommending and prescribing probiotics for patients. Hypothetically, probiotics may translocate out of the gut, causing bacteremia or fungemia, as well as contamination of the product, and, therefore, caution is advised when they are used in immunocompromised, hospitalized, or postoperative patients.

In addition, commercially available probiotics may be contaminated with allergens, such as cow’s milk protein, and, therefore, should be avoided in patients with severe allergies. An abstract from the Celiac Disease Center presented at the 2018 Digestive Disease Week found that there is significant contamination of probiotics with...
gluten, and, thus, celiac patients should be cautious when using these products. In addition, there are not enough safety data on the use of probiotics during pregnancy, although published studies thus far have not found any AEs. Pregnant women also should avoid any unpasteurized products.

Another important aspect of counseling patients when recommending probiotics is to discuss the utility of eating yogurt as a source of probiotics. Some yogurts made in the United States are pasteurized, a process that kills live bacterial cultures. In addition, studies have shown that live cultures in yogurt may not survive in the low pH of the product; they may not persist during prolonged shelf time or transit through the acidic stomach; and they may not resist degradation in the small intestine by hydrolytic enzymes and bile salts. Therefore, it is not known how much of the live cultures reach the distal gut and colonize the microbiota after the above processes, leading to questions about the clinical utility of ingesting yogurt for the probiotic content. Other foods to consider that contain live cultures include kimchi (a Korean fermented cabbage dish), sauerkraut (fermented cabbage), miso (a fermented soybean-based paste), pickles, kombucha (a fermented tea), and apple cider vinegar (made from fermented apple sugars).

**Conclusion**
The data remain strongest for the use of probiotics in pouchitis at a dose of 3 g per day of VSL#3 for primary prophylaxis, and 6 g per day for secondary prophylaxis. Symptomatic relief of infectious diarrhea also may be achieved with a dose of 6×10⁹ CFU of *L. casei* strain GG twice a day for 5 days. There is not enough evidence to use probiotics alone to treat *C. difficile* infection, but there are probiotic regimens that are effective as a preventive measure in people at high risk for infection while they are receiving antibiotic therapy. The evidence for probiotics in IBS and hepatic encephalopathy is promising. With regard to IBD, currently there are not enough supporting data to use probiotics.

When discussing probiotic use with patients, ensure you’ve discussed the risks, benefits, and contraindications of their use. Consider concentrated, rigorously tested probiotic strains, in addition to foods that are able to deliver live bacterial cultures past the initial stages of digestion. Make sure patients are taking the correct regimen for the appropriate indication, and caution them that the data for other diseases are preliminary and likely will advance in the coming years. As such, the recommendations on probiotic strains and dosing may change as research continues in this field.
Renal tubular acidosis & hypokalemic paralysis as a clinical presentation of primary Sjögren’s syndrome

Abstract
Sjögren’s syndrome is an autoimmune disease with multisystem involvement and varied clinical presentation. We report the clinical course and outcome of a case who presented with repeated episodes of hypokalemia mimicking hypokalemic periodic paralysis and metabolic acidosis, which was later diagnosed as distal renal tubular acidosis secondary to primary Sjögren’s syndrome. A 50-year-old lady, who was previously diagnosed as hypokalemic periodic paralysis presented with generalized weakness and fatigue. She was found to have severe hypokalemia with normal anion-gap metabolic acidosis consistent with distal renal tubular acidosis. Subsequent evaluation revealed Sjögren’s syndrome as the cause of her problems. Kidney biopsy done to evaluate significant proteinuria revealed non-proliferative morphology with patchy acute tubular injury and significant chronic interstitial nephritis. The patient responded well to potassium supplementation and oral prednisolone. Presentation of this case highlights the necessity of close vigilance while managing a case of repeated hypokalemia, which could be one of the rare clinical manifestation of Sjögren’s syndrome.

1. Introduction
Sjögren’s syndrome (SS) is a slowly progressing autoimmune disease characterized by lymphocytic infiltration of the exocrine glands, mainly the lacrimal and salivary glands, resulting in impaired secretory function. The disease has an estimated prevalence of 0.3 to 1 per 1000 persons and a peak incidence at approximately 50 years of age with female-to-male predominance of 9:1.

Renal involvement is seen in 5% of patients with SS, most common of which being chronic interstitial nephritis. Renal tubular acidosis (RTA) occurs in up to 25% of patients with the disease, most of which are usually asymptomatic. We report a case requiring multiple hospital admissions with a clinical diagnosis of hypokalemic periodic paralysis previously presented to us with severe hypokalemia associated with metabolic acidosis, which was later diagnosed to be secondary to Sjögren’s syndrome.

2. Case report
A 50-year-old woman presented to the emergency department (ED) of Chitwan Medical College, Bharatpur, Chitwan Nepal with the history of weakness of both lower limbs for two days that was preceded by muscle cramps of three days’ duration. Her weakness was insidious in onset and gradually progressive in nature affecting the upper limbs by next day with no history of altered sensorium, seizure and bladder or bowel involvement. Her past medical history was positive for repeated episodes of weakness and fatigue associated with hypokalemia for the past three years, which was managed in the line of hypokalemic periodic paralysis that responded well to supplemental potassium alone. She also had similar problems episodically for the past three years. She denied history of vomiting and intake of diuretics, alcohol or laxatives. Previous medical records revealed negative results for antibody against acetylcholine receptor that ruled out myasthenia gravis.

On physical examination, vital signs were within normal limit and higher mental functions were intact. Her oral cavity was dry and there was no lymphadenopathy. Motor power was 3/5 on the lower limbs and 4/5 on the upper limb affecting both proximal and distal group of muscles. Deep tendon reflexes were diminished bilaterally. There was no sensory deficit and cranial nerve examination was unremarkable. Cardiovascular,
respiratory, gastrointestinal and thyroid examination findings were normal.

She was found to have hypokalemia (documented serum K+ of 1.6 meq/L; normal range 3.5–5.5 meq/L) (Table 1). ECG showed a sinus bradycardia with global T wave inversion and the presence of subtle U wave.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>10.0 (g/dl)</td>
</tr>
<tr>
<td>WBC</td>
<td>5600 (per mm3)</td>
</tr>
<tr>
<td>Platelets</td>
<td>298,000 (per mm3)</td>
</tr>
<tr>
<td>ESR</td>
<td>67 (mm/1st hour)</td>
</tr>
<tr>
<td>Serum Na+</td>
<td>148 (mEq/L)</td>
</tr>
<tr>
<td>Serum K+</td>
<td>1.6 (mEq/L)</td>
</tr>
<tr>
<td>Serum Urea</td>
<td>29 (mg/dL)</td>
</tr>
<tr>
<td>Serum Creatinine</td>
<td>1.0 (mg/dL)</td>
</tr>
<tr>
<td>Random blood sugar</td>
<td>130 (mg/dL)</td>
</tr>
<tr>
<td>Serum Magnesium</td>
<td>2.5 (mg/dL)</td>
</tr>
<tr>
<td>Serum Calcium</td>
<td>8.36 (mg/dL)</td>
</tr>
<tr>
<td>Serum pH</td>
<td>7.20</td>
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<tr>
<td>pCO2</td>
<td>18.8 (mmHg)</td>
</tr>
<tr>
<td>HCO3</td>
<td>7.1 (mEq/L)</td>
</tr>
<tr>
<td>pO2</td>
<td>89 (mmHg)</td>
</tr>
<tr>
<td>Serum Chloride</td>
<td>130 (mmol/L)</td>
</tr>
<tr>
<td>Anion Gap</td>
<td>11.9 (mmol/L)</td>
</tr>
<tr>
<td>Serum Vitamin 25(OH) D</td>
<td>6.40 (ng/ml)</td>
</tr>
<tr>
<td>Parathyroid hormone</td>
<td>145 (pg/ml)</td>
</tr>
<tr>
<td>TSH</td>
<td>8.74 (mIU/ml)</td>
</tr>
<tr>
<td>Urine pH</td>
<td>5.0</td>
</tr>
<tr>
<td>Urine K+</td>
<td>34.6</td>
</tr>
<tr>
<td>HIV, HBsAG, Anti-HCV</td>
<td>Negative</td>
</tr>
</tbody>
</table>

Serum Anion Gap = Na – (Cl + HCO3)

In the emergency department, the patient was started on intravenous potassium supplementation at the rate of 20 meq/hour via central line and was admitted to the intensive care unit (ICU), where treatment was continued and serial monitoring of potassium level was done. Consecutive serum potassium level at 6th, 12th and 48th hour after initiation of treatment were 1.75 mmol/L, 2.1 mmol/L and 3.7 mmol/L respectively. Intravenous magnesium supplementation and injection sodium bicarbonate were also given. After 12 hours of treatment, her clinical condition improved significantly with normalization of the muscle power. With the urinary pH of 5.0, negative urine culture and no history of diuretic usage, vomiting and diarrhea and the arterial blood gas (ABG) showing hyperchloremic normal anion gap metabolic acidosis in a patient with severe hypokalemia (serum potassium 1.7 mmol/L), the diagnosis of distal renal tubular acidosis (DRTA) was made. With the history of xerostomia and xerophthalmia without any secondary causes for them, SS was suspected, which was later confirmed by the significantly raised titers of anti-Ro/SSA and/or anti-La/SSB antibodies and positive schirmer test as per the latest classification criteria.

She was started on oral prednisolone at 1 mg/kg/day after which ptosis showed partial recovery in the first 7 days. She was discharged with the same dose of prednisolone and was advised for regular follow up in nephrology clinic. The patient attended the Nephrology clinic after 7 days with palpable purpuric rashes in the both of the lower limbs associated with minimal pedal edema (Figure 1).

Fig. 1: Palpable purpura on the lower limb.
She was re-evaluated and found to have normal hemogram and bleeding profile; and negative perinuclear anti-neutrophil cytoplasmic antibodies (P-ANCA) and cytoplasmic anti-neutrophil cytoplasmic antibodies (C-ANCA). Urine examination showed 2+ albumin without associated hematuria and 24-hour urinary protein was 1600 mg, for which she underwent kidney biopsy. Light microscopy showed non-proliferative glomerular morphology (Figure 2) with patchy acute tubular injury and multifocal chronic interstitial inflammation (Figure 3). Direct immuno-fluorescent examination revealed no significant glomerular immune deposits. Transmission electron microscopy revealed relatively well preserved visceral epithelial cell foot processes (Figure 4) and no evidence of glomerular or extraglomerular electron dense deposits. Endothelial tubuloreticular inclusions were not seen. Proximal tubular epithelial cells did not reveal abnormal inclusions or giant mitochondria.

The patient is on regular follow up and the oral steroids is getting tapered gradually. She is doing well with improvement in proteinuria, resolution of acidosis and hypokalemic episodes.

3. Discussion
Our patient presented with the complaints of muscle weakness secondary to severe hypokalemia (serum K+ 1.6 meq/L). On further evaluation in our center, she had normal anion gap hyperchloremic metabolic acidosis (HCMA). Despite lack of a more comprehensive evaluation, the biochemical findings of renal potassium loss in association with HCMA was supportive of the diagnosis of distal renal tubular acidosis (RTA) in our patient. Further history obtained from the patient revealed that she had a history of foreign body sensation in the eyes, and dry mouth for the past three years, which prompted us to evaluate for the possibility of Sjögren’s syndrome as the root cause of her recurrent clinical problems. Significantly raised titers of anti-Ro/SSA and anti-La/SSB antibodies and positive schirmer test confirmed Sjögren’s syndrome. She later developed significant proteinuria, for which kidney biopsy was done that showed non-proliferative morphology with patchy acute tubular injury and focal chronic interstitial inflammation. She was started with oral prednisolone and was kept on regular follow ups with significant clinical improvements.
Sjögren’s syndrome is a systemic autoimmune disorder characterized by a unique set of signs and symptoms predominantly caused by a cell-mediated autoimmunity against exocrine glands. Systemic manifestations occur in approximately 30 to 40% of the patients with primary Sjögren’s syndrome. Lymphocytic infiltration can cause interstitial nephritis, autoimmune primary biliary cholangitis, and obstructive bronchiolitis. Immune complex deposition can result in palpable purpura, cryoglobulinemia-associated glomerulonephritis, interstitial pneumonitis, and peripheral neuropathy.

The most common non-exocrine organ affected in Sjögren’s syndrome is kidney with the prevalence ranging between 2-67%. Most common form of renal involvement in Sjögren’s syndrome is interstitial nephritis followed by distal renal tubular acidosis (dRTA), nephrogenic diabetes insipidus and different forms of glomerular diseases, of which membranoproliferative glomerulonephritis (MPGN) and membranous nephropathy (MN) are the most common. Although dRTA is common in Sjögren's syndrome, it is usually asymptomatic and in most cases it remains undetected. Hypokalemia is the most common electrolyte abnormality in patients with dRTA. The causes of hypokalemia include decreased distal tubular Na+ delivery, secondary hyperaldosteronism, defective H+-K+ ATPase, and bicarbonaturia. Hypokalemic paralysis seen in SS is rare and may sometimes mimic hypokalemic periodic paralysis (HPP). However, there are case reports of single presentation of severe hypokalemic paralysis, which was later confirmed as Sjögren’s syndrome.

A diagnosis of primary Sjögren’s syndrome is often considered based on the classic symptoms of mouth and eye dryness, fatigue, and pain. However, systemic complications sometimes provide the first clue to the disease as seen in our case, in which the presenting complaint was muscle weakness secondary to severe hypokalemia and metabolic acidosis. Anti-SSA antibodies (antibodies against Sjögren’s syndrome–related antigen A) are present in two thirds of patients and should be assessed in all suspected cases of primary Sjögren’s syndrome. Biopsy of minor salivary glands is typically recommended for establishing a diagnosis of primary Sjögren’s syndrome in the absence of anti-SSA antibodies. Schirmer’s test to assess the ocular dryness is a useful examination. A recent set of classification criteria for SS were published by the ACR/EULAR in 2016 and the score of ≥4 is required for the diagnosis.

Management of primary SS is symptomatic. In the acute setting, when the patient presents with hypokalemia, the priority will be to reverse the severe hypokalemia with intravenous potassium supplementation, followed by correction of the underlying acidosis. Long term use of potassium supplementation might be required for majority of the patients. Use of muscarinic agonists (pilocarpine hydrochloride and cevimeline hydrochloride) is recommended for the treatment of oral dryness and, to a lesser extent, ocular dryness. Neuropathic pain in patients with primary Sjögren’s syndrome is typically treated with gabapentin, pregabalin, or duloxetine. Although no immunomodulatory drug has been proved to be efficacious in primary SS, combination of corticosteroids and other immunosuppressive drugs have been reported to slow the progression of renal damage in Sjögren’s syndrome. Agents that are commonly used include hydroxychloroquine, prednisone, methotrexate, mycophenolate sodium, azathioprine, and cyclosporine. Few biologic agents have been rigorously studied in primary SS, and none have shown significant efficacy in multiple studies. The heterogeneity in the etiopathogenesis and clinical manifestation of the disease, in conjunction with a variable response to clinical therapeutics, warrants a more individualized approach to achieve improved long-term outcomes in patients with primary SS.

Our patient had repeated episodes of hypokalemia and metabolic acidosis in the past, which responded symptomatically to potassium supplementation alone. Thus, she was labelled as a case of hypokalemic periodic paralysis but detailed work ups for the etiopathogenesis of her problem was missed.

4. Conclusion
Although Sjögren’s syndrome might have a varied clinical presentation and presentation of a person with renal symptoms in the form of hypokalemia as the first symptom might create the confusion to reach the diagnosis. This case highlights the importance of high index of suspicion for possibility of Sjögren’s syndrome, especially in the middle-aged females, who present with hypokalemia and metabolic acidosis.

Consent
The patient has given informed written consent for this case report to be published.

Disclosure
The authors confirm that this case report has not been submitted or published at any form previously.

Conflicts of Interest
The authors declare that they have no conflicts of interest regarding the publication of this paper.
References


Hungry for Health: Fasting's Medical Benefits

John Watson

For most of us, a growling stomach is a siren song calling us to our refrigerator. However, for researchers and adherents of intermittent fasting (the practice of voluntarily abstaining from food and non-water beverages), hunger is something not to vanquish but rather to embrace.

Fasting has been shown for years to be an effective non-pharmacologic strategy for counteracting some of the most entrenched modern ailments, from cardiovascular disease and cancer to diabetes and diminishing cognition. The stumbling block was that this evidence was derived primarily from studies in rats and mice, which meant that intermittent fasting remained an interesting, but somewhat fringe, field of research. That has decidedly changed, though, with the recent publication of some small but promising investigations showing positive outcomes in humans.

"In the early 1990s, my own science colleagues viewed fasting as irrelevant, and it was largely ignored by the medical community," explained Valter Longo, PhD, a forerunner of fasting research and director of the Longevity Institute at the University of Southern California, Los Angeles. "Now things are changing very rapidly, and fasting is the most widely adopted diet in those under age 34 in the United States."

Fasting is the most widely adopted diet in those under age 34 in the United States.

"Intermittent fasting" is an admittedly vague umbrella term but one that is nonetheless useful for describing a wide variety of regimens.

The most popular fasting regimen is undoubtedly the 5:2 diet, in which participants restrict themselves to approximately 500-600 calories 2 days a week but eat as they normally would for the remaining 5 days. It comes garnished with all-important celebrity endorsements (for example, Jimmy Kimmel and Benedict Cumberbatch) and glossy coverage in magazines you would find at any grocery store checkout lane.

Other common regimens include time-restricted feeding (eat a standard amount of calories, but only within a limited time frame), alternate-day fasting (eating nothing one day, then whatever you like the next), and periodic fasting (abstaining from food and energy-containing beverages for continuous days, sometimes stretching out to 3 weeks). In addition, researchers such as Longo are investigating the efficacy of fasting-mimicking diets for reducing markers of aging and risks for age-related diseases.

Because there have been no large randomized controlled trials comparing these regimens, we cannot yet establish superiority for any. Trends uncovered in clinical studies...
Why Fasting May Work
When our bodies enter a fasting state, we deplete the stores of glucose in our livers and convert to fat-derived ketone bodies. Depending on your physical output during the fasting period, you can enter a ketogenic state within hours.

Proponents of fasting as a dietary intervention will probably have little difficulty communicating why there might be benefits to substituting ketones for glucose and the myriad negative health effects it can cause when poorly regulated. However, they may find more resistance in overcoming the common belief that fasting slows down metabolic rates, which raises the question: If your body is compensating for lack of food in this manner, wouldn’t this simply offset or limit any advantages to be gained?

In fact, this long-standing assumption began to change toward the end of the 20th century, when research emerged indicating that fasting for durations of a few days had the opposite effect of increasing metabolism. The full spectrum of physiologic mechanisms contributing to increased metabolism during early food restriction is complex, involving such factors as circadian rhythm and upticks in the fat-burning hormone norepinephrine. However, the utility of this approach is borne out by clinical studies of metabolic outcomes. A recent review identified 16 such studies that, although primarily consisting of cohorts of less than 50 patients, nonetheless show different fasting regimens produced notable decreases in glucoregulatory markers, lipids, inflammatory markers, and weight.

The increasing popularity of fasting diets among the general public may also be due to how easily these align with the consensus that there is something amiss with the modern diet. Although our bodies retain the ability to get by quite capably for long periods in a ketogenic state, we happen to live in a society where the predominant eating schedule makes doing so extremely difficult.

“If you look back in the literature, the recommendation that we eat three meals a day with some snacking on top is mainly based on studies of diabetics, and the notion was that you don’t want to have big spikes in glucose,” said Mark P. Mattson, PhD, chief of the Laboratory of Neurosciences at the National Institute on Aging, and professor of neuroscience at Johns Hopkins University in Baltimore, Maryland. “But it turns out that intermittent fasting actually improves glucose regulation in both animals and humans.”

If you consider that our bodies evolved over millennia to function in one way (hunter-gatherer systems defined by periodic food scarcity) but have been wrenched into another system in a relatively short period, it takes only a small mental leap to see how this may play a role in our contemporary crisis of food-related illnesses.

The epidemic of obesity...occurred in the past 40 years with the eating pattern of three meals a day plus snacks.

“The epidemic of obesity, including childhood obesity, occurred in the past 40 years with the eating pattern of three meals a day plus snacks,” Mattson added. “So clearly, that is not necessarily a healthy eating pattern. If people can avoid overeating by skipping meals, once they adapt to that, it can only be a good thing.”

The Fasting Brain
Mattson’s research centers on a possibly more surprising benefit of fasting: its ability to enhance cognition and brain function. He and others have provided abundant animal data showing that fasting-related ketogenic states lead to cellular and molecular adaptions in the brain that confer such benefits as resistance to stress, injury, and disease.

“Another interesting finding is if you take rats or mice and reduce their calorie intake aggressively—a 40%-50% reduction in calories approaching starvation—their heart, liver, gut, and muscles all decrease in size, but the brain remains the same size.”

Here, too, we have a compelling evolutionary explanation. Ketones are an exceptional energy source for the brain, more so than the unreliable fluctuations of glucose. It is likely that mammals who excelled at surviving long periods of food deprivation were naturally selected for optimal brain function in that state.

Mattson and colleagues at the National Institute on Aging are currently running a trial in which participants at risk for cognitive impairment owing to age (55-70 years) and metabolic status (body mass index ≥ 30 kg/m2, insulin resistant but nondiabetic) are randomly assigned to receive either the 5:2 diet or control (healthy eating). After 2 months, they are tested for...
cognition and psychological factors, in addition to undergoing functional MRI on network activity in the brain and spinal taps for brain-derived neurotrophic factor, which animal studies suggest is critical for learning and memory.

"On the basis of what we know about the impact of aging and obesity on cognition and brain function in human subjects and the effects of intermittent fasting on cognition and nerve cell network activity in animal studies, we're predicting that intermittent fasting will improve performance and the cognitive test, and enhance the fidelity of communication between brain regions that are critical for cognition," Mattson said.

In Fasting to Fight Cancer, Timing May Be Everything
Recent clinical research on fasting's role in breast cancer suggests that its positive impact may depend not just on whether people abstain from eating, but also when.

In a 2015 epidemiologic analysis of women participating in the 2009-2010 US National Health and Nutrition Examination Survey, researchers were able to show, for the first time, that longer nighttime fasting duration was significantly associated with improved glycemic regulation, and thereby reduced risk for breast cancer. In a study the following year, researchers looked at over 2400 patients who were in remission from early-stage breast cancer. In those who self-reported nightly fasting of less than 13 hours, there was a statistically significant 36% increase of the risk for breast cancer recurrence compared with those whose nightly fasting lasted more than 13 hours.

"This finding was the first time that anyone had ever made an association between a clinical outcome of breast cancer occurrence and prolonged nightly fasting," explained Dorothy D. Sears, PhD, associate director of the Center for Circadian Biology, and an associate professor at the University of California, San Diego, who worked on both studies.

According to Sears, there are good reasons why nighttime eating would have negative effects. Although insulin works well in the morning and early afternoon, in the evening it begins to be counteracted by melatonin and growth hormone.

"That's bad, because sugar in the blood causes reaction with proteins and the blood vessels," she said. "Lots of proteins in the body can become glycated, or sugar-coated, which causes a form of irreversible damage."

"Another negative effect of having high glucose and insulin at night or for an extended period in the night is that it can drive the growth of tumors," Sears continued.

The Future of Fasting
All of the researchers interviewed for this article agreed that the data supporting intermittent fasting as a clinical intervention are currently limited to a few indications, and are derived from relatively small studies. It is difficult to know the true benefits of this treatment, much less the adverse events that could accompany its application. They cautioned against the adoption of fasting in such populations as frail and elderly persons, hypoglycemic patients, and children and adolescents.

There is justifiable excitement that a simple, nonpharmacologic intervention could have a notable impact for patients with life-threatening conditions. There is nonetheless a justifiable excitement that a simple, nonpharmacologic intervention could have a notable impact for patients with life-threatening conditions, such as breast cancer or cardiovascular disease. However, according to Sears, this hasn't made obtaining funding for robust fasting studies any easier.

"It would be really wonderful to see larger, appropriately powered studies funded. That takes support from the research community who's reviewing the grants, to invest and to recognize the promise," she said.

Then there is the issue of financial incentives. Clinical trials are primarily subsidized under the hope that a marketable treatment will emerge at the end of a prolonged and expensive period of investigation. There is no clear way to profitably market food abstinence. Diet books do not make it into Big Pharma's development pipeline.

But if our bodies are evolutionarily conditioned to survive and perhaps even excel through hunger, our appetite for shortcuts may be equally hardwired. This past spring, a team of biologists from the Massachusetts Institute of Technology reported that mice fasting for 24 hours were able to regenerate their intestinal stem cells at double the normal rate. In accompanying media coverage, the team expressed hope that one day, these results would lead to the creation of a drug that mimics fasting without the actual need for fasting.

If these and other like-minded researchers are able to make good on their aspirations, in the future it may be fine once again to treat that growling in your stomach with a trip to the refrigerator, so long as you stop by your medicine cabinet for dessert.
Exploring the Relationship between Depression and Dementia

Rita Rubin, MA

Diagnosing and treating depression in people with mild cognitive impairment (MCI) or with dementia presents special challenges, but doing so can improve the quality of their lives as well as the lives of their caregivers and, in the case of MCI, might even delay progression to dementia.

Researchers are still trying to tease out the relationship between depression and dementia. While depression does not appear to cause dementia, it likely is a risk factor, just as dementia is a risk factor for depression, said George Alexopoulos, MD, founder and director of the Weill-Cornell Institute of Geriatric Psychiatry. At least 20% of people with dementia develop a depressive syndrome, Alexopoulos said.

Often, though, the depression comes first. Some studies suggest that depression in early life is a risk factor for dementia, while depression later in life can be a prodrome of dementia, Alexopoulos said. Although findings are mixed, a 2014 review of the literature concluded that there is convincing evidence to suggest that depression can be a risk factor and a prodromal symptom of dementia.

In a more recent large longitudinal cohort study published in 2017 in JAMA in life did have a higher risk of dementia than those who did not. However, the association was greater in men who were depressed when they entered the study. Treatment with antidepressants did not decrease the risk of depression-associated dementia, leading the authors to conclude that late-life depression should be considered an early sign of dementia, not a modifiable risk factor.

“Anytime you have the first episode (of depression) at a later age, that’s always concerning for a neurodegenerative disorder,” said Anna Burke, MD, a geriatric psychiatrist and the director of neuropsychiatry at Barrow Neurological Institute in Phoenix, who was not involved with either study.
Raj Shah, MD, an associate professor of family medicine with the Rush University, Alzheimer Disease Center in Chicago recommends that a first episode of depression in older individuals be considered a sentinel event, the same way a fall is. Both events should spur questions about whether patients need to have their medication adjusted or whether the fall or the mood change is a marker of other conditions, Shah said.

**Difficult Diagnosis**

Depression is often overlooked when it accompanies dementia, Burke said.

“The problem is the DSM-5 [Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition)] criteria we use for major depressive disorder don’t necessarily fit for this population, much like in children, where depression presents differently,” she said. As with children, adults living with dementia and depression might not talk about emotional pain or feeling down, Burke said. Instead, they might exhibit irritability—“they may just get a little more feisty,” she said—and an increase in somatic symptoms, such as aches and pains and gastrointestinal complaints.

“Sometimes people don’t get diagnosed with depression because there is such a huge overlap in symptoms between depression and dementia as well as growing older,” Burke said. Symptoms common to both depression and dementia include loss of interest in activities and hobbies, social withdrawal, and impaired thinking. Because the symptoms overlap, caregivers might not recognize depression in people with dementia. “I’m often the first person to bring it up,” Burke said. “Even when people do seek treatment in the community, many physicians are not focused on treating anything beyond the memory changes. Nobody ever really discusses the behavioral changes, the changes in mood.”

Still, Alexopoulos said, “If you see the patient at the wrong time, you may miss it. Patients with dementia underreport depression, and caregivers are unreliable reporters.” As David Steffens, MD, MHS, explained, “It’s hard to notice a change in mood when somebody can’t really voice how they’re feeling.”

But that doesn’t mean depression is insignificant in the setting of dementia. “One reason to treat depression is that depression makes underlying cognitive impairment much worse,” said Steffens, chairman of psychiatry at the University of Connecticut. “You want to give them their best cognitive chance.” Besides antidepressants, he said, psychiatrists have sometimes used electroconvulsive therapy to treat severe depression in people with mild dementia.

**Drug Therapy**

The prescribing of antidepressants to people with dementia appears to be increasing, according to a UK study published in 2017. Trends in diagnosis and treatment of people with dementia suggest that the proportion prescribed antidepressants rose from 28% to 36.6% from 2005 to 2015. Antidepressants don’t seem to work as well in people with dementia, possibly because “depression in dementia is a different illness” than depression in people with normal cognition, Alexopoulos said. Cognitive control dysfunction in dementia appears to decrease the effectiveness of some selective serotonin reuptake inhibitors (SSRIs), he and his coauthors wrote in a 2015 article. “I think it is appropriate to try to treat with as little medication as you can,” in part because polypharmacy can lead to delirium syndromes in patients with dementia, Alexopoulos said.

Although the study of Australian men found that taking antidepressants did not reduce the risk of depression-associated dementia, recent research suggests that the drugs might slow the progression to dementia in people with MCI and depression. That study, published in 2017, found that taking the antidepressant citalopram (Celexa), an SSRI, for more than 4 years was associated with a delay in progression from MCI to Alzheimer disease by about 3 years. “Three years is a big deal in this age group,”
Alexopoulos said. Experiments in mice and healthy humans have shown that citalopram reduces amyloid plaque, one of the hallmarks of Alzheimer disease. Treating depression in people with MCI with antidepressants might slow the progression to dementia, but little is known about whether drugs and other interventions developed to treat Alzheimer disease have any effect on depression. Most clinical trials of potential Alzheimer disease treatments do not consider neuropsychiatric symptoms such as depression or irritability as primary research targets, even though “these symptoms are widely recognized as the most stressful and challenging manifestations of dementia,” concluded authors of a recent review article. Only 17.7% of the relevant studies they found on clinicaltrials.gov tested the effect of pharmacological or nonpharmacological interventions on neuropsychiatric symptoms, they wrote.

**Beyond Medication and Talk Therapy**

People with MCI might still be able to benefit from cognitive behavioral therapy or psychotherapy, but that becomes less likely as they decline, Burke said. “A huge part of psychotherapy is being able to remember what happened in a session.” Even individuals whose dementia is too advanced for talk therapy can still benefit from lifestyle changes, though, Burke said. Engaging them in social activities and modifying their environment to minimize triggers that make them anxious or irritable can help improve their quality of life, she said.

A recent pilot study suggested that increasing exposure to daylight can reduce depression in people with dementia. The 12-week study involved 77 people living in eight dementia care communities. At four of the communities, staff took study participants to a room with windows for socialization from 8 AM to 10 AM each day. At the other four communities, staff took study participants to socialize in the mornings in a room illuminated only with typical artificial light. At the end of the study, participants who had socialized in the rooms with daylight had a statistically significant decrease in their scores on the Cornell Scale for Depression in Dementia, while the other participants did not. More studies are needed to determine the appropriate timing, duration, wavelength, and intensity of light exposure for adults with dementia, the researchers concluded.

Another recent study suggested a perceived lack of social engagement is also associated with depressive symptoms in people with dementia.

Researchers measured social engagement, medication use, and depressive symptoms in 402 community-dwelling adults whose average age was 86 years. The data were collected during the first interview at which the participants met the criteria for a dementia diagnosis. The researchers found a link between perceived social isolation and the severity of depressive symptoms but not between antidepressant use and severity of depressive symptoms.

Because the study participants were newly diagnosed, their dementia was mild to moderate. “At that stage, people can still engage,” coauthor Shah said. “If we breakdown some of the stigma around the diagnosis of dementia, it will help people build cultures of support and inclusiveness.”
Obesity Is a Disease, Not a Choice, Experts Advise

Pam Harrison

TORONTO — Effective weight management is going to require a paradigm shift in the way healthcare professionals think about obesity, a leading expert in the field suggests.

Otherwise, patients are doomed to failure and blame, despite the fact the medical community should be shouldering some of the responsibility for not having developed more effective interventions, said Lee Kaplan, MD, PhD, director of the Obesity, Metabolism and Nutrition Institute at Massachusetts General Hospital in Boston.

"My colleagues and I believe — and the Obesity Society and other professional organizations agree — that obesity is a disease," Kaplan told delegates here at the Pediatric Academic Societies 2018 meeting.

As such, obesity must be driven by pathophysiologic processes, just like type 2 diabetes and other chronic diseases, stressed Kaplan.

Like diabetes, obesity is also never "cured," although a patient’s body mass index (BMI) can be under excellent control. Patients "still have the disease of obesity, even though they no longer meet the definition of obesity by our measurements," Kaplan explained.

If obesity is, in fact, a chronic disease, then physicians need to treat it as a chronic disease. And there are many good reasons to do so, he pointed out. First, obesity carries substantial adverse health risks. Type 2 diabetes, for example, is common in the setting of obesity, as are hypertension, dyslipidemia, sleep apnea, and fatty liver disease.

People on the Mediterranean diet did better in terms of cardiovascular risk reduction if they had obesity, but they did so despite an average weight loss of less than one pound.

Common treatable comorbidities typically dictate the treatment that patients with obesity receive, but treatment for obesity itself is often overlooked. In addition, treatments known to improve the comorbidities of obesity are often incorrectly assumed to help obesity itself. A salient example is the oft-recommended Mediterranean diet to promote weight loss in patients with obesity.

Results from several large trials have shown that the Mediterranean diet has little effect on body weight, despite frequent claims to the contrary. In one landmark study (N Engl J Med. 2013;368:1279-1290), people who followed the Mediterranean diet reduced their risk for cardiovascular disease significantly, but the diet had no appreciable effect on body weight.

"People on the Mediterranean diet did better in terms of cardiovascular risk reduction if they had obesity, but they did so despite an average weight loss of less than one pound," Kaplan pointed out.

"We have to be careful about what we tell our patients because if we tell them they are going to lose weight or prevent weight gain on a particular diet and it doesn't work out, then patients and parents themselves will say, 'they don't know what they are talking about' and give up," he said.

Paradigm Shift

Perhaps the most powerful argument for shifting away from thinking that obesity is a lifestyle choice comes from a global study in which researchers tracked trends in BMI from 1980 to 2013 (Lancet. 2014;384:766-781). In that study, the proportion of adults with a BMI of 25 kg/m² or greater relentlessly increased over time in both developed and developing countries.

"In fact, no country has experienced a decrease in obesity rates over essentially the past 40 years, which is a pretty sobering statistic," Kaplan observed.

"We may disagree over what the primary cause of obesity is, but the final pathway, by its nature, has to be pathophysiological, not merely voluntary control of energy balance," he said.

Why this shift in thinking is so pivotal comes down to understanding what drives people to overeat and gain weight, Kaplan continued.

Physicians who treat obesity naturally take a history to identify triggers for eating, exercise patterns, stress levels, sleep patterns and related circadian
rhythm imbalances, and any drugs that can promote obesity. Overeating does not cause obesity, obesity causes overeating.

"We take that history in detail and then we say to the patient, 'eat less and exercise more';" Kaplan quipped. But this statement reveals little understanding of the biologic basis of obesity or its heterogeneity. The body defends a fat mass just like it defends a mass of red blood cells, he explained.

"If you try to perturb your red blood cells by donating blood, your body will bring it back to where it was before you gave blood," he pointed out. Similarly, if a patient undergoes liposuction to remove fat, the fat will grow back to where it was before removal, and it will grow back "lumpier and bumpier" than before.

"If there is a pathophysiology that maintains extra body fat beyond what is normal or healthy, then that pathophysiology will drive us to overeat in the case of obesity," Kaplan said.

"Overeating does not cause obesity, obesity causes overeating. Analogously, undereating does not cure or solve the problem of obesity, effective treatment of obesity causes undereating," he stressed.

This brings physicians to an important question: What works in obesity management and what, predictably, does not.

**What Might Work in Weight Loss**

If obesity is a pathophysiologic state, then the treatments used to modify this state need to be physiologic in nature to drive down the elevated fat mass set point that propels people to overeat, Kaplan explained.

The obesity treatment arsenal includes a healthy diet, exercise, stress reduction, improved sleep health and the re-establishment of normal circadian rhythms, antiobesity medications (such as metformin and liraglutide) that promote weight loss, and bariatric surgery.

Interventions that don’t usually work, at least over the long term, include calorie restriction on a diet chemically unchanged from what patients were eating before (what Kaplan jokingly referred to as the half-Twinkie diet); malabsorptive drugs like orlistat (Xenical, Roche), the only antiobesity drug currently approved by the US Food and Drug Administration specifically for the treatment of pediatric obesity; and devices like the intragastric balloon that restrict food intake or cause malabsorption. More exercise, if patients are already exercising regularly, is unlikely to promote significant long-term weight loss, Kaplan added.

Each antiobesity intervention "works well in only a small subgroup of patients. There is an enormous variability in response to these interventions," he cautioned. This suggests that there are multiple subtypes of obesity, which, if defined better, could be used to predict how well a patient might respond to a particular intervention. But accurate predictive models have not yet been developed.

In the meantime, Kaplan and his team are exploring the potential of a genetic risk score to help determine the likelihood of an individual’s response to a particular therapy.

"The power of genetics to help guide treatment of obesity is largely untapped," Kaplan said. "But as we learn more about the heterogeneity of obesity, I anticipate that we will be able to provide more individualized and effective treatments, which ultimately will lead to more effective obesity-prevention strategies."

**Individualized Treatment**

The concept of obesity as a physiologically driven chronic illness that requires treatment with physiologic-based interventions makes sense, said Amy Fleischman, MD, director of the Optimal Weight for Life Program at Boston’s Children’s Hospital. And she agrees with Kaplan that treatment must be individualized to maximize the chance of success.

"We have a variety of offerings in our clinical program," Fleischman told Medscape Medical News. "We offer individual visits, group visits, exercise programming, and nutritional groups because we believe that different things work for different children and families."

"We also focus on treating the whole family," she added. Another key element for success is to identify small steps that patients and their families feel are doable, rather than imposing larger goals that they might not be able to sustain.

"In growing kids, the goal is sometimes not weight loss at all," she explained. "Even in our tertiary care center, where we see extreme obesity, we initially focus on slowing the acceleration of weight gain. The first goal in a growing child is stabilization of the BMI percentile. When kids are still getting taller, their BMI will improve over time with a slowing in the acceleration of weight gain," Fleischman added.

Kaplan serves as a scientific consultant to AMAG, Gelesis, GI Dynamics, Johnson & Johnson, Novartis, Novo Nordisk, Rhythm, Sanofi, and Zafgen. Fleischman has disclosed no relevant financial relationships.
ETC

6 Scientific Benefits of Playing Videogames

JACINTA BOWLER

The jury is in – video games are not the mind-melting devil creations that your parents made them out to be. Not only can gaming be a whole lot of fun, but recent research has revealed there's also a range of scientific benefits to playing videogames – everything from increasing brain matter to pain relief. Here are six of the best benefits to tell your friends next time you blow off drinks to game:

1. 3D video games could increase memory capacity
In a 2015 study in The Journal of Neuroscience, researchers from the University of California, Irvine recruited 69 participants, and asked a third to play Super Mario 3D World for two weeks, a third to play Angry Birds, and the rest to play nothing. "Because of their engaging experiences and enriching 3D virtual environments, the same video games that have been played for decades by children and adults alike may actually provide our brain with meaningful stimulation," the researchers wrote. The people who played Mario ended up doing better on follow-up memory tasks, while the others showed no improvement pre- and post-gaming. "Video gamers who specifically favour complex 3D video games performed better," the researchers concluded.

2. Gaming could be good for pain relief
This one is the best excuse for playing video games on your next sick day – a 2012 literature review published in the American Journal of Preventive Medicine found that in the 38 studies examined, video games improved the health outcomes of 195 patients on every front, including psychological and physical therapy. Plus, in 2010, scientists presented research at the American Pain Society's conference, which found evidence that playing video games, especially virtual reality games, are effective at reducing anxiety or pain caused by chronic illness or medical procedures. "The focus is drawn to the game not the pain or the medical procedure, while the virtual reality experience engages visual and other senses," said Jeffrey Gold from the University of Southern California.

3. There's evidence games help dyslexic kids improve their reading
Video games can help kids, too! A 2013 study published in Cell investigated the effect that playing action games, like 'Rayman Raving Rabbids', could help dyslexic children aged 7 to 13 year read faster, with no loss in accuracy. The results were equal or better to traditional reading treatments, which can be more time consuming and not as fun. The researchers think that the fast pace in these games helped the kids increase their attention spans, although this hypothesis is yet to be tested.

4. Tetris could help limit trauma
Trusty old Tetris might be good for more than just time wasting if this new study is anything to go by. Last year, 37 patients that arrived at a hospital emergency department in Oxford, UK, to be treated for a traffic accident were randomly selected to play 20 minutes of Tetris. Another 34 patients didn't get given the game, but were asked to log their regular activity

Source: www.sciencealert.com/tech 26 Apr 2017
instead – including things such as texting, crosswords, and reading. The Tetris players had significantly less flashbacks to the traumatic traffic event than those that didn’t – about 62 percent less on average. The research, published last month in Molecular Psychiatry, concludes that the "brief, science-driven intervention offers a low-intensity means that could substantially improve the mental health of those who have experienced psychological trauma."

5. Some research shows that video games might actually make you smarter
A study published in PLoS ONE in 2013 goes as far as saying that your cognition might be enhanced when you start up your Xbox or PlayStation. The researchers took five groups of non-gamers, and made them play a phone game for one hour a day over four weeks. They found that all video games, both action and non-action games, improved cognitive function in the participants – measured by tests such as short term memory tasks.

6. Gaming is linked to an increase in brain matter
And finally – a 2014 study published in Molecular Psychiatry by researchers from the Max Planck Institute in Germany from the found that playing Super Mario 64 caused an increase in the size of brain regions. Specifically the bits of the brain responsible for spatial orientation, memory formation, strategic planning, and fine motor skills. When the researchers looked at 24 participants who had played the game for 30 minutes a day for two months under an MRI machine they found that they had increased grey matter in the right hippocampus, right prefrontal cortex, and the cerebellum, compared to a control group that hadn't played any game. "This proves that specific brain regions can be trained by means of video games", said one of the researchers, Simone Küh, at the time. So there you go – doctors have totally just backed your decision to play video games all weekend. You can thank us later.
Apollo International Polyclinic (AIPC)

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AIPC through telemedicine services consult with the relevant specialized doctors and expertise across the world, with an aim to benefit the patients from the best international experts as well.

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that they can get rid of shadow of the disease, and to achieve that becomes our self-confidence. Here by, AIPC team of specialized doctors, pharmacists, nurses, lab technicians with their own field specific specialties work together in guiding through diagnosis, treatment and recovery.

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- Pharmacists: Our pharmacists will monitor all the drugs prescribed to the patients, looking onto any adverse reactions and assure the efficacy on all the prescribed drugs. Your health is our priority.
- Lab Technicians: Our personnel in lab are very determined to provide the best and precise reports on your health related examinations. We are committed to be brand for accuracy on lab reports.

**Advanced Technology of Apollo International Polyclinic**

**1. Atomization**

Used for ENT, Gynecology, Urology and Anorectal related problems.

- Directly kills pathogens.
- Anti-inflammatory.
- Analgesic activity to achieve therapeutic purposes.
- The drugs given will evenly distribute and adhere to the skin and mucous membrane surface.

**2. Microwave Therapy**

**Indications:**
- Chronic inflammation, surgical incision.
- Anus inflammation, breast hyperplasia, mastitis.
- Prostatitis, benign prostatic hyperplasia.
- Helps to absorb the collected fluids from any parts of the body. For example: nasal cavity, ear.

**Contraindications:**
- Bleeding tendency.
- Active tuberculosis.
- Severe local edema.

**3. Red-light (Hot)**

Used for ENT, Gynecology, Urology and Anorectal related problems.

**Indications:**
- Anti-inflammatory.
- Decreases pain.
- Cure of the boils, carbuncle, herpes zoster, mastitis, soft tissue injury and other anti-inflammatory.
- It produces photochemical effects on organisms.
- The red blood cells absorb the largest red light which can increase cell metabolism.
- Helps to promote wound healing.
- Male: Genital warts, penis hyperplasia can also be used for circumcision.
- Gynaecological: Cervical erosion, cervical polyps.
- For recovery of the wounds.

**Contraindications:**
- Light sensitive reaction history.
- Patients with malignant tumors, bleeding disorders.
- Various severe diseases such as cardiovascular diseases, liver diseases, fever patient who are sick right now should not be treated.
- Patient with coagulopathy should be treated with caution.

**4. ZD invitro electric field hyperthermia machine (Short wave therapy)**

**Indications:**
- Chronic prostatitis, benign prostatic hyperplasia.
- Pelvic inflammatory disease, annex inflammation.

**Contraindications:**
- Urethral and bladder stones.
- Unhealed wounds, bleeding disorders.
- Pacemaker in situ and the metal prosthetics.
- Active tuberculosis.
- Pregnancy
- Menstrual female.
- Patient should not be placed in short wave therapy after surgery.
- Cardio vascular compensatory dysfunction.
- Body temperature regulation disorders.

**Precautions of ZD invitro**

- Ask the patient to take away the metal items such as watches, mobile phones, keys, belt, etc.
- Ask the patient to empty the bladder before the treatment, dry the residual urine (that is left in the urethral mouth and underwear urine).
- If the patient is sweating then they should not be placed in ZD machine.

**5. Intermediate Frequency Treatment (IFT):**

Used for ENT and any part of the body.

**Indications:**
- To promote blood circulations.
- To activate nerves endings.
- To reduce pain.

**6. Cold Red light:**

Used for Gynecology, Urology and Anorectal problems

**Indications:**
- Same as Hot Red light.
- This light is given on the day of surgery.
- This is given to those patients who has allergy with hot red light. For eg. Itching of the light exposed area.
7. Sexual Rehab:
For Urological problems.

Indications:
- To improve the erectile dysfunction.
- Prostatitis
- Helps to promote in penile blood flow.

8. Pelvic Treatment:
For Gynecological problem.

Indications:
- Pelvic inflammatory diseases. (PID)
- Dysmenorrhea
- Ovarian cysts, Endometrial cysts.
- Minor operations of cervical erosion can be given pelvic treatment.
- It helps to promote blood circulation, reduce inflammatory and reduce pain.

Contra-indications:
- Pregnancy, heavy menstrual bleeding.

9. Washing machine ozone:
For Gynecology.

Indications:
- Vaginitis
- To clean the surface of the cervix by inserting spaculum with potassium permanganate.
- If there is highly infection in the uterus, ozone therapy is given as the doctor’s prescription for the limited time.

10. Colposcopy:
For Gynecology (Patients can see their conditions of cervical erosion through their naked eyes in computer).

Indications:
- To detect the (degree) Grade of cervical erosion.
- Cysts, cervical polyps.

11. Sexual dysfunction detection machine:
For Urology.

Indications:
- Helps to detect the cause of erectile dysfunction and impotence.

12. Cystoscopy:
Used for Urology and Gynecology.

Indications:
- Blood in urine.
- Frequent urinary tract infections.
- Pelvic pain.
- Helps to know the cause of blockage.
- Enlarged prostate gland.
- Non-cancerous growths.
- Problems with the ureters (tubes connecting bladder to kidneys).

13. Anal endoscopy:
For Anorectal : Patients can see fissure, fistula, internal and external hemorrhoids through their naked eyes in computer.

Indications:
- To diagnose internal and external hemorrhoids, papilloma (cancerous cells).
- Fissures, fistula.

14. Nasal, Throat and Ear endoscopy:
For ENT : Patients can see their problems through their naked eyes in computer.

Indications:
- Nasal problems
- Throat problems.
- Ear problems.

15. Rectal Microwave:
For Urology.

Indications:
- Prostatitis
- Benign prostatic hyperplasia.

16. DNR Low temperature plasma technology:
DNR therapy is a kind of Minimally invasive surgery for ENT patients.

17. Sterility Testing
For Gynecological patients.

- Infertility testing and treatment for women.
- More focus on health of women with miscarriage happened earlier.

18. HCPT Machine for hemorrhoids surgery.
For Anorectal problems.

- Successful treatment of fissures, fistula and hemorrhoids

We pride ourselves on patient and employee safety, support lifelong learning for professional and support staff, and continue to explore innovative ways to deliver compassionate and prompt care, to those we serve.

Disclaimer: This is merely for the information on advancement of healthcare system and services of Nepal. This bulletin does not intends to promote any hospital/clinic.
Why NPL Social Welfare Organization’s Health Care Program in Sunakothi Community of Lalitpur?

NPL Social Welfare Organization is a NGO that is working on various social and health issue of a community and different parts of the country. Financial, technical and other necessary supports are provided by Nepal Pharmaceutical Lab Pvt. Ltd, Fleur Himalayan Ltd., Mrs. Kamaleswari Amatya family, Mrs. Janaki Devi Pradhananga family as well as Lalit Yog Social Service Institute etc. NPL (Nepal Pharmaceuticals Lab Pvt. Ltd) and NPL Social Welfare Organization’ office is situated at Pulchowk, Lalitpur.

NPL Social Welfare Organization have major focus on achieving Sustainable Development Goals (SDG goals) which provide a powerful aspiration for improving one world – laying out where we collectively need to go and how to go there. Third SDG goal is good health and well being which ensures healthy lives and promote wellbeing.

The global trend is that people are living longer, but support systems for elderly are often ignored. Investments in health through healthcare systems are a reinvestment in development of society. Good health is fundamental to enable people for achieving their full potential and contributing to the development of society. Achieving optimal health including access to necessary health care, food, water, clean air, sanitation, hygiene and medicine is a fundamental right.

Health promotion is the process of enabling people to increase control over their health. So health promotion is focused on preventive health care rather than a medical model of curative care. Health promotion involves public policy that addresses health determinants such as income, housing, food security and quality working conditions.

Active stakeholders’ engagement activities are an integral part of our sustainability commitments. Hence, we believe the most effective social and charitable investments are made through strategic relationships with organizations dedicated to serving our commitments, day in and day out.

Healthy life and prosperous society is major component of NPL Social Welfare Organization, Therefore, we are working on improving health status of people, improving the working environment of people and various health care and livelihood promotional activities. We always give emphasis to the social value of community since social value form an important part of the culture of society. People of Sunakothi are indulged with similar kind of practices so we have chosen elderly people of Sunakothi for the health care program. However, elderly have a wealth of experiences and they need proper care and support.

Sunakothi community is located outside ring road, on the way of Chapagao, about 4 km (2.5 mi) south of the main Lalitpur town in Lalitpur District. According to Nepal Census, 2011, Sunakothi has a population of 10,092 living in 2397 Households. Among the total population, 3000 of them are elderly population. Most of the people of Sunakothi are Newars, engaged in agriculture, supplemented by wood related furniture, general stores and few are involved in foreign employment, job, and other business.

One of the most interesting programs carried out by people of Sunakothi was to honor the elderly people who have had already done their jankhu (elderly Newari people of 77 years above) which is managed by local community organization named Bhringareswar Mahadev Mandir and Bridha Sewa Samiti. Janku means Bhimratharohan. Every full moon of the month (Purnima day), they are
honored with various social religious program, gifts and delicious food. People of Sunakothi have high regards and values for their elderly population who is regarded as assets of the society. Despite of so many policies to uplift and value elderly population, lacking part of the implementation with proper strategies is the major challenges in grass root level.

Improving the access to health care and health services is the only stepping stone to the more important issue of promoting health and wellbeing of the elders. The health promotion issues of elderly are often ignored. Enabling environment and participatory approaches are essential to empower elder persons and to value and support their contribution to their family and society and ultimately for social development.

Rationale of initiating elderly people health promotion program
A constant increase in the percentage of aged persons in the population is creating humanitarian, social and economic problems in many underdeveloped countries like Nepal. An ageing population tends to have a higher prevalence of chronic diseases, physical disabilities, mental illnesses and other co-morbidities. Health related problems of elderly people cannot be viewed in isolation. Poor knowledge and awareness about the risk factors, food and nutritional factors, psycho-emotional concerns (viz. isolation, mental stress, difficulty in keeping themselves occupied), financial constraints (viz. definite reduction in income), health care system (lacking effective health insurance system for elderly people and inadequacies in the government health care system) etc. are the major glitches and cast a significant impact on the quality of life of the elderly people.

Elderly people (post Jankhu or more than 77 years old) and women group were chosen as target group for this Health Promotion program of NPL Social Welfare Organization in coordination with local community organization Bhringareswar Mandir Sudhar and Bridha Sewa Samiti. Study carried out by NPL Social Welfare Organization found out that the elderly people who have had their jankhu were suffering from various health problems such as hypertension, diabetes, gastritis, heart disease, respiratory disease, joint pain, hearing problem, eye sight problem, weakness, pain in various part of the body etc. as they had less immunity than that of younger people. Depression was more prevalent among elders with poor social support, low income, having no spouse, non-pensioner and low educational status. Family had traditionally been the main source of support for the elderly. The traditional sense of duty and obligation of the younger generation towards their older generation was being eroded. So, it was recommended that the elderly people group in each Ward or Community should be made eligible for 10% of the development grant given to each Ward each year for protection, health schemes or program and social security in community level.

Health Care Program Phase I (camp) for 110 elderly people who have had their janku from Sunakothi, Ward 26 and 27 of Lalitpur Metropolitan Municipality was conducted at Bhringareshwor Mahadev Mandir, Sunakothi, Lalitpur on 1st Poush 2074, Saturday with the co-operation of local community organization.

Our Objectives:
• To find out major health problems of the geriatric population of Sunakothi.
• To solve the various health problems of geriatric population of Sunakothi.
• To aware people about the proper and timely checkup of any health issue.
• To give counseling to people about various problems that they might be facing.
• To screen various diabetic and blood pressure patient which are growing more dangerously.

Program Description:
During the process of program management planning, we conducted surveying the environment, setting the direction, observed the problems and challenges and did our best for implementation supplemented with monitoring and follow up for remedies.

A team of nine members including three medical doctors, six nurses along with lab technicians from National Hospital and Cancer Care Center participated in geriatric health promotion program (people aged group 77 and above) organized by NPL Social Welfare Organization. Volunteers from local organization members of Bhringareshwor Mahadev Mandir Sudhar and Bridha Sewa Samiti also gave their full support in organizing the camp.

Local Health Post Incharge, Local Leaders including Ward Chairman of area 26 and 27 were also invited at the time of inauguration. They had positive feeling about the program.

Overall, the program provided free services which included:
• General health checkup i.e. weight, blood pressure, diabetes
• Specific urine tests. (Pap smear test was planned but old ladies refused to do it)
• Health Checkup to identify
problems and counseling for the same by Doctors

- Distribution of the medicines

**The responsibilities were divided as**

1) Volunteers of the local organization and NPL Social Welfare Organization for venue setting, management and monitoring of the program, information flow process.
2) Medical staffs of National hospital and Cancer Care Center for proper Health Checkup, Counseling, and medicine distribution, supported by the related Organization’s volunteers.

**Methods applied:**

- Community Participation
- Involvement of local organization, local government, and Non-governmental organization including (private and public company), family members and individual, since to sustain any program involvement of every related sector is important.
- Learning by doing: Demonstration
- General Awareness
- Interactive communication
- Accomplishment and remedial

**We were able to:**

- Find out various health issues of geriatric population.
- Conduct the health promotion camp properly and effectively.
- Involve community people in our program.
- Give adequate information on their current health issues.
- Effectively demonstrate methods of various medicinal intakes.
- Counseling on proper balance diet and methods to prevent disease.

**Problems and challenges**

Major problems and challenges during the program were as follows:

- Elderly people do not take medicines properly and timely due to which some of them even felt dizziness.
- Most of the name of elderly people was similar so the test report often got exchanged.
- Language barrier since most of elderly people speak only Newari language.
- In old age, the authority and decision making is shifted to other adult of household

**Best solution for implementation**

- Learning Newari language or take support to communicate with elderly people.
- Distributing identity card of elderly people
- Involving women in health care program as women of family play vital role taking caring of whole family members.
- Conducting health awareness program along with screening program.

**Monitoring and follow up**

Follow up on the program is continued by NPL Social Welfare Organization with the support of Local Committee.

As the outcome of our health camp, it was found that hypertension and diabetes were one of the major health problems of the community people. So, we started conducting the routine Blood Pressure and diabetes screening in the community not only for elderly people but also for women group and young ones as many people are unaware of the prevailing of hypertension and diabetes. So, we conducted health education and promotitional program subsequently.

We had to aware the people that non- communicable disease like hypertension and diabetes can exist in our body without any sign and symptoms. Hence, we had to conduct health education and awareness program, life style modification program, life skill program, life promotion program among people of Sunakothi.

Evaluation and feedback have been collected based on reduction in cases and management of hypertension and diabetes cases. We did research on it with structured questionnaire form and observation.

**Summary of findings**

Elevated blood pressure and diabetes are the biggest contributing risk factor to global death and global burden of disease – causing heart attacks and other cardiovascular complications, strokes, kidney problems etc. The important drivers of hypertension and diabetes identified were related to lifestyle, dietary practices, genetics and environment etc. Generally, 1 in 4 people is suffering from hypertension and 1 in 10 people is suffering from diabetes in current scenario. Increasing awareness helps people to improve uptake of better lifestyle practices. Screening of blood pressure and diabetes helps to identify high risk groups and benefit them by overall low risk of future mortality and morbidity. It influences people to be involve in healthy activities rather than to be engaged in sedentary lifestyles.

NPL Social Welfare Organization appreciated a nationwide blood pressure screening campaign, May Measurement Month to raise awareness, screening, provide counseling and communicate the findings to the Ministry of Health and other relevant stakeholders and advocate for specific interventions aimed at reducing the national burden of disease worldwide, initiated led by International Society of Hypertension (ISH) and endorsed by World
Hypertension League (WHL). NPL Social Welfare Organization supported financially to organize conference in Kathmandu to disseminate the preliminary findings aiming concerned stakeholders, sharing the experiences of the volunteers, hearing the voices of people, providing future direction and guidance from the experts and felicitating the selfless volunteers for being part of the campaign to bring it into this success & distributing certificates to volunteers and gifts to contributors. NPL Social Welfare Organization also got opportunity to present its own experiences and data findings of effective health promotion program of Sunakothi community using PowerPoint and projector.

Lastly, with the goal of reducing morbidity, mortality and disability due to diabetes and hypertension observed in rapidly urbanizing society and community due to change in life styles and structural factors exposing to disease and its risk factors, this coming year, NPL Social Welfare Organization is planning to implement and conduct the health promotion program and activities in rapidly urbanizing society and community. We will also plan how to best disseminate the results to the broader community and facilitate ongoing dialogue within the broader healthcare system to ensure dissemination of our findings to decision makers responsible for the delivery of health care services.
Felicitation of Advisory Board & technical committee in grateful recognition of their generous support & guidance since the initial days of 'The Himalayan Health'.

We are always thankful & expecting your patronage & guidance ahead.
Answer to THH Crossword 063

Across
1. Liquid waste produced by the kidneys which mainly a watery solution of salt and substances is called urea and uric acid. (5)
2. The smallest unit of living structure capable of independent existence, composed of a membrane-enclosed mass of protoplasm and containing a nucleus or nucleoid. (4)
3. A part of the brain that has a vital role in controlling many bodily functions including the release of hormones from the pituitary gland. (12)
4. NPL Esthertica’s Hydrocortisone 1% w/w cream (5)
5. NPL - LAPEN Cardiac Care’s Telmisartan Brand. (5)

Down
1. ………….. veins are in the neck and drain blood from the head, brain, face and neck and convey it toward the heart. (7)
2. LAPEN - Diabetes’ Care Sitagliptin and Metformin Tablet (7)
3. NPL Division II’s Montelukast Chewable Tablet (6)
4. NPL Division I’s Iron supplement Tablet (8)
5. ………….. gland that makes and stores hormones that help regulate the heart rate, blood pressure, body temperature, and the rate at which food is converted into energy (7)

Entries should reach to the editor by 20th Chaitra 2075. In case of more than one correct entry, the winner will be decided by lucky draw.
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