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# Management of Acute Febrile Illness: Doxycycline, the Empirical Antibiotic of Choice

Acute fever or acute febrile illness is one of the most common presenting complaints to the physicians in OPDs and in emergency care, in children and in adults alike. Fever itself is not a disease; it is both a symptom and a sign of disease.

India, being a tropical country, acute fever has myriad causes. Most fevers are infectious in origin due to bacterial, viral or parasitic protozoan infections notable among which are dengue, typhoid fever, malaria, Chikungunya, scrub typhus and rickettsial infections, Japanese encephalitis, leptospirosis, respiratory tract infections, sexually transmitted infections. The cause usually depends on the disease endemicity and seasonality of infections.

Such a diverse infectious etiology that often overlaps, presents a challenge to the treating physician. These infections often present with similar clinical features. A diagnosis is not always possible based on clinical presentation alone and correct diagnosis is reached only with specific diagnostic tests. Hence, a common approach to acute fever is the use of empirical antibiotics and adjunctive supportive treatment with antipyretics.

When choosing an empirical antibiotic, we do not want to miss deadly fevers such as scrub typhus, leptospirosis, the diagnosis of which requires expensive investigations. The cost of investigations in acute fever may run in hundreds and thousands, and the cost of empirical antibiotics may be less than one hundred rupees.

To understand the rationale of use of empirical antibiotics in a patient with acute febrile illness, a brief review of pathogenesis of fever is relevant here. The body temperature is determined by a balance between pyrogens and cryogens; pyrogens cause fever, cryogens are antipyretic. The febrile response is mediated by the release of endogenous pyrogens, which are cytokines. There are three main pyrogenic cytokines: Interleukin (IL)-6, IL-1, ciliary neurotrophic factor (CNTF) and tumor necrosis factor (TNF)-$\alpha$, which are produced by neutrophils, macrophages and lymphocytes in response to exogenous pyrogens, which are mainly microorganisms or their toxins.[1] These pyrogenic cytokines stimulate the hypothalamus to raise the thermoregulatory set point resulting in increase in body temperature.

Elevated levels of cytokines are the hallmark of various bacterial and viral infections.[2] The use of agents that reduce cytokine production or their activity has thus been explored as a potential therapeutic option. The rationale of using antibiotics as anticytokine therapy comes from evidence, which has shown that antibiotics can modify cytokine production.[3] These immunomodulatory effects inhibit production of proinflammatory cytokines.

A broad-spectrum antibiotic such as doxycycline can be a rational first choice of antibiotic in patients presenting with acute fever. It is bacteriostatic[4] and also has anti-inflammatory activity including antiviral activity against herpes simplex virus, rotavirus and dengue virus.[2]

Doxycycline is effective for treating respiratory tract infections such as community-acquired pneumonia (CAP) and acute exacerbations of chronic bronchitis (AECB).[4] It has been used as chemoprophylaxis and treatment for malaria,[5] sexually transmitted infections,[6] management of acne vulgaris[7] and is regarded as the drug of choice for scrub typhus[8] and for rickettsial infections.[9] Doxycycline has been used in patients with enteric fever and brucellosis.[10] In endemic areas, antibiotic treatment of typhoid fever is usually empirical. Concurrent treatment with doxycycline may be required to cover for typhus and leptospirosis.[11]

In addition, doxycycline may have a role in dengue fever because of its immunomodulatory effect in reducing the proinflammatory cytokines (IL-6 and TNF) and also due to its ability to inhibit replication of the dengue virus *in vitro*.[12] Disease severity in dengue virus infection has been linked to an increase in various cytokine levels.[13] Therefore, by decreasing pro-inflammatory cytokine levels, doxycycline can provide a clinical benefit to dengue patients at high risk of complications.[14]

Updated recommendations from the American Academy of Pediatrics (AAP) now permit doxycycline for ≤21 days in children of all ages.[15] Doxycycline binds less readily to calcium than other tetracyclines, and the risk of dental staining with short courses of doxycycline is minimal.

Another important point to be considered is that empirical antibiotic must also have a low probability of resistance. Most of us prescribe azithromycin or cefuroxime as empirical antibiotics in fever of duration more than 3 days. Penicillin till today is sensitive in streptococcal sore throat. Doxycycline is another antibiotic with low probability of resistance.[16]

Hence, while awaiting lab reports, if you want to prescribe an empirical antibiotic meanwhile, doxycycline appears to be a rational, safe and inexpensive choice given its proven effectiveness, fewer adverse effects, oral route of administration, once-daily dose, low probability of developing resistance and low cost,[12,17] which is especially pertinent in a resource-poor setting as India.

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AMERICAN FAMILY PHYSICIAN

# Health Maintenance in Postmenopausal Women

I. CORI BAILL, ANALIA CASTIGLIONI


## ABSTRACT

Cardiovascular disease is the leading cause of death and disability in postmenopausal women older than 50 years. Clinicians should use the pooled cohort risk assessment equations or another risk calculator every three to five years to estimate a woman's 10-year risk of atherosclerotic cardiovascular disease, including myocardial infarction and stroke. Major guidelines concur that women at average risk of breast cancer benefit from screening mammography at least every other year from 50 to 74 years of age. Several effective options for colorectal cancer screening are recommended for women 50 to 75 years of age. Cervical cancer screening should occur at three- or five-year intervals depending on the test used, and can generally be discontinued after 65 years of age or total hysterectomy for benign disease. Screening for ovarian cancer is not recommended. Clinicians should consider screening for sexually transmitted infections in older women at high risk. Postmenopausal women should be routinely screened for depression, alcohol abuse, and intimate partner violence.


**Keywords:** Postmenopausal, cardiovascular disease, stroke, cerebrovascualr disease, breast cancer, ovarian cancer, cervical cancer, colorectal cancer, osteoporosis, falls, sexually transmitted infections, psychosocial issues, vaccination, guideline, prevention

Postmenopausal women have a number of unique health-promotion and disease-prevention needs. However, many effective preventive health strategies for postmenopausal women are underutilized.[1] This article reviews evidence-based preventive services recommendations for asymptomatic postmenopausal women from the U.S. Preventive Services Task Force (USPSTF), which are supported by the American Academy of Family Physicians. Relevant guidelines from other professional groups are also described.

## CARDIOVASCULAR DISEASE SCREENING AND PREVENTION

Cardiovascular disease (CVD) is the leading cause of death and disability in women older than 50 years, exceeding the number of deaths from malignant neoplasms, diabetes mellitus, and chronic lower respiratory diseases combined.[2] The prevalence of CVD increases rapidly at the onset of menopause and continues to increase through the postmenopausal period.

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*Source*: Adapted from Am Fam Physician. 2017;95(9):561-570.

### Cardiovascular Risk Stratification

Periodic cardiovascular risk assessment in postmenopausal women can identify risk factors and enable implementation of risk-reduction strategies (Tables 1[3-16] and 2[17,18]). The 2013 American College of Cardiology/American Heart Association (ACC/AHA) guideline recommends using the pooled cohort risk assessment equations (http://tools.acc.org/ASCVD-Risk-Estimator/) every three to five years to calculate the 10-year risk of atherosclerotic CVD, including myocardial infarction and stroke.[6,19-21] The guideline supports the use of statins for primary prevention of atherosclerotic CVD in high-risk patients and for secondary prevention in all patients with a history of atherosclerotic CVD. Although concerns have been raised that the pooled cohort equations overestimate risk, other risk scores, including the traditional Framingham risk score, also overestimate risk by 25% to 115%.[22,23] The pooled cohort equations and Framingham risk score apply only to women younger than 80 years, limiting their use in the older population.

### Coronary Heart Disease

The complex effects of hormones on the cardiovascular system result in different presentations of coronary heart disease in women, with a higher incidence of angina, a lower burden of obstructive coronary artery disease (CAD) on angiography, and a poorer prognosis compared with men. In addition, postmenopausal women are more

**Table 1.** Cardiovascular Risk Factor Screening Recommendations for Postmenopausal Women

| Risk factor | Organization | Recommendation | Comments |
|---|---|---|---|
| Diabetes mellitus | USPSTF,[3] ADA[4] | USPSTF: Screen all adults 40 to 70 years of age who are overweight. | A1C: normal is < 5.7%; impaired glucose tolerance = 5.7% to 6.4%; diabetes is ≥ 6.5%[4] |
| | | ADA: If no risk factors, begin screening at 45 years of age and repeat every three years. | Fasting glucose (mg per dL): normal is < 100 (5.6 mmol per L); impaired glucose tolerance = 100 to 125 (5.6 to 6.9 mmol per L); diabetes is ≥ 126 (7.0 mmol per L)[4] |
| | | Both: Offer or refer patients with abnormal screening to intensive behavioral counseling interventions to promote healthful diet and exercise. | Two-hour oral glucose tolerance test (mg per dL): normal is < 140 (7.8 mmol per L); impaired glucose tolerance = 140 to 199 (7.8 to 11.0 mmol per L); diabetes is ≥ 200 (11.1 mmol per L)[4] |
| Dyslipidemia | USPSTF[5] | Identification of dyslipidemia and calculation of 10-year CVD event risk requires universal lipid screening in adults 40 to 75 years of age. | Measure total, high-density lipoprotein, and low-density lipoprotein cholesterol levels in nonfasting or fasting patients. |
| | | Periodic measurement of total, low-density lipoprotein, and high-density lipoprotein cholesterol levels is required to implement this recommendation. | Optimal screening interval is unknown; a reasonable interval is every five years, with shorter or longer intervals based on risk and lipid levels.<br>Age at which to stop has not been established. |
| | ACC/AHA[6] | Screen adults 20 to 79 years of age who do not have CVD every four to six years to calculate 10-year CVD risk. | — |
| Hypertension | Joint National Committee[7,8] | Screen every two years if blood pressure < 120/80 mm Hg, or annually if 120/80 to 139/89 mmHg. | Treat to a blood pressure goal of 150/90 mm Hg for persons ≥ 60 years (140/90 mm Hg in persons < 60 years and in those with diabetes or chronic kidney disease). |
| | USPSTF[9] | Screen annually. | Obtain measurements outside of the clinical setting for diagnostic confirmation. |
| Overweight and obesity* | AHA/ACC/ Obesity Society[10] | Measure height and weight, and calculate BMI at annual visits or more frequently. | Waist circumference ≥ 35 in (89 cm) for women is considered elevated and indicative of increased cardiometabolic risk. |
| | | In overweight and obese adults, measure waist circumference annually. | Waist circumference measurement is unnecessary in patients with BMI ≥ 35 kg per $m^2$. |
| | American College of Obstetricians and Gynecologists[11] | Calculate BMI in all adult women. | — |
| | USPSTF[12] | Calculate BMI (interval not specified). | Obese patients should be offered or referred to intensive, multicomponent behavioral interventions.<br>Offer or refer overweight/obese patients with additional CVD risk factors to intensive behavioral counseling interventions to promote a healthful diet and physical activity.[13] |
| Tobacco use | USPSTF[14] | Ask all adults about tobacco use, advise them to stop using tobacco, and provide behavioral interventions and U.S. Food and Drug Administration–approved pharmacotherapy for smoking cessation. | The 5 A's intervention (ask, advise, assess, assist, and arrange) is an evidence-based model to address patient smoking.[15] Many other guides exist. Brief intervention with phone follow-up is also effective.[16] |

ACC = American College of Cardiology; ADA = American Diabetes Association; AHA = American Heart Association; BMI = Body mass index; CVD = Cardiovascular disease; USPSTF = U.S. Preventive Services Task Force.

*Overweight: BMI of 25 to 29.9 kg per $m^2$; obesity class I: BMI of 30.0 to 34.9 kg per $m^2$; obesity class II: BMI of 35.0 to 39.9 kg per $m^2$; obesity class III: BMI > 40.0 kg per $m^2$.

Information from references 3 through 16.

**Table 2.** Lifestyle Recommendations for Postmenopausal Women

| Topic | Organization | Recommendation |
|---|---|---|
| Diet | AHA/ACC[17] | Recommended diets should include vegetables, fruits, and whole grains, and should limit sweets, sugar-sweetened beverages, and red meats; no more than 5% to 6% of calories should come from saturated fat and/or trans fat. |
| | | Diets should be adapted to personal and cultural food preferences. |
| Physical activity | AHA/ACC[17] | Adults should engage in moderate- to vigorous-intensity aerobic physical activity for an average of 40 minutes three or four times per week. |
| | American College of Sports Medicine/AHA[18] | All healthy adults 18 to 65 years of age should engage in moderate-intensity aerobic physical activity (e.g., brisk walking) for at least 30 minutes on five days per week, or vigorous-intensity aerobic physical activity (e.g., jogging) for at least 20 minutes on three days per week. |

ACC = American College of Cardiology; AHA = American Heart Association.

Information from references 17 and 18.

likely to develop heart failure with preserved ejection fraction.[24] Table 3 provides a summary of screening recommendations for CVD risk factors.[25-30]

### Stroke and Atrial Fibrillation

Cerebrovascular disease accounts for a higher proportion of cardiovascular events and mortality in women, with 50,000 more U.S. women than men dying from strokes each year.[2] Unique risk factors for stroke in postmenopausal women include the use of hormone therapy and a higher prevalence of hypertension in older persons. In a nationwide study of Finnish women who discontinued menopausal hormone therapy, the risk of cardiac- or stroke-related death increased 26% to 66% in the first year after discontinuation.[31] Women have a higher stroke risk and mortality in the setting of atrial fibrillation compared with men. Risk assessment for stroke using the $CHA_2DS_2$-VASc score (http://reference.medscape.com/calculator/chads-vasc-af-stroke) accounts for this increased risk by adding an extra point for women.[24,32,33]

### Aspirin and Statins for Primary Prevention

The USPSTF and ACC/AHA recommend aspirin and statins for primary prevention of CVD in select high-risk patients who are at low risk of adverse effects from these medications[5,6,34] (Table 4[5,6,22,34-37]).

## CANCER SCREENING

### Breast Cancer

There is agreement across multiple organizational guidelines that average-risk women benefit from screening mammography at least every other year from 50 to 74 years of age (Table 5).[38-41] For high-risk women, the USPSTF found insufficient evidence to judge the balance of benefits and harms for screening magnetic resonance imaging.[41] The American Cancer Society and the National Comprehensive Cancer Network recommend considering the addition of annual magnetic resonance imaging in women whose lifetime breast cancer risk is at least 20%, as defined by models largely dependent on family history, a history of atypical hyperplasia on breast biopsy, or who were exposed as a child to therapeutic chest radiation.[38,40]

The USPSTF recommends that postmenopausal women at high risk of breast cancer and low risk of medication adverse effects be offered tamoxifen or raloxifene.[42] Based on expert opinion, the American Cancer Society and the National Comprehensive Cancer Network include aromatase inhibitors, exemestane, or anastrozole as additional options.[38,43]

Breast cancer prevention trials historically defined high-risk women as those with a 1.66% or greater five-year risk of invasive breast cancer as calculated by the Gail model (Breast Cancer Risk Assessment Tool, http://www.cancer.gov/bcrisktool/Default.aspx).[44] However, this cutoff includes almost all women older than 65 years, many of whom will not experience a net benefit from the use of risk-reducing medication.[42] A 3% or greater five-year risk of invasive breast cancer is more likely to identify postmenopausal candidates for chemoprophylaxis.[45] The Tyrer-Cuzick model (International Breast Intervention Study breast cancer risk evaluation tool, http://www.ems-trials.org/riskevaluator) incorporates the Gail model risk factors, as well as age, use of hormone therapy, and body mass index.[46] It defines high risk as more than 20% lifetime risk.

The USPSTF recommends genetic counseling and, if indicated, *BRCA* testing in women with Ashkenazi Jewish ethnicity or a family history of breast cancer before 50 years of age, bilateral breast cancer, breast and ovarian cancer, breast cancer in at least one male family

**Table 3.** Cardiovascular Screening Recommendations for Postmenopausal Women

| Condition | Organization | Screening modality | Recommendation |
|---|---|---|---|
| Asymptomatic carotid stenosis | ACC Foundation/AHA, et al.[25] | Duplex ultrasonography | Screening is not recommended in the general population. |
| | USPSTF[26] | Duplex ultrasonography | Screening is not recommended in the general population. |
| Coronary artery disease | ACC/AHA[27] | Exercise testing | Consider screening exercise testing in patients with multiple risk factors for CHD to guide risk-reduction therapy, in women older than 55 years who are sedentary and plan to start a vigorous exercise program, and in patients with public safety occupations. |
| | USPSTF[28] | Resting or exercise electrocardiography | Do not routinely screen adults at low risk of CHD events. |
| | | | Evidence is insufficient to recommend for or against routine screening in adults at increased risk of CHD events. |
| Lower extremity peripheral artery disease | ACC Foundation/AHA[29] | Ankle-brachial index | Consider screening if: |
| | | | < 50 years with diabetes mellitus and an additional cardiovascular risk factor |
| | | | ≥ 50 years with a history of smoking or diabetes |
| | | | ≥ 65 years |
| | USPSTF[30] | Ankle-brachial index | Evidence is insufficient to screen for peripheral artery disease and cardiovascular risk factors with the ankle-brachial index in adults. |

ACC = American College of Cardiology; AHA = American Heart Association; CHD = Coronary heart disease; USPSTF = U.S. Preventive Services Task Force.
Information from references 25 through 30.

member, multiple cases of breast cancer in the family, or one or more family member with two primary types of *BRCA*-related cancer.[47] The American College of Obstetricians and Gynecologists advises genetic testing if risk assessment is consistent with a 20% to 25% lifetime risk of breast and ovarian cancer.[39]

### Ovarian Cancer

The USPSTF recommends against screening for ovarian cancer.[48] Preliminary results from the U.K. Collaborative Trial of Ovarian Cancer Screening, which used a multimodal screening protocol combining history, changes in the cancer antigen 125 level over time, and high-resolution ultrasonography, suggested a possible mortality benefit.[49] However, it remains uncertain if implementation of a proprietary algorithm will produce more benefits than harms.[50,51]

### Cervical Cancer

Most cervical cancers arise in women who were never screened or received inadequate screening.[52] Postmenopausal women should receive human papillomavirus and cytology cotesting every five years, or cytology alone every three years, until 65 years of age (eTable A). Human papillomavirus screening every three years can be considered for women older than 25 years.[52,53] Screening should be discontinued in women who undergo total hysterectomy for benign disease.[54] Women who undergo subtotal hysterectomy (removal of the uterus with retention of the cervix) should continue regular screening.[52,54]

### Colorectal Cancer

The American College of Gastroenterology recommends colonoscopy every 10 years beginning at 50 years of age in average-risk patients, including those who have a first-degree relative diagnosed with colorectal cancer or an advanced adenoma at 60 years or older.[55] Patients with relatives diagnosed before 60 years of age should be screened every five years beginning at 40 years of age or 10 years younger than the relative at the time of diagnosis. The USPSTF recommends screening for colorectal cancer beginning at 50 years of age and continuing through 75 years of age, then individualized decision making in patients 76 to 85 years of age[56] (Table 6[55,56]). High-risk women who may require more intensive screening and/or genetic testing include those with a history of genetic disorders (e.g., familial adenomatous polyposis), inflammatory bowel disease, or a previous adenomatous polyp or colorectal cancer.[56]

## OSTEOPOROSIS SCREENING

Many postmenopausal women with osteoporosis do not receive preventive care for fractures.[57,58] eTable B

**Table 4.** Aspirin and Statin Use for Primary Prevention of Cardiovascular Disease in Postmenopausal Women

| Intervention | Organization | Recommendation | Comments |
|---|---|---|---|
| Aspirin | AHA/American Stroke Association[35] | Low-dose aspirin is recommended for adults whose risk is sufficiently high for the benefits to outweigh the risks; a 10-year atherosclerotic CVD risk of 6% to 10% is suggested.* | — |
| | USPSTF[34] | Low-dose aspirin is recommended for primary prevention of CVD in adults 50 to 59 years of age who have a 10-year atherosclerotic CVD risk of 10% or greater,* are not at increased risk of bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin for at least 10 years.<br>Recommendations for persons 60 to 69 years of age are less robust and should be individualized.<br>The evidence is insufficient to recommend use in persons 70 years and older. | Benefits include prevention of myocardial infarction, ischemic stroke, and with long-term use, reduced incidence of colorectal cancer. Aspirin use may result in small to moderate harms, including gastrointestinal bleeding and hemorrhagic stroke. Individual bleeding risk can be estimated using the HAS-BLED score (http://www.mdcalc.com/has-bled-score-for-major-bleeding-risk).[36,37] |
| Statins | American College of Cardiology/ AHA[6,22] | Groups in which statin benefits outweigh risks:<br>• Adults with LDL cholesterol level > 190 mg per dL (4.92 mmol per L)<br>• Adults 40 to 75 years of age with diabetes mellitus and LDL cholesterol level 70 to 189 mg per dL (1.81 to 4.90 mmol per L) who do not have clinical atherosclerotic CVD<br>• Adults with LDL cholesterol level 70 to 189 mg per dL and a 10-year atherosclerotic CVD risk > 7.5%* who do not have clinical atherosclerotic CVD or diabetes<br>Statin use can be considered in adults 40 to 75 years of age with normal LDL cholesterol levels and a 10-year atherosclerotic CVD risk of 5% to < 7.5%* who do not have clinical atherosclerotic CVD or diabetes. | Before initiating statin therapy, physicians and patients should discuss:<br>• Potential for CVD risk-reduction benefits<br>• Potential for adverse effects and drug–drug interactions<br>• Heart-healthy lifestyle<br>• Management of other risk factors<br>• Patient preferences<br>In patients with an atherosclerotic CVD risk of 5% to 7.5%, other risk factors may be considered to initiate statin therapy: LDL cholesterol level ≥ 160 mg per dL (4.14 mmol per L), family history of premature cardiovascular disease, high-sensitivity C-reactive protein level ≥ 2 mg per L (19.05 nmol per L), coronary artery calcium score ≥ 300 Agatston units, ankle-brachial index < 0.9, or elevated lifetime atherosclerotic CVD risk. |
| | USPSTF[5] | Adults 40 to 75 years of age with no history of CVD, at least one CVD risk factor, and a calculated 10-year CVD event risk of 10% or greater* benefit from low- to moderate-dose statins for the prevention of CVD events and mortality.<br>Adults 40 to 75 years of age with no history of CVD, at least one CVD risk factor, and a calculated 10-year CVD event risk of 7.5% to 10%* have a small net benefit. Clinicians may offer a low- to moderate-dose statin for these patients.<br>The evidence is insufficient for adults 76 years and older with no history of CVD, and the balance of benefits and harms cannot be determined. | The decision to initiate therapy in these populations should reflect an assessment of the patient's specific circumstances and his or her preference for a potential small benefit relative to the potential risks and inconvenience of a lifelong daily medication. |

AHA = American Heart Association; CVD = Cardiovascular disease; LDL = Low-density lipoprotein; USPSTF = U.S. Preventive Services Task Force.

*A risk calculator is available at http://tools.acc.org/ASCVD-Risk-Estimator.

Information from references 5, 6, 22, and 34 through 37.

**Table 5.** Breast Cancer Screening Recommendations for Average-Risk Women

| Organization | Mammography | Clinical breast examination | Breast self-examination | Breast self-awareness |
|---|---|---|---|---|
| American Cancer Society [38] | Annually in women 45 to 54 years of age; biennially in women 55 years and older; do not screen women with a life expectancy of less than 10 years | Not recommended | — | — |
| American College of Obstetricians and Gynecologists[39] | Annually beginning at 40 years of age | Every one to three years for women 29 to 39 years of age, then annually | Consider for high-risk patients | Recommended |
| National Comprehensive Cancer Network[40] | Annually in women 40 to 74 years of age; biennial screening not recommended | Every one to three years for women 25 to 40 years of age | No benefit | Recommended in women older than 25 years |
| U.S. Preventive Services Task Force[41] | Biennially in women 50 to 74 years of age; individualize decision to screen women 40 to 49 years of age | Insufficient evidence | — | — |

Information from references 38 through 41.

**Table 6.** Colorectal Cancer Screening Recommendations for Postmenopausal Women

| Organization | Screening population | Comments | Screening methods |
|---|---|---|---|
| American College of Gastroenterology[55] | Black women 45 years and older; all other women 50 years and older<br>Screening obese women 45 years and older and women with more than a 20 pack-year history of smoking may be cost-effective and beneficial | Guidelines contain additional notes on genetic testing and management of patients with familial adenomatous polyposis (> 100 adenomas) and hereditary nonpolyposis colorectal cancer (usual number of polyps). | Colonoscopy every 10 years is the preferred screening test; alternatives include flexible sigmoidoscopy every five to 10 years and CT colonography every five years.<br>If screening methods above are declined, annual FIT is the preferred screening method; alternatively, FOBT or multitargeted fecal DNA testing may be performed every three years. |
| U.S. Preventive Services Task Force[56] | All average-risk adults 50 to 75 years of age<br>Healthy adults 76 to 85 years of age who have never been screened, if comorbid conditions do not limit life expectancy | One-third of eligible U.S. adults have never been screened; black patients may develop disease at a younger age. | Screening tests are not presented in order of preference; rather, the goal is to maximize the number of persons who are screened. Methods: guaiac-based FOBT or FIT every year; multitargeted fecal DNA testing every one to three years; CT colonography or flexible sigmoidoscopy every five years; colonoscopy every 10 years; flexible sigmoidoscopy every 10 years with FIT every year. |

CT = Computed tomography; FIT = Fecal immunochemical testing; FOBT = Fecal occult blood testing.

Information from references 55 and 56.

summarizes osteoporosis screening recommendations. The optimal interval for repeat screening in postmenopausal women with normal or mildly decreased bone mineral density is uncertain.[58] Diagnostic and treatment criteria for osteoporosis rely on hip and lumbar spine dual-energy x-ray absorptiometry measurements.[58]

In addition to adequate calcium and vitamin D intake and weight-bearing exercise, multiple drug therapies

are approved by the U.S. Food and Drug Administration to reduce fracture risk, including bisphosphonates, parathyroid hormone, raloxifene, and estrogen.[58]

## FALL PREVENTION

According to the USPSTF, effective fall prevention measures include daily intake of 600 to 800 IU of vitamin D, weight-bearing exercise, balance training three times per week, muscle strengthening twice per week, and 150 minutes per week of moderate-intensity or 75 minutes per week of vigorous-intensity aerobic physical activity.[59] Vision correction, medication discontinuation, protein supplementation, education and counseling, and home hazard modification may be helpful in select cases, but are not routinely recommended.

## STI SCREENING AND PREVENTION

An estimated 65% of women 51 to 64 years of age engage in sexual intercourse at least once per week.[60] Relationship transitions, the availability of erectile dysfunction treatments, and underutilization of condoms contribute to the increasing incidence of sexually transmitted infections (STIs) in older women.[61,62] Thinning, less elastic postmenopausal vaginal epithelium facilitates transmission of STIs via coital trauma. One American study found that 1% of widowed women 67 to 99 years of age developed an STI during a nine-year study.[63] The USPSTF recommends that high-risk sexually active women receive intensive behavioral counseling to reduce STI risk, and annual screening for chlamydia, gonorrhea, syphilis, and human immunodeficiency virus (HIV) infection.[62] Regardless of risk, all women should receive HIV screening at least once before 65 years of age. Counseling resources are available through the Centers for Disease Control and Prevention at http://www.cdc.gov/std/prevention/default.htm.

## PSYCHOSOCIAL ISSUES

The USPSTF recommends routinely screening postmenopausal women for depression, alcohol abuse, and intimate partner violence (eTable C).

## VACCINATIONS

Postmenopausal women benefit from receiving vaccines recommended by the Advisory Committee on Immunization Practices, including those that provide protection against herpes zoster, influenza, pneumococcus, and tetanus, diphtheria, and pertussis (Table 7).[64] The adult immunization schedules are available at http://www.cdc.gov/vaccines/hcp/acip-recs/index.html.

**Table 7.** Vaccine Recommendations for Postmenopausal Women

| Vaccine | Recommended schedule | Comments |
|---|---|---|
| Herpes zoster | Single dose | Licensed for use beginning at 50 years of age; the Advisory Committee on Immunization Practices recommends herpes zoster vaccination for adults 60 years and older, but does not recommend it for adults 50 to 59 years of age who do not have chronic medical conditions. |
| Influenza | Annually | No age limit. |
| Pneumococcal | Single dose of PCV13 followed by a dose of PPSV23 no earlier than one year later; PCV13 and PPSV23 should not be coadministered; if a dose of PPSV23 is inadvertently given earlier than the recommended interval, the dose need not be repeated | Recommended for all immunocompetent adults 65 years and older who have not previously received pneumococcal vaccine; adults who received PPSV23 before 65 years of age and in whom an additional dose is now indicated should receive the subsequent dose no earlier than one year after PCV13 and no earlier than five years after the most recent dose of PPSV23; for adults 65 years and older who have immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leaks, or cochlear implants, the recommended interval between PCV13 and PPSV23 is at least eight weeks. |
| Tetanus | Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) one time, then tetanus and diphtheria toxoids (Td) every 10 years | Tdap conveys pertussis immunity, so one additional dose should be administered after 19 years of age. |

**Note:** In addition to the vaccines listed above, meningococcal vaccination and combined hepatitis A and B vaccination can be considered for high-risk women. The measles, mumps, and rubella vaccine may be appropriate for women born before 1957.

PCV13 = 13-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine.

Information from reference 64.

**eTable A.** Cervical Cancer Screening Recommendations

| Age | Preferred testing methods | Acceptable testing method |
|---|---|---|
| 30 to 65 years | HPV and cytology cotesting every five years; there is no indication for annual screening in average-risk women. | Cytology alone every three years; in women older than 25 years, FDA-approved primary HPV screening every three years can be considered as an alternative to current cytology-based cervical cancer screening methods. |
| > 65 years | Screening should be discontinued at 65 years of age in women with a history of negative screening results (three consecutive negative cytology results or two consecutive negative cotesting results in the previous 10 years, with the most recent test within five years) and no history of CIN 2 or higher.* | — |

**Note:** Women who have undergone hysterectomy (with removal of the cervix) and have no history of CIN 2 or higher do not require cytology or HPV screening regardless of age. The American Society for Colposcopy and Cervical Pathology mobile app may help in applying screening recommendations (http://www.asccp.org/Bookstore/ASCCP-Mobile-App).

CIN = Cervical intraepithelial neoplasia; FDA = U.S. Food and Drug Administration; HPV = Human papillomavirus.

*Exceptions: Women with a history of CIN 2 or 3, or adenocarcinoma in situ should continue screening for 20 years after regression or management, even if screening extends beyond 65 years of age; women should continue screening even if they have had a total (cervix removed) hysterectomy if they have a history of CIN 2 or higher in the past 20 years or cervical cancer at any point (cytology alone every three years for 20 years after initial surveillance); high-risk women (e.g., those with human immunodeficiency virus infection, immunocompromised women such as solid organ transplant recipients, women exposed to diethylstilbestrol in utero) require annual screening throughout their lives.

Information from:

Committee on Practice Bulletins—Gynecology. Practice bulletin no. 168: cervical cancer screening and prevention. Obstet Gynecol. 2016;128(4):e111-e130.

Huh WK, Ault KA, Chelmow D, et al. Use of primary high-risk human papillomavirus testing for cervical cancer screening: interim clinical guidance. Obstet Gynecol. 2015;125(2):330-337.

U.S. Preventive Services Task Force. Cervical cancer: screening. March 2012. http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/cervical-cancer-screening?ds=1&s=Cervix. Accessed March 1, 2016.

**eTable B.** Osteoporosis Screening Recommendations for Postmenopausal Women

| Organization | Recommendation |
|---|---|
| American College of Obstetricians and Gynecologists[B1] | BMD testing is recommended for women 65 years and older, and for postmenopausal women younger than 65 years who have risk factors. |
| National Osteoporosis Foundation[B2] | BMD testing is recommended for women 65 years and older, and for postmenopausal women younger than 65 years, based on risk factors. |
| USPSTF[B3] | Dual-energy x-ray absorptiometry screening is recommended for women 65 years and older, and for younger women whose fracture risk is equal to or greater than that of a 65-year-old white woman who has no additional risk factors; the USPSTF advises using a Fracture Risk Assessment Tool–generated 9.3% 10-year risk threshold to screen women 50 to 64 years of age.* |
| World Health Organization[B4] | Indirect evidence supports screening women 65 years and older, but no direct evidence supports widespread screening programs using BMD testing. |

BMD = Bone mineral density; USPSTF = U.S. Preventive Services Task Force.

*The Fracture Risk Assessment Tool is available at http://www.shef.ac.uk/FRAX.

Information from:

[B1]Committee on Practice Bulletins-Gynecology, American College of Obstetricians and Gynecologists. ACOG practice bulletin no. 129. Osteoporosis. Obstet Gynecol. 2012;120(3):718-734.

[B2]Cosman F, de Beur SJ, LeBoff MS, et al.; National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis [published correction appears in Osteoporos Int. 2015;26(7):2045-2047]. Osteoporos Int. 2014;25(10):2359-2381.

[B3]U.S. Preventive Services Task Force. Osteoporosis: screening. January 2011. http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/osteoporosis-screening. Accessed June 21, 2016.

[B4]World Health Organization. What evidence is there for the prevention and screening of osteoporosis? May 2006. http://www.euro.who.int/__data/assets/pdf_file/0009/74475/E88668.pdf. Accessed June 22, 2016.

**eTable C.** Psychosocial Considerations for Postmenopausal Women

| Topic | Comments | Suggested screening method |
|---|---|---|
| Alcohol misuse/abuse | The USPSTF recommends that clinicians screen persons 18 years and older for alcohol misuse and provide persons engaged in risky or hazardous drinking with brief behavioral counseling interventions to reduce alcohol misuse.[C1] | CAGE questionnaire*[C2]<br>• Have you ever felt you should Cut down on your drinking?<br>• Have people Annoyed you by criticizing your drinking?<br>• Have you ever felt bad or Guilty about your drinking?<br>• Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (Eye opener)? |
| Depression | The USPSTF recommends screening all adults, including older adults, for depression.[C3]<br>Depression is more common in women than in men, but not more common in postmenopausal women. | Patient Health Questionnaire, Hospital Anxiety and Depression Scale, Geriatric Depression Scale |
| Intimate partner violence† | The U.S. Department of Health and Human Services has recommended that screening and counseling for intimate partner violence should be a core part of women's preventive health visits.<br>More than one in three women in the United States have experienced rape, physical violence, or stalking by an intimate partner[C4]; 14% of noninstitutionalized older adults experienced financial exploitation, neglect, or physical, psychological, or sexual abuse during the past year[C5]; women with disabilities are four times more likely to have experienced sexual assault in the past year than women without disabilities.[C6]<br>Physicians should screen all women for intimate partner violence at periodic intervals[C7]; computer-based screening may be preferred by some patients.[C8] | Sample questions:<br>• Has your current partner ever threatened you or made you feel afraid?<br>• Has your partner ever hit, choked, or physically hurt you?<br>• Has your partner ever forced you to do something sexually that you did not want to do, or refused your request to use condoms?<br>• Has your partner prevented you from using a wheelchair, cane, respirator, or other assistive device?<br>• Has your partner refused to help you with an important personal need such as taking your medicine, getting to the bathroom, getting out of bed, bathing, getting dressed, or getting food or drink, or threatened not to help you with these personal needs? |

USPSTF = U.S. Preventive Services Task Force.

*The CAGE questionnaire is one of several available screening instruments. Incorporating the questions into the general history is recommended rather than using the questionnaire as a stand-alone screening tool. Item responses are scored 0 or 1, with a higher score indicating alcohol problems. A total score of 2 or greater is considered clinically significant.

†A pattern of assaultive and coercive behavior that may include physical injury, psychological abuse, sexual assault, progressive isolation, stalking, deprivation, intimidation, and reproductive coercion to control an intimate partner. Elder abuse and neglect are forms of intimate partner violence.

Information from:

[C1]U.S. Preventive Services Task Force. Alcohol misuse: screening and behavioral counseling interventions in primary care. May 2013. http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/alcohol-misuse-screening-and-behavioral-counseling-interventions-in-primary-care?ds=1&s=alcohol. Accessed June 23, 2016.

[C2]Ewing JA. Detecting alcoholism. The CAGE questionnaire. JAMA. 1984;252(14):1905-1907.

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[C5]U.S. Government Accountability Office. Elder justice: stronger federal leadership could enhance national response to elder abuse. http://www.gao.gov/products/GAO-11-208. Accessed June 22, 2016.

[C6]Martin SL, Ray N, Sotres-Alvarez D, et al. Physical and sexual assault of women with disabilities. Violence Against Women. 2006;12(9):823-837.

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# Practice Guidelines

## PHARMACOLOGIC TREATMENT OF HYPERTENSION: ACP AND AAFP RELEASE RECOMMENDATIONS FOR ADULTS 60 YEARS AND OLDER

Hypertension is a common chronic condition occurring in almost 65% of persons older than 60 years. Proper treatment can lower the risk of cardiovascular, renal, and cerebrovascular disease, as well as mortality; however, there is debate regarding ideal blood pressure (BP) targets. Comorbid conditions should also be considered when choosing a BP target in persons 60 years and older. The American College of Physicians (ACP) and American Academy of Family Physicians (AAFP) have made recommendations for all clinicians to treat hypertension in this patient population, based on the benefits and harms of higher (less than 150 mm Hg) and lower (140 mm Hg or less) systolic BP targets.

### Higher vs. Lower BP Targets

#### Benefits

Although trials have shown that treating high BP in older persons is beneficial, the evidence was based primarily on persons with moderate or severe hypertension (BP greater than 160 mm Hg) initially who later reached levels greater than 140 mm Hg with treatment. Based on high-quality evidence, all-cause mortality, stroke, and cardiac events are reduced in persons with initial BP levels of at least 160 mm Hg who later attained BP levels lower than 150 mm Hg.

High-quality evidence from a subgroup analysis evaluating trials of persons attaining BP levels less than 140 mm Hg vs. levels of 140 mm Hg or greater indicated that the risk reduction was comparable for mortality and cardiac events; however, stroke reduction was marginally better in persons attaining levels of 140 mm Hg or greater.

Based on moderate-quality evidence, a target BP of 130 to 140 mm Hg in persons with a history of stroke or transient ischemic attack (TIA) lowered the recurrence of stroke; however, cardiac events and all-cause mortality were not reduced.

No studies evaluated how comorbidities might affect the possible benefits of more aggressive BP treatment, and data were insufficient regarding treatment in persons with diastolic hypertension, but without systolic hypertension.

#### Harms

In four of 10 studies, lower BP targets were associated with a greater number of persons withdrawing because of adverse effects. Based on moderate-quality evidence, there were no differences in cognitive decline or dementia, fractures, or quality of life when comparing higher and lower BP targets. No information on electrolyte abnormalities, which commonly occur with hypertension treatment, was provided, nor did any studies evaluate the effects of comorbidities on harms.

### Recommendations

To lower the risk of mortality, stroke, and cardiac events in persons with a persistent BP level of 150 mm Hg or greater, treatment should be aimed at attaining a level of less than 150 mm Hg. High-quality evidence showed a reduction in these events at this target, with most persons experiencing benefit, regardless of the presence of diabetes mellitus. Studies in which patients' baseline mean BP levels were higher than 160 mm Hg indicated the best and most consistent benefit.

Medications for hypertension treatment include thiazide-type diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, and beta blockers.

To reduce the risk of stroke recurrence, starting or increasing medications should be considered in persons with a history of stroke or TIA to achieve a BP of less than 140 mm Hg. Based on moderate-quality evidence, a target of 130 to 140 mm Hg vs. higher targets in this population does reduce recurrent stroke without any statistically significant effect on cardiac events or all-cause mortality.

To lower the risk of stroke or cardiac events, starting or increasing medications should be considered to obtain a BP level less than 140 mm Hg in some persons with high cardiovascular risk. This decision should be individualized, taking into account comorbidities, other medications used, adverse effects, and expense. Typically, factors associated with increased cardiovascular risk

*Source:* Adapted from Am Fam Physician. 2017;95(9):588-589.

include known vascular disease, diabetes, metabolic syndrome, chronic kidney disease with an estimated glomerular filtration rate less than 45 mL per min per 1.73 $m^2$, and older age. The SPRINT study, which used a target of 120 mm Hg vs. 140 mm Hg in high-risk patients, showed a statistically significant reduction in cardiovascular events and all-cause mortality in persons without diabetes or a history of stroke, and an initial baseline BP of less than 140 mm Hg. However, the ACCORD study, which was limited to patients with type 2 diabetes, did not find a statistically significant reduction in nonfatal myocardial infarction or stroke, or death from cardiovascular causes. Stroke events were reduced; however, there were more serious adverse effects with a target of less than 120 mm Hg than with less than 140 mm Hg.

For all recommendations, treatment goals should be determined after discussing the benefits and harms of each BP target with patients.

## Clinical Considerations

Before initiating or altering treatment, an accurate BP measurement should be obtained. Because elevated BP does occur in office settings for some patients, several measurements in the office may be needed. Ambulatory and home monitoring can also be considered. Nonpharmacologic treatment consisting of dietary or lifestyle changes and increased physical activity can be considered before prescribing medication or combined with medications. Because persons who are 60 years and older are often taking other medications, the burden of additional treatment and possible medication interactions should be assessed when making treatment decisions for hypertension. Generic medications should be prescribed whenever possible. When making treatment decisions, physicians should keep in mind that evidence in persons with frailty or comorbidities is limited.

■■■■

# Make sure

## DURING MEDICAL PRACTICE

**SITUATION:** A patient with hypertension and type 2 diabetes and moderately increased albuminuria showed progression to chronic kidney disease (CKD).


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**LESSON:** Make sure that all patients with hypertension at risk for CKD are given the renoprotective drugs. In addition to providing 24-hour BP control, clinical studies in patients with diabetes show that telmisartan improves renal endothelial function, prevents progression from microalbuminuria to macroalbuminuria, slows the decline in glomerular filtration rate and reduces proteinuria in overt nephropathy.

*Cardiovasc Diabetol. 2010;9:60.*

# Photo Quiz

## ACQUIRED NAIL DISORDER IN AN OLDER PERSON

A 78-year-old man who had not seen a physician in many years had pain in his feet, but no history of trauma. He wore sneakers and was able to walk well without a cane or walker. He had not cut his toenails for an extended period and had poor hygiene. He was independent in activities of daily living. He had no relevant medical history and was not taking medications.

On physical examination, his lower extremities were cool with thin, dry, and scaly skin. Bilateral thick, elongated, and curved toenails 5 to 8 cm long were digging into the skin (Figure 1). Keratin debris was noted over the toes and interdigital spaces, and there was trace pitting edema on both legs. Dorsalis pedis pulses were diminished bilaterally. Sensation was grossly decreased to light touch.

### Question

Based on the patient's history and physical examination findings, which one of the following is the most likely diagnosis?

A. Onychauxis.

B. Onychogryphosis.

C. Onychorrhexis.

D. Onychoschizia.

E. Trachyonychia.

### Discussion

The answer is B: onychogryphosis. The condition is characterized by thickened, discolored, severely elongated, curved nails with claw-like deformity (ram's horn nail). Onychogryphosis occurs mostly in older or homeless persons as a result of chronic neglect, trauma, or poor nail care.[1-4] Although it occurs most commonly in the great toenails, any nail can be affected. Underlying peripheral vascular disease, poor circulation, and associated onychomycosis may occur, as in this patient.[1-4]

*Source:* Adapted from Am Fam Physician. 2017;95(8):519-520.

**Figure 1.**

Treatment of patients with onychogryphosis includes trimming the nails with an electric burr and filing subungual hyperkeratosis. Rough edges of the toenail should be smoothed down. Other treatments include avulsion of the nail plate and surgical or chemical destruction of the nail matrix with phenol or a carbon-dioxide laser.[5-7] The choice of treatment should take into account peripheral vascular circulation, treatment compliance, and potential complications. Periodic repeated treatments are usually required for maintenance.[5] Any coexisting fungal infection should be treated appropriately.[1,2]

Onychauxis is a thickening of the nail plate with discoloration that occurs in older persons. It may be associated with subungual hyperkeratosis of the nail bed. Presenting symptoms may include pain and onycholysis, and underlying fungal infection, hemorrhage, or ulceration of the nail bed.[3-5]

Onychorrhexis is increased nail brittleness with longitudinal ridging and fissuring of the nail plate. It can occur with several conditions, such as hypothyroidism, anemia, or bulimia. It may also be associated with use of nail polish remover or nail picking.[3,4]

Onychoschizia is splitting of the distal lamella of the nail horizontally at the free edge. It is often due to frequent water or detergent exposure.[4]

Trachyonychia, also known as twenty-nail dystrophy, is an idiopathic condition characterized by longitudinal

**Summary Table**

| Condition | Limb abnormalities |
|---|---|
| Onychauxis | Thickening of the nail plate with discoloration in older persons; may be associated with subungual hyperkeratosis of the nail bed |
| Onychogryphosis | Thickened, discolored, severely elongated nails; curled, claw-like deformity (ram's horn); underlying peripheral vascular disease, poor circulation, or associated onychomycosis may occur |
| Onychorrhexis | Increased nail brittleness with longitudinal ridging and fissuring of the nail plate |
| Onychoschizia | Splitting of the distal lamella of the nail horizontally at the free edge; often due to water or detergent exposure |
| Trachyonychia | Thinned nail with longitudinal ridges, pitting, and roughening of the proximal nail surface |

ridges, pitting, and roughening of the nail surface. This condition may also occur with inflammatory diseases, such as lichen planus, psoriasis, or alopecia areata.[3,4]

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CHAT WITH DR KK

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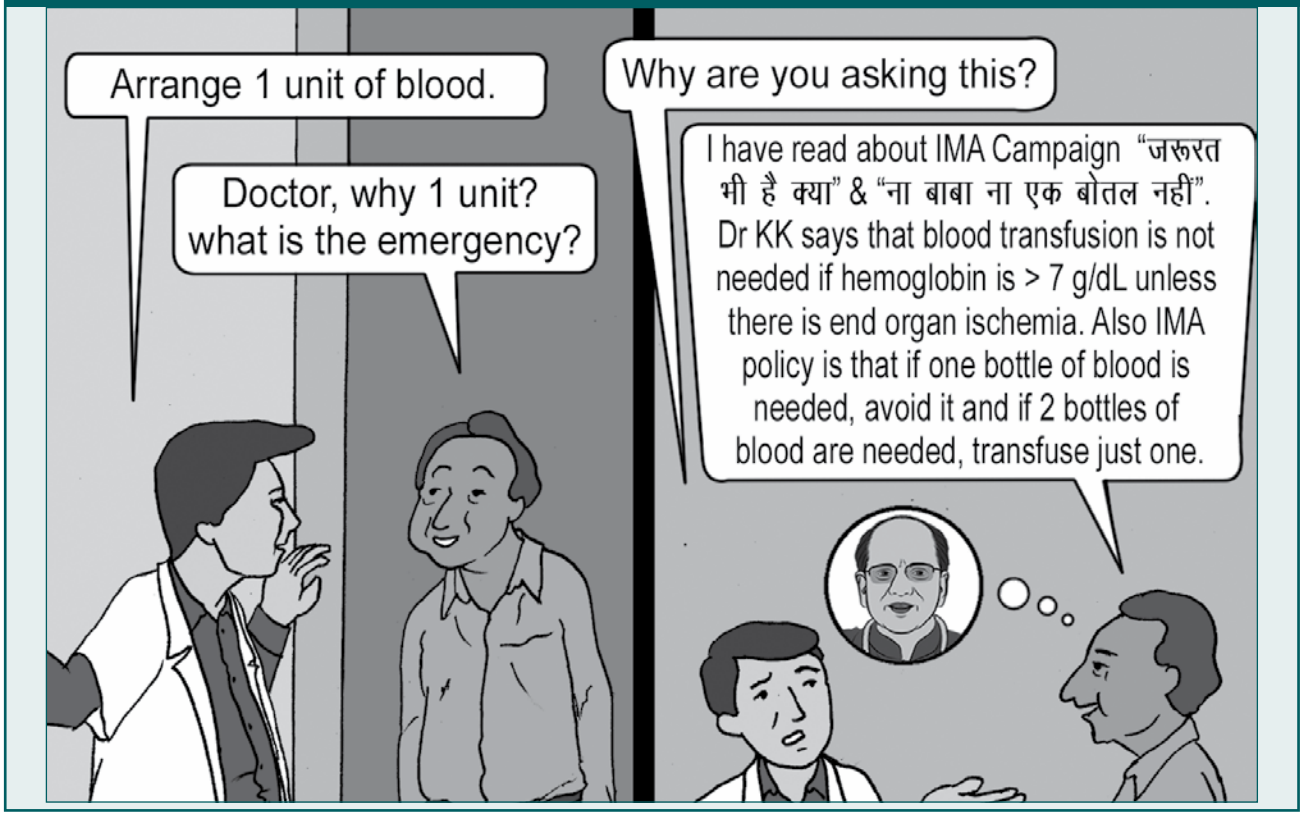

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# Study of Healthcare-associated Infections

PH MISHRA*, PALLAVI BANERJEE†, HEEMA GOSAIN‡

## ABSTRACT

Management of hospital-acquired infection is a very important aspect of healthcare management. A nosocomial infection affects approximately 2 million patients annually in acute care facilities in our country and their annual patient care costs several millions of rupees. Studies shows that nearly one-third of nosocomial infections can be prevented by a well-organized infection control program. But only <10% are actually prevented. Healthcare waste is an important source of healthcare-associated infection (HAI) and should be considered as a reservoir of pathogenic microorganisms, which can cause contamination and give rise to infection. If waste is inadequately managed, these microorganisms can be transmitted by direct contact, air or by a variety of vectors. Infectious waste contributes in this way to the risk of nosocomial infections, putting the health of hospital personnel and patients, at risk. The aim of the Hospital Infection Control Program is dissemination of information, surveillance activities, investigation, prevention and control of nosocomial infections in the hospitals.

**Keywords:** Hospital-acquired infection, hospital waste management, Hospital Infection Control Committee

This study describes the measures taken in a tertiary care hospital to control infection and its effect. There are big human and economic burdens of healthcare-associated infections (HAIs). The appropriate resources and activities required for an effective Infection Prevention and Control Program (IPCP) are very important to minimize the incidence and adverse outcomes of these infections.

The goals of IPCPs are to minimize these and other negative effects by contributing to patient safety through protecting patients from infections; protecting healthcare workers and visitors to healthcare facilities from infections; and accomplishing these goals in the most cost-effective manner whenever possible, thus reducing the economic impacts of HAIs on individual health facilities, health systems and the national healthcare industry.

HAIs occur in relation to healthcare interventions including invasive, diagnostic, surgical and medical procedures. Examples of HAIs include bloodstream, surgical site, urinary tract, pulmonary and skin and soft tissue infections. Transmission of infectious diseases, such as SARS, tuberculosis, influenza, *Clostridium difficile* (*C. difficile*), norovirus and antibiotic-resistant organisms (e.g., MRSA [methicillin-resistant *Staphylococcus aureus*] and VRE [vancomycin-resistant enterococci]) to patients within the healthcare delivery system are also considered HAIs.

IPCPs were first introduced in the1950s. Initially referred to as Infection Control Programs, these hospital-based programs focused on the control of hospital-acquired infections, which were referred to as nosocomial infections. As healthcare increased in complexity and sophistication and expanded beyond acute care, the mandate of IPCPs should have expanded to encompass infections in all settings across the healthcare continuum. Contrary to expectations; however, IPCPs have seen their resources either decrease or remain static and consequently have failed to achieve the needs of the expanding mandate.

HAIs contribute to significant morbidity, mortality and economic costs and the risk of hospital-acquired infections is increasing. These infections are the most common complication affecting hospitalized patients. Effective IPCPs reduce nosocomial infections by at least 30% and have repeatedly been shown to be effective in controlling infection outbreaks in the healthcare setting. Appropriate resources, both in quantity and in quality, are required to support effective IPCPs.

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## AIM OF THE STUDY

The aim of the study is to see the effect of Hospital Infection Control Program in the intensive care unit (ICU) of a tertiary care hospital.

## MATERIAL AND METHODS

This study was conducted in the ICU of a tertiary care super specialty hospital (Indian Spinal Injuries Centre) by observing and monitoring the effect of implementing Hospital Infection Control Program in postoperative cases over a period of 7 days from the date of surgery. Indian Spinal Injuries Centre is a tertiary care specialized center for spinal injury patient, orthopedics and joint replacement.

### Infection Control Program

Hospital control program team consists of two infection control nurses and one infection control officer (microbiologist) who are responsible for infection control work. There is a multidisciplinary Hospital Infection Control Committee chaired by medical superintendent and microbiologist is the member secretary and other members are from different clinical and nonclinical specialties, nursing and housekeeping.

## REVIEW OF LITERATURE

A nosocomial infection (derived from the Greek words nosos [disease] and komein [to care for], and later the Latin word for hospital nosocomium) is defined as an "Infection that is not present or incubating when the patient is admitted to hospital or other healthcare facility".

The time frame for diagnosis of a nosocomial infection will thus clearly be dependent on the incubation period of the specific infection; 48-72 hours after admission is generally deemed indicative of nosocomial, rather than community-acquired infection.

Although generally associated with hospital admission (hence the term hospital-acquired infection), nosocomial infections can arise after admission to any healthcare facility and the term HAI is increasingly being used. Such infections are common and associated with great morbidity and mortality. Indeed, one provocative headline stated "Hospital-acquired infections kill 5,000 patients a year in England".

The information for this news piece was taken from a government report on hospital-acquired infection in England, which suggested that there are at least 1,00,000 cases of hospital-acquired infection every year in England, costing the UK National Health Service some £1 billion each year. In addition to their association with increased morbidity and mortality, nosocomial infections are frequently associated with drug-resistant microorganisms, including MRSA and extended-spectrum β-lactamase (ESBL)-producing Gram-negative bacteria, which can pose considerable therapeutic problems.

Medicolegal issues can also arise, since patients or their families sometimes blame the hospital or staff for the infection, and demand compensation. Nosocomial infections can affect any part of the body, but respiratory tract infections are most frequent, followed by central line infections, urinary tract infections and wound infections.

## PATHOPHYSIOLOGY

The development of nosocomial infection is dependent on two key pathophysiological factors: decreased host defences and colonization by pathogenic, or potentially pathogenic, bacteria.

Although these two factors can arise independently, for infection to result both must be present to some degree. Direct contact can include spread from the hands of healthcare workers or visitors, but also from contaminated equipment and infusions.

## UNDERLYING HEALTH IMPAIRMENT

Certain conditions predispose to bacterial colonization, and hence nosocomial infection, by impairing host-defense mechanisms. Patients with chronic lung disease are at an increased risk of developing nosocomial infection. Poor nutrition and chronic debilitation are associated with reduced immune defense, explaining the increased risk of nosocomial infections in such patients.

## THE ACUTE DISEASE PROCESS

The underlying disease process as well as the severity of disease can affect the risk of developing nosocomial infection. Patients with a primary diagnosis of trauma or burns are at an increased risk. Trauma patients too have altered immune responses, making them more likely to develop infection.

Perhaps unsurprisingly, severity of illness as assessed by severity scores has also been associated with the development of nosocomial infection, but rather associated with other risk factors for infection, such as prolonged length of stay.

## INVASIVE DEVICES

In a report from the National Nosocomial Infection Surveillance (NNIS) system, involving data from 4,98,998 patients, 83% of episodes of nosocomial pneumonia were associated with mechanical ventilation, 97% of urinary tract infections arose in patients with a urinary catheter in place and 87% of primary bloodstream infections were in patients with a central line.

## TREATMENT METHODS

Various therapeutic strategies are associated with a raised risk of nosocomial infection. Cook and colleagues noted that the administration of paralytic agents was an independent predictor of nosocomial pneumonia in their study of 1,014 mechanically ventilated patients. Sedative drugs, corticotherapy, antacids, stress-ulcer prophylaxis, previous antibiotic therapy and multiple blood transfusions have all been identified as risk factors.

## EPIDEMIOLOGY

The quoted incidence of nosocomial infection varies, according to the setting i.e., the type of hospital or ICU the population of patients, and the precise definition used (hospital-acquired, ICU acquired, nosocomial pneumonia). One of the largest databases related to nosocomial infection in intensive care. In this 1-day point prevalence study, information was obtained on all patients who occupied a bed in an ICU over 24 hours in 1992: 10,038 patients were recruited from 1,417 western European ICU. Of these patients, 4,501 were infected and of those 2,064 (21% of the total number) had an ICU-acquired infection. There was a relation between the prevalence of nosocomial infection and mortality according to country, with greater incidence of infection and higher mortality rates in the southern European countries of Portugal and Greece than in Scandinavia and Switzerland (Fig. 1).

Other studies have quoted incidence rates between 9% and 37%, dependent largely on the populations studied and the definitions used. Differences in surveillance techniques can also affect detection of nosocomial infection and, hence, rates. However, we are becoming less invasive in our treatment techniques (less aggressive surgical procedures are used, fewer Swan-Ganz catheters are being placed, noninvasive mechanical ventilation is being applied when possible and appropriate) and are more aware of techniques that could prevent nosocomial infection

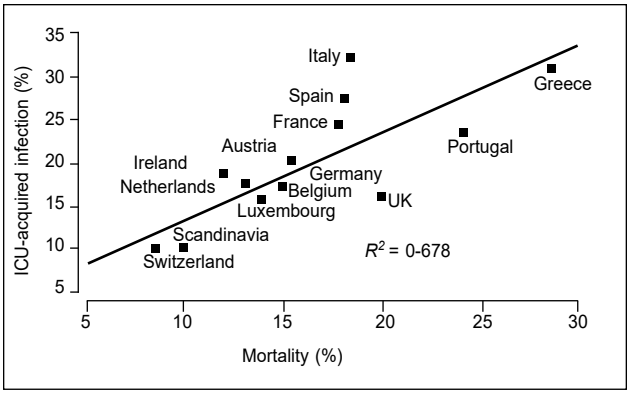


**Figure 1.** Correlation between prevalence rate of ICU-acquired infection and mortality rate by country.

(antibiotic-coated catheters, avoidance of nasotracheal intubation thus limiting sinusitis), which could result in a reduced incidence of infections. In a study on one ICU, comparing data over 25 years, the incidence of bacteremia increased from 1.8% in 1971-75 to 5.5% in 1991-95, with the largest increase seen between 1986-90 and 1991-95. Dagan and co-workers, however, reported a fall in the nosocomial infection ratio from 25.2% in 1987 to 20% in 1992.

## EFFECT OF NOSOCOMIAL INFECTION

The effect of nosocomial infection in terms of morbidity, mortality and increased resource use is substantial. Nosocomial infection is associated with an increased length of stay, which results in an additional cost of about US$ 3.5 billion per year, without taking into account antibiotic or other therapeutic costs. Crude mortality rates associated with nosocomial infection vary from 12% to 80%, dependent on the population studied and the definitions used.

## ORGANISMS

Any organism can be implicated in nosocomial infection, and many infections are polymicrobial. Recent years have seen a swing in the pattern of infecting organisms towards Gram-positive infections. The surveillance and control of pathogens of epidemiologic importance (SCOPE) project data revealed that Gram-positive cocci were isolated in 64% of 10,617 episodes of nosocomial bacteremia, whereas Gram-negative bacilli were isolated in only 27% of cases.

The EPIC study identified the following as the most commonly reported nosocomial pathogens: *S. aureus* (30%), *Pseudomonas aeruginosa* (29%), coagulase-negative staphylococci (19%), yeasts (17%), *Escherichia coli*

(13%), enterococci (12%), Acinetobacter spp. (9%) and Klebsiella spp. (8%). Other studies have noted similar patterns of causative microorganisms.

## ANTIMICROBIAL RESISTANCE

Antimicrobial resistance patients who remain in hospital for long periods can have successive infections and are more likely to develop nosocomial infections due to resistant pathogens. In the EPIC study, 60% of the *S. aureus* for which methicillin resistance patterns were reported, were resistant (as high as 80% in Italy, France, and Greece), and 46% of *P. aeruginosa* were resistant to gentamicin. Legras and colleagues similarly reported that 58% of the *S. aureus* in their study in French ICUs were methicillin-resistant. The NNIS reports increased rates of resistance for many microorganisms when comparing data from 2000 with those pooled from the period 1995 to 1999 (Fig. 2).

One approach to try and reduce the frequency of resistant organisms is to use antibiotic rotation or cycling. Gruson and colleagues noted that antibiotic rotation and restricted use of ceftazidime and ciprofloxacin caused a fall in the number of cases of VAP-associated with resistant Gram-negative bacilli, and an increase in the numbers of methicillin-sensitive *S. aureus.*

Raymond and co-workers introduced a quarterly rotation of empirical antibiotics in their ICU and noted great reductions in the incidence of antibiotic-resistant Gram-positive coccal infections (7.8 infections per 100 admissions vs. 14.6 infections per 100 admissions, $p < 0.0001$), antibiotic-resistant Gram-negative bacillary infections (2.5 infections per 100 admissions vs. 7.7 infections per 100 admissions $p < 0.0001$), and mortality associated with infection (2.9 deaths per 100 admissions vs. 9.6 deaths per 100 admissions, $p < 0.0001$) during rotation. Other groups have reported similar benefits from such strategies, which require continued input from infectious disease specialists if they are to be employed effectively.

## SPECIFIC NOSOCOMIAL INFECTIONS

### Respiratory

The respiratory tract is the most common site of nosocomial infection in the ICU. In the EPIC study, pneumonia accounted for 47% of nosocomial infections, the figure rising to 65% if all respiratory infections were included.

### Urinary Tract

This is the second most common site of nosocomial infection (accounting for 8-35% of infections), although the consequences of nosocomial urinary tract infection are usually less severe than for other types of nosocomial infection. Urinary tract infections are generally associated with the presence of a urinary catheter. Silver hydrogel-coated catheters might reduce the incidence of nosocomial urinary tract infection in general hospital patients, although results of several studies, including one in patients in intensive care, noted no significant differences.

Antibiotic-coated catheters (with nitrofural or ciprofloxacin) have been effective in animals and *in vitro*, but no results from clinical tests have been published and concerns exist as to the effects of such catheters on the development of antimicrobial resistance. Prevention of nosocomial urinary tract infections should thus aim at avoiding catheter placement whenever possible, but when necessary, reducing the duration of catheterization.

### Catheter-related Infections

Catheter-related bloodstream infections are associated with pronounced increases in length of time in ICU and hospital costs.

### Other Sites

Nosocomial infections from other sources are generally decreasing in incidence. One good example of how change in practice can affect infection rates is the case of nosocomial sinusitis, a nosocomial infection specific to ICU. Results of studies indicate that nosocomial sinusitis, carrying an increased risk of nosocomial pneumonia, was significantly more common in patients with nasal devices, such as nasogastric or nasotracheal tubes, than in those without.

In a randomized trial, Rouby and colleagues reported that radiological sinusitis developed in 95% of patients intubated with a nasal tube compared with 23% in patients with an oral tube. Use of the orotracheal route for intubation, rather than the nasotracheal route, has reduced the incidence of nosocomial sinusitis.

## FUTURE PERSPECTIVES

The roles of understaffing and staff composition as predisposing factors for nosocomial infection need to be emphasised. Fridkin and colleagues noted that the patient-to-nurse ratio was an independent risk factor for catheter-related bloodstream infection in

their population of surgical patients in intensive care. Infection surveillance can reduce nosocomial infection rates when incorporated with infection prevention programs, but needs to be improved and implemented and combined with continuing educational programs to encourage compliance with basic infection control procedures. Infection surveillance is increasingly undertaken and various surveillance systems have been developed.

## DEFINITIONS OF HOSPITAL-ACQUIRED (NOSOCOMIAL) INFECTIONS

The Centers for Disease Control and Prevention (CDC) defined hospital infection as follows:

Hospital-acquired infection (nosocomial infection) is the occurrence of infection after hospital admission, without evidence that the infection was present or incubating at the time of admission. A nosocomial infection usually occurs within 30 days after hospital stay or within 1 year in case of infection associated with insertion of a prosthetic device.

**Types of HAI:** All types were recorded. Infections in more than one site in the same person were registered as separate infections.

The following are clinical infection categories:

- Urinary tract infection (excluding asymptomatic bacteriuria
- Upper respiratory tract infection
- Lower respiratory tract infection
- Gastroenteritis
- Postoperative wound infection; incision site superficial
- Postoperative wound infection, deep-seated
- Skin and soft tissue infection, burn infection
- Skin and soft tissue infection, other infections
- Intra-abdominal infection
- Osteomyelitis
- Septicemia
- Meningitis
- Intravascular-access-device infection/infection in tracheal incision
- Infections in newborns.

## OBSERVATIONS

This study shows that if IPCP is implemented and monitored it can bring down HAI even in a hospital treating spine injuries (Where patients are unable to take care and move hence there are more chances of infection) (Table 1 and Fig. 2).

## DISCUSSION

### Impacts of HAIs: An Overview

Society as a whole suffers negative consequences from HAIs. These infections, including their investigation and treatment, have both immediate and future implications

**Table 1.** Infection Control Data for Indian Spinal Injuries Centre

| | Dec 11 | Jan 12 | Feb 12 | March 12 | April 12 | May 12 |
|---|---|---|---|---|---|---|
| UTI | 4.4 | 3.6 | 3.7 | 3.2 | 2.4 | 2 |
| BSI | 1.4 | 0.7 | 0 | 0 | 0 | 0 |
| SSI | 1.8 | 1.3 | 1.1 | 1 | 0.8 | 0.6 |
| VAP | 0 | 0 | 16.2 | 6.2 | 0 | 0 |

UTI = Urinary tract infection; BSI = Bloodstream infection; SSI = Surgical site infection; VAP = Ventilator-associated pneumonia.

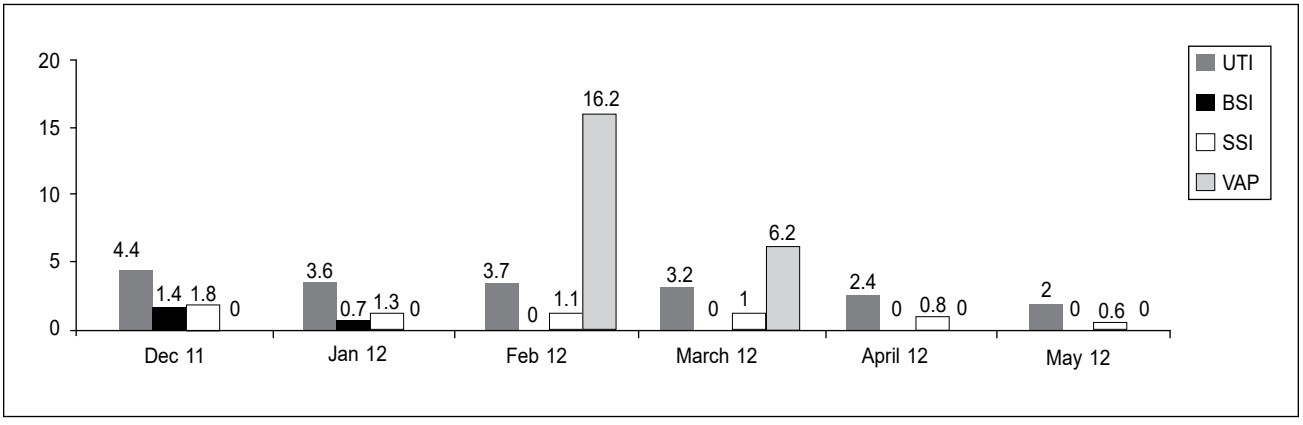


**Figure 2.** Infection control data for Indian Spinal Injuries Centre.

for the individual, the healthcare system, and the local, national and global communities. Although there are limited data describing the societal impact of HAIs, some emerging examples illustrate their breadth and gravity.

### Costs and Rates of HAIs

The management of HAIs exacerbates rising healthcare costs, although the exact attributable cost to society is unknown. Related financial impacts of HAIs include an increased time away from home for the individual with an infection and if employed, the individual experiences loss of work and wages or at least an increased use of sick leave.

The indirect costs, such as a family members' time lost from work in caring for the affected individual, must be considered in addition to the direct costs of increased use of resources, but have not been well-quantified. Overall, HAIs have a detrimental effect on the individual's quality-of-life and are very costly. The HAI financial burden to the healthcare system has been estimated by measuring a number of indices including increased:

- Number of readmissions to hospital
- Length of stay
- Use of antimicrobials
- Surveillance and isolation measures for AROs
- Laboratory and radiological services attributable to diagnosing and managing HAIs
- Overall direct or indirect costs
- Cost attributable to outbreaks.

Effective infection control program should include the following:

- Organized surveillance and control activities
- One infection control practitioner for every major Health Facility
- A trained hospital epidemiologist
- A system for reporting surgical wound infection rates and other infection back to the practicing surgeons and physicians.

### Essentials of the Standard Precautions to be Used in the Care of all Patients

#### Hand Hygiene

- Performed between patient contacts, after touching blood, secretions, excretions and contaminated items, whether or not gloves are worn.

Can be performed with:

- Alcoholic hand sanitizer
- Use of plain soap and water for routine hand washing.
- Use of antimicrobial agent for specific circumstances.

#### Gloves

- Wear gloves when touching blood, body fluids, secretions, excretions and contaminated items. Put on clean gloves just before touching mucous membranes and nonintact skin.

#### Mask, Eye Protection, Face Shield

- Wear a mask and eye protection or a face shield during procedures and patient care activities that are likely to generate splashes or sprays of blood, body fluids, secretions and excretions.

#### Gown

- Wear a gown during procedures and patient-care activities that are likely to generate splashes or sprays of blood, body fluids, secretions or excretions.

#### Patient-care Equipment

- Ensure that reusable equipment is not used for the care of another patient until it has been cleaned and reprocessed appropriately.

#### Environmental Control

- Ensure that the hospital has adequate procedures for the routine care, cleaning and disinfection of environmental surfaces.

#### Linen

- Handle used linen, soiled with blood, body fluids, secretions and excretions in a manner that prevents skin and mucous membrane exposures and that avoids transfer of microorganisms to other patients and environments.

#### Occupational Health and Blood Borne Pathogens

- Take care to prevent injuries when using needles, scalpels, and other sharp instruments or devices.
- Use ventilation devices as an alternative to mouth-to-mouth resuscitation methods.

#### Place of Care of the Patient

- Place a patient, who contaminates the environment or who does not assist in maintaining appropriate hygiene, in an isolated (or separate) room.

### Goals for Infection Control

There are three principal goals for hospital infection control and prevention programs regardless of the healthcare setting or service mix:

- Protect the patient
- Protect the healthcare worker, visitors and others in the healthcare environment
- Accomplish the previous goals in a timely, efficient, and cost-effective manner, whenever possible.

### Priority Outcome Areas

The priority outcome areas identified are:

- Management commitment, leadership and accountability
- Monitoring infection control and reducing infection rates
- Prevention of adverse events
- Protecting healthcare workers and visitors
- Surveillance.

### Management Commitment, Leadership and Accountability

The hospital management is responsible for ensuring management supports and allocates appropriate resources for effective prevention, monitoring and control of infection.

### Prevent Adverse Events

The hospital management has a risk management approach and ensures that senior management support an effective risk management program, which incorporates strategies for addressing infection control issues.

### Monitor IC and Reduce Infection Rates

Interruption of the transmission of or potential transmission of infectious disease, outbreak investigations and control, and performance improvement activities.

### Protect Staff and Visitors

The hospital management is responsible for the provision of a safe environment for patients, staff and visitors.

### Surveillance

There is a defined program for nosocomial infection surveillance which includes the collection, analysis and reporting back of data to those who need to know and take action. The Infection Control Team and Hospital Infection Control Committee play a major role in this. HAI rates could be reduced over a period of 6 months by simple approach like implementing and monitoring hand hygiene compliance among staff and those handling the patients.

## DO'S AND DON'TS

### Infection Control

#### Do's

- Ensure that all isolation/cohort areas are supplied with gloves/gowns, aprons and hand-hygiene supplies.
- Encourage and facilitate hand-hygiene practices
- Ensure ongoing and terminal cleaning of isolation areas.

#### Don'ts

- Transfer isolated/cohorted individual unless clinically essential.
- Prolong patient's placement in isolation area on cessation of symptoms/clearance of specimens/ completion of treatment and/or advice by specialist.

### Infection Control in Healthcare Environment Cleaning of Patient Care Devices

#### Do's

- Perform most cleaning, disinfection and sterilization of patient-care devices in a central processing department in order to control quality.
- Meticulously clean patient-care items with water and detergent or with water and enzymatic cleaners before high-level disinfection or sterilization procedures.
- Remove visible organic residue (e.g., residue of blood and tissue) and inorganic salts with cleaning.
- Use cleaning agents that are capable of removing visible organic and inorganic residues.
- Clean medical devices as soon as possible after use (e.g. at the point of use because soiled materials become dried onto the instruments). Dried or baked materials on the instrument make the removal process more difficult.
- Perform either manual cleaning (i.e., using friction) or mechanical cleaning (e.g., with ultrasonic cleaners, washer-disinfector, washer-sterilisers).
- Inspect equipment surfaces for breaks in integrity that can impair either cleaning or disinfection/ sterilization.

### Disinfectant Fogging

#### Don't

- Perform disinfectant fogging for routine purposes in patient-care areas.

### Disposal of Biohazard Materials

#### Do's

- Ensure segregation of waste at point of origin into designated colored bags depending on type of waste as per BMW (Management of Handling Rules, 1998).
- Ensure that janitor wears gloves, mask, apron when handling biomedical waste.
- Bag all used linen at point of origin. While changing linen avoid unnecessary agitation.
- Bag all linen, tie it up and keep aside.
- Use dedicated trolley for waste and for used linen.
- Disinfect waste trolley with FDA approved disinfectant after each use.
- Use material that do not generate fumes in wards and critical care units.
- Discard sharps in the dedicated sharps container.

### Best Practices for Prevention and Monitoring of Catheter-associated Urinary Tract Infections

#### Do's

Limit the use of indwelling urethral catheters to the following:

- Perioperative use for selected surgical procedures
- Urine output monitoring in critically ill patients
- Management of acute urinary retention and urinary obstruction
- Assistance in pressure ulcer healing for incontinence
- Properly secure indwelling catheters after insertion
- Maintain a sterile, continuously closed drainage system
- Collect a small sample of fresh urine for examination by aspirating urine from the sampling port with a sterile needle and syringe after cleansing the port with disinfectant
- Maintain unobstructed urine flow
- Empty the collecting bag regularly, using a separate collecting container for each patient
- Keep the collecting bag below the level of the bladder at all times.

#### Don'ts

- Disconnect the catheter and drainage tube unless the catheter requires irrigation.
- Screen for asymptomatic bacteriuria in catheterized patients.
- Treat asymptomatic bacteriuria in catheterized patients except before invasive urologic procedures.
- Irrigate catheter.
- Perform continuous irrigation of the bladder with antimicrobials as a routine infection prevention measure.
- Use systemic antimicrobials routinely as prophylaxis.
- Change catheters frequently.
- Routinely use silver-coated or other antibacterial catheters.

### Best Practices for Prevention and Monitoring of Surgical Site Infections

#### Do's

- Keep preoperative hospital stay as short as possible.
- Control serum blood glucose level in all diabetic patients adequately.
- Use electric clippers rather than razors or depilatories for hair removal. Hair should be removed immediately before the operation.
- Use an acceptable antiseptic agent for skin preparation, such as alcohol (usually 70-92%), chlorhexidine (4%, 2% or 0.5% in alcohol base) or iodine/iodophors (usually 10% aqueous with 1% iodine or with 7.5%).
- Perform the surgical scrub for duration of 3-5 minutes.
- Select a prophylactic antimicrobial agent based on its efficacy against the most common pathogens causing surgical site infection for a specific operation.
- Administer a antimicrobial prophylaxis, ideally within 30 minutes, but not longer than 2 hours before the initial incision.
- Maintain positive pressure ventilation in the operating room with respect to the corridors and adjacent areas.
- Maintain a minimum of 15 air changes per hour in the operating room, of which at least 3 should be of fresh air.
- Keep operating room doors closed except when needed for passage of equipment, personnel and the patient.

- Limit the number of personnel entering the operating room, to necessary ones only.
- Wet vacuum the operating room floor after the last operation of the day or in night with an EPA-approved hospital disinfectant.
- Protect an incision closed primarily with a sterile dressing for 24-48 hours postoperatively.
- Wash hands with an antiseptic agent before and after dressing changes or on any contact with the surgical site.
- Identify SSI using CDC definition without modification among surgical in patients and out patients.

### Don'ts

- Extend antibiotic prophylaxis postoperatively.
- Routinely use vancomycin for prophylaxis.
- Perform special cleaning or disinfection of operating rooms after contaminated or dirty operations.
- Perform routine environmental sampling of the operating room. Perform microbiologic sampling of operating room environmental surfaces or air only as part of an epidemiologic investigation.
- Use flash sterilization for routine reprocessing of surgical instruments.

## Best Practices for Prevention and Monitoring of Intravascular Catheter-related Infections

### Do's

- Educate healthcare workers regarding the indications for intravascular catheter use, proper procedures for the insertion and maintenance of intravascular catheters.
- Observe hand hygiene before and after palpating catheter insertion sites, as well as before and after inserting, replacing, accessing, repairing or dressing an intravascular catheter.
- Maintain aseptic technique for the insertion and care of intravascular catheters.
- Disinfect clean skin with an appropriate antiseptic before catheter insertion and during dressing changes. Although a 2% chlorhexidine-based preparation is preferred, but tincture of iodine, an iodophor or 70% alcohol can also be used.
- Select the catheter, insertion technique and insertion site with the lowest risk for complications (infectious and noninfectious) for the anticipated type and duration of intravenous therapy (IV) therapy.
- Promptly remove any intravascular catheter that is no longer essential.
- Replace all catheters as soon as possible and after no longer than 48 hours when adherence to aseptic technique can not be ensured (i.e., when catheters are inserted during a medical emergency)
- Use a subclavian site (rather than a jugular or a femoral site) in adult patients to minimize infection risk for tunneled central venous catheter (CVC) placement.
- Conduct surveillance in ICUs and other patient populations to determine catheter-related bloodstream infection (CRBSI) rates, monitor trends in those rates and assist in identifying lapses in infection control practices.

### Don'ts

- Routinely culture catheter tips.
- Routinely use arterial or venous cut down procedures as a method to insert catheters.
- Apply organic solvents (e.g., acetone and ether) to the skin before insertion of catheters or during dressing changes.
- Use topical antibiotic ointment or creams on insertion sites (except when using dialysis catheters) because of their potential to promote fungal infections and antimicrobial resistance.
- Routinely replace central venous or arterial catheters solely for the purposes of reducing the incidence of infection.
- Routinely replace venous catheters in patients who are bacteremic or fungemic if the source of infection is unlikely to be the catheter.
- Use filters routinely for infection-control purposes.
- Administer intranasal or systemic antimicrobial prophylaxis routinely before insertion or during use of an intravascular catheter to prevent catheter colonization or bloodstream infection.
- Routinely use antibiotic lock solutions to prevent CRBSI. Use prophylactic antibiotic lock solution only in special circumstances (e.g. in treating a patient with a long-term cuffed or tunneled catheter or port, having a history of multiple CRBSIs despite optimal maximal adherence to aseptic technique.

## CONCLUSION

HAIs increased morbidity, mortality and resource expenditure throughout the hospital setting and particularly in the ICU. A multidisciplinary approach to prevention that involves the whole intensive-care team including management is essential if we are to succeed

in preventing infections. Awareness of risk factors and attention to simple preventive measures such as hand hygiene can reduce the incidence and effect of these infections.

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# Effect of Various Surface Treatment on the Push-out Bond Strength of Glass Fiber Posts Bonded to Human Root Dentin: An *in vitro* Study

AVK NARENE*, P SHANKAR†, A KARTHICK*

## ABSTRACT

This *in vitro* study evaluated whether surface treatment for glass fiber posts has an effect on the push-out strength bonded to human root dentin. Fifty freshly extracted maxillary central incisors were endodontically treated and post-space preparation done. A total of 50 FRC Postec randomly divided into five groups (10 teeth each) were subjected to four different surface treatments: Silane only (II), cojet and silane (III), 10% sodium ethoxide and silane (IV), 10% hydrogen peroxide (V). The control group (I) did not receive any surface treatment. The root canals were treated with 37% phosphoric acid and Excite DSC and all the posts were luted with Variolink II dual cure resin. A push-out test was done to measure bond strength at different levels of the root. Data were analyzed with one-way ANOVA and post-hoc Tukey HSD test. The results showed no significant difference between control group and silane treatment. Cojet and silane (III) showed the highest bond strength of 15.50 ± 4.2 MPa, which was statistically significant than all the other group ($p < 0.001$). The coronal segment showed the highest mean bond strength of 13.74 ± 6.1 MPa ($p < 0.001$).

**Keywords:** Post, push-out bond strength, surface treatment

The challenge of restoring endodontically treated teeth has spawned a considerable diversity in foundation restorations and a plethora of publications in dental literature.[1] Pulpless teeth pose several challenges due to the loss of tooth structure by caries, defective restoration and endodontic access preparations.

Use of post system for the rehabilitation of endodontically treated teeth requires planning for restoring function of the tooth as well as structural and esthetic strategy. Currently, increasing demand for esthetic posts and cores has led to the development of zirconia and fiber posts.[2] These post systems have been developed to improve the optical effect of esthetic restorations.[3] Newer adhesive systems and resin-based luting agents create a genuine adhesive continuum between the tooth and the post-core complex. The use of these bondable materials allows the practitioner to unify the structure and morphology of root systems.[4]

Zirconium oxide posts demonstrate high fracture resistance due to high flexural strengths, which is comparable to that of cast gold and titanium posts. But the fracture of zirconium oxide posts often results in unrestorable damage to the tooth, whereas *in vitro* studies on fracture strength of fiber re-inforced composite (FRC) posts show more favorable mode of failure. The modulus of elasticity of FRC posts is closer to that of dentin and distributes stress evenly over a broad surface area.[5,6]

Fiber posts are bonded with resin luting cements, which allows the formation of a single unit where tooth, post and core function as a cohesive unit - monoblock configuration.[7] The clinical success of post retention depends on the bonding of post to the luting cement and luting cement with the dentin.[8] Surface treatments are methods by which general adhesive properties of a material are enhanced by facilitating chemical and micromechanical retention between different constituents.[9,10] Various methods of surface treatments for fiber posts are sand blasting, hydrogen

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peroxide ($H_2O_2$), silane, potassium permanganate, sodium ethoxide, etc.

Taking into consideration that the primary cause of failure of fiber posts is debonding, the objective of this study was to test the effect of various surface treatments on the push-out bond strength of glass fiber posts. The null hypotheses tested in this study were:

- The use of silane coupling agent alone does not have effect on the bond strengths of fiber posts
- There is no measurable difference in bond strength after different surface treatment
- There is no measurable difference in bond strength at different levels of root.

## METHODOLOGY

Fifty freshly extracted single rooted human maxillary central incisors free of caries and fractures without any significant canal curvatures and with type 1 canal configuration were selected and stored in 0.9% physiologic saline until root canal treatment was performed. Crowns were decoronated to the level of cementoenamel junction for all samples using a diamond disc and pulp was extirpated using barbed broaches.

An initial 10 size K-file was passed in the canal till its tip could be seen at the apex and the length was measured. Working length was calculated by subtracting 1 mm from the measured length of the initial 10 size K-file. The coronal third of the canal was prepared using GG drills from sizes 4-1, while apical and middle third was prepared with K files manually using step back technique. Three percent sodium hypochlorite, 17% EDTA (ethylenediaminetetraacetic acid) and 0.9% physiological saline were the standard irrigants used in the study. Master apical size of #35 was standardized and obturation was done by lateral condensation technique with AH Plus sealer.

Post-space preparation was done using the corresponding drill supplied by the manufacturer leaving 5 mm of apical gutta-percha for all the samples. The canals were then irrigated with distilled water and dried with paper points. The canal walls of all the experimental samples were then etched with 37% orthophosphoric acid gel for 15 seconds using an applicator tip.

The canal walls were then irrigated with distilled water to remove the excess etchant from the canal and dried with paper points. The bonding agent Excite DSC (Ivoclar Vivadent) was applied with the Microbrush all over the prepared post-space of the root canal and light cured for 20 seconds from the orifice. All the samples were randomly assigned into five experimental groups of 10 teeth each.

**Box 1.** Surface Treatment of Posts

- Group I (n = 10): No surface treatment
- Group II (n = 10): Silane treatment only (The posts were surface-treated with silane coupling agent (Monobond-S) for 60 seconds and then gently air-dried)
- Group III (n = 10): Cojet and silane treatment (The posts were sandblasted (Cojet) for 30 seconds and then treated with silane coupling agent for 60 seconds and then gently air-dried)
- Group IV (n = 10): 10% $H_2O_2$ and silane treatment (The posts were immersed in 10% $H_2O_2$ for 5 minutes, washed with distilled water and treated with silane solution for 60 seconds and then gently air-dried)
- Group V (n = 10): Sodium ethoxide and silane treatment (The posts were immersed in freshly prepared solution of sodium ethoxide for 5 minutes, washed with distilled water and treated with silane solution (Monobond-S) for 60 seconds and then gently air-dried).

The fiber post-FRC Postec (Ivoclar Vivadent) - 1.0 mm diameter (Tip) (n = 50) was grouped as shown in Box 1.

All the posts were then luted with Variolink II (Ivoclar Vivadent) dual cure resin cement. After luting the samples were stored in 100% humidity at 37°C and were subjected to a temperature of 45°C for 3 minutes, 5 times a day for 15 days.

### Push-out Bond Strength Testing

The apical 5 mm of the samples containing gutta-percha was cut down with a diamond disc. From the remaining coronal segment of the samples, 3 cross sections of 2 mm thickness from apical area were obtained and the thickness was checked with a digital vernier calipers.

The specimens were then placed in an acrylic mold of 2 mm diameter and then subjected to push-out bond strength testing. Each section was attached to the acrylic mold with cyanoacrylate adhesive ensuring that the coronal surface faces the mold and the post was centered over the hole of 2 mm diameter in the mold

The push-out mold was then placed in Lloyds Instron universal testing machine. The cross head was lowered at a speed of 1 mm/min until the post was dislodged. Push-out bond strengths were calculated for each section. All the values obtained were tabulated and subjected to statistical analysis.

## RESULTS

The highest mean push-out strength values were recorded in Group III (Cojet and Silane treatment) 15.50 ± 4.2 MPa followed by Group V (Sodium ethoxide and Silane treatment) 12.04 ± 3.9 MPa and Group IV (10% $H_2O_2$ and Silane treatment) 11.9 ± 3.5 MPa as shown in Table 1. These results were analyzed using one-way-ANOVA and post-hoc Tukey HSD test. Group III (Cojet and Silane treatment) was significant with all the other groups at $p < 0.001$ level. There was no significant difference between Group I (No surface treatment) 10.43 ± 3.8 MPa and Group II (Silane treatment) 10.73 ± 3.5 MPa at $p < 0.05$ proving that there was no increase in bond strength of fiber posts that had undergone silane treatment only.

In all the experimental groups, the coronal segment showed the highest mean bond strength of 13.74 ± 6.1 MPa. The lowest bond strength was observed with the apical segments (10.58 ± 5.1 MPa). Coronal segments show a statistical significance ($p < 0.001$) when compared with the apical and middle segments.

## DISCUSSION

The restoration of endodontically treated teeth is one of the extensively studied topics in endodontics and yet remains controversial from many perspectives. There are varieties of posts that are available today which may vary in composition, mechanical properties and structural geometry (Custom made cast post, prefabricated post, titanium post, zirconia and fiber posts).[11] Fiber-reinforced technology is already used for a wide range of applications in dentistry - splints, complete dentures, fixed dentures, retainers, etc. Fibers have also been used for endodontic post build-up restorations to reinforce composite resins.

Surface treatments are methods by which general adhesive properties of a material are enhanced by facilitating chemical and micromechanical retention between different constituents. As it has been hypothesized that the primary mode of failure of fiber posts is debonding, various surface treatment methods have been suggested to improve the bond between the post and the luting cement like sand blasting, silanization, $H_2O_2$, sodium ethoxide etching, etc.[12,13]

Silanes are hybrid organic-inorganic compounds that can mediate adhesion between matrices through their intrinsic dual reactivity. Although the use of silane coupling agents as adhesion promoters in fiber reinforced materials is well-established, their use in pre-treatment of fiber posts still remains controversial.[14,15] Bond integrity is challenged by the limited capacity to dissipate polymerization shrinkage stresses (C factor) in long narrow post-spaces that exhibit highly unfavorable cavity geometry.[16-18]

The efficacy of one step (self-etch) adhesives in forming a durable bond with root dentin is questioned.[19] It was shown that the hybrid layers created by self-etch adhesives are not uniform and contain nanovoids that are permeable to water. This may adversely affect the longevity of bonded root canal fillings and posts. The increased collagenolytic activity in root dentin due to the less acidic primers of self-etch adhesives have also been demonstrated recently.[20] Therefore, a total etch technique was followed in this study.

Excite DSC, dual polymerizing single bottle agent was used as the bonding agent. The uniform formation of hybrid layer lies in the wetting of the adhesive entirely over the etched surfaces. The importance of microbrush in reaching the narrowest and deepest portion of root canal preparations has been shown by Vichi et al[21] and Ferrari et al.[8] This results in a deep diffusion of resin into the tubules and the formation of uniform hybrid layer and lateral branches. In an attempt to simulate the oral condition, a thermocycling protocol was done to all the test samples.

In a recent study of the bonding of resin cements to fiber posts, it was found that the strength of the bond depended on the post material, the surface treatment of the post and the resin cement.[22] The role of silane

**Table 1.** Push-out Bond Strength of Coronal, Middle and Apical Specimens

| Groups<br>Subgroups | I (MPa) | II (MPa) | III (MPa) | IV (MPa) | V (MPa) |
|---|---|---|---|---|---|
| Coronal | 11.9 ± 6.3 | 12.5 ± 7.2 | 17.1 ± 7.0 | 13.5 ± 4.9 | 13.7 ± 5.5 |
| Middle | 10.5 ± 5.5 | 10.7 ± 6.9 | 15.2 ± 5.8 | 11.9 ± 5.2 | 12.0 ± 7.2 |
| Apical | 8.9 ± 7.3 | 9.0 ± 6.8 | 14.2 ± 4.9 | 10.3 ± 6.6 | 10.5 ± 7.3 |
| Mean | 10.43 ± 3.8 | 10.73 ± 3.5 | 15.5 ± 4.2 | 11.9 ± 3.5 | 12.04 ± 3.9 |

in the bonding of ceramics and composites has been established but its role in fiber post adhesion yet remains controversial. Silane due to its low viscosity would assist substrate wetting, and once an intimate contact between the interfacing materials is established, the Van der Waals forces would become effective providing physical adhesion, which may lead to a tertiary monoblock structure from the existing secondary monoblock.

The results showed no significant difference in Group I and II (No surface treatment and silane (10.43 ± 3.8 MPa and 10.73 ± 3.5) proving no increase in bond strength of fiber posts that had undergone only silane treatment. Hence, the first null hypothesis tested holds good. These results were in accordance with the study by Perdigao et al[23] and Newman et al.[24] The highest mean push-out strength values were recorded in Group III (Cojet and Silane) 15.50 ± 4.2 MPa followed by Group V (Sodium ethoxide and Silane) 12.04 ± 3.9 MPa and Group IV (10% $H_2O_2$ and Silane) 11.9 ± 3.5 MPa. The results show a statistically significant difference at $p < 0.001$ levels.

The highly cross-linked polymers of the matrix of the glass FRC posts used in this study do not have any free functional group for reaction.[22,23] This could be the possible reason for insignificant effect of the silane when no surface treatment was done. Etching solutions such as sodium ethoxide, hydrogen peroxide, potassium permanganate have been commonly employed for partially removing the resinous superficial layer of the fiber posts containing epoxy resin matrix. Increased bond strength has been observed after the combined etching and silanization coupling from various studies than silane treatment alone.

In the present study, mechanical roughening using cojet followed by silane treatment achieved the highest bond strength of 15.5 MPa compared to chemical etching (10% $H_2O_2$, sodium ethoxide) and silane treatment. These were significant to $p < 0.001$ level. In addition to that findings, etching with chemical solutions yielded higher bond strength values than Group I and II (Silane and Non-Silane). Thus, second null hypothesis tested has been proven to be false.

The coronal segment showed the highest mean bond strength of 13.47 ± 6.1 MPa. The lowest bond strength was observed with the apical segments. Coronal segments show a statistical significance ($p < 0.001$) when compared with the apical and middle group. But no statistical difference was observed between the middle and apical segments ($p > 0.001$). These results were consistent with the studies of Boff et al,[6] Kalkan et al[16] and Perdiago et al.[23] But these were in contrary with those of Teixeira et al in which apical segments revealed the highest bond strength which may be due to the fact that bond strength was related more to the area of solid dentin than the density of tubules.

Adhesion to root dentin is a viable procedure but structural differences exist between coronal and radicular dentin. Tubule density is greatest in the coronal and middle third than the apical third of the root. As adhesion is enhanced by the penetration of resin into the tubules, if there were a greater number of tubules per $mm^2$, a stronger bond would be expected. Additionally, the coronal portion of the canal is the most accessible part for the canal space, making it easier for thorough application of the adhesive and therefore formation of resin tags is more uniform than the deeper areas of the canal. Hence, the third null hypothesis tested has been proven to be false. Thus, mechanical roughening of the post (Cojet) and silanization has proven to be more effective than the use of the etching solutions and silane.

## CONCLUSION

Within the limitations of the present study it has been found that:

- Silanization without any surface treatment has negligible effect on the bond strength of fiber post.
- Cojet with silane treatment has proven to be more effective than silanization done along with etching solutions.
- There is a marginal increase in bond strength when the posts were silanated after etching with 10% $H_2O_2$ and sodium ethoxide.
- Highest push-out strength was achieved at the coronal third of the root when compared with the middle and apical third.

Further studies on these fiber post systems are required to validate the results of the present study. More parameters like microleakage, flexural strength, modulus of elasticity, etc. needs to be evaluated.

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## Safe Driving Limit

The legal permissible limit of blood alcohol content (BAC) is 0.03% or 30 μL alcohol in 100 mL blood alcohol as detected in a test by a Breath Analyzer.

- Two pegs in the first hour and one per every 1 hour after that will give a blood alcohol concentration of 0.05 (g/100 mL).

**"Blood-alcohol maximum-per-drink" number**

If you divide the number 3.8 by your body weight in pounds, you should obtain a number between 0.015 and 0.40. This is your personal "blood-alcohol maximum-per-drink" number. This is the maximum percentage alcohol that will be added to your blood with each "drink" you take.

For the purposes of this calculation, a "drink" is a 12-ounce, 4% alcohol, bottle of beer or a 4-ounce glass (a small wine glass) of 12% alcohol wine, or a one-ounce shot glass of 100 proof liquor (most bars's mixed drinks have this amount of alcohol). (Microbrewery beer, malt liquor, pint bottles of beer, large [6 oz.] wine glasses, 20% alcohol ["fortified"] wines and very stiff or large mixed drinks should be counted as "1½" drinks.)

# Serum Sclerostin Level in Patients of Type 2 Diabetes Mellitus and Its Correlation with HbA1c and Bone Turnover Markers

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## ABSTRACT

**Aims and objectives:** The aims were to observe the circulating level of sclerostin in type 2 diabetes mellitus patients and its relationship with glycemic control and markers of bone turnover. **Material and methods:** The study was an observational study conducted at JNMCH, Aligarh, Uttar Pradesh, with 50 male patients between 40 and 60 years of age, who were diabetic as per the ADA criteria. It excluded patients having diseases affecting bone metabolism (Paget disease, liver dysfunction, vitamin D deficiency, renal insufficiency, hematological disorder) or patients who had or were receiving treatment with drugs altering bone metabolism (calcium, vitamin D, calcitonin, thiazide, steroids, anticonvulsant). After obtaining the approval by Institutional Ethics Committee and the consent of patients, the subjects underwent investigations to assess for glycemic control, along with estimation of the serum levels of calcium, phosphate, 25-hydroxyvitamin D [25(OH)D], bone-specific alkaline phosphatase (BSAP) and sclerostin. Bone mineral density (BMD) was measured at L2-L4 by DEXA scan. **Results:** The mean level of serum sclerostin in our study was 79.84 pmol/L. The mean values of serum calcium, serum phosphate, 25(OH) D and BSAP were 8.75 mg/dL, 3.35 mg/dL, 24.66 pg/mL and 28.8 U/L, respectively. There was inverse correlation between sclerostin and BSAP ($r = –0.225$, $p < 0.004$) and levels of vitamin D ($r = –0.638$, $p < 0.001$). The serum sclerostin levels were negatively correlated with BMD ($r = –0.701$, $p < 0.001$) and positively with HbA1c ($r = 0.846$, $p < 0.001$). **Conclusion:** The circulating sclerostin level is increased in poorly controlled diabetes and is correlated with BMD and BSAP. It may be contributing to the deranged bone metabolism in diabetics. Additional studies are needed to evaluate the role of sclerostin on bone metabolism in this population.


**Keywords:** Type 2 diabetes mellitus, sclerostin, bone turnover markers

The incidence of type 2 diabetes mellitus (T2DM) and osteoporosis is increasing day by day and when present simultaneously, result in additive effect on morbidity and mortality of the patient. Osteoporosis is characterized by decreased bone mineral density (BMD) and deterioration of bone microarchitecture. Dual-energy X-ray absorptiometry (DEXA) is currently the criterion standard for the evaluation of BMD. DEXA provides the patient's T-score, which is the BMD value compared with that of control subjects who are at their peak BMD. The World Health Organization (WHO) criteria define a normal T-score value as within 1 standard deviation (SD) of the mean BMD value in a healthy young adult. Values lying farther from the mean are stratified as follows:

- T-score of -1 to -2.5 SD indicates osteopenia
- T-score of -2.5 SD or lower indicates osteoporosis
- T-score of -2.5 SD or lower with fragility fracture(s) indicates severe osteoporosis.

T2DM is associated with poor quality of bone due to impaired blood glucose, poor glycemic control, decreased levels of insulin-like growth factor, impaired vitamin D and calcium metabolism, possible vascular abnormalities, associated neuropathy, acidosis, ketosis, associated abnormalities of sex hormone levels and history of repeated falls in patients of diabetes mellitus.

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Sclerostin is a glycoprotein coded by *SOST* gene, located on chromosome 17 locus q11.2 with C terminal cysteine-like domain, with a length of 213 residues. It was previously considered as nonclassical bone morphogenic protein but recent studies reveal that it competitively binds to low-density lipoprotein receptor-related protein (LRP)-5 or -6 and inhibits Wnt signaling pathways. Wnt signaling pathway leads to expansion of osteoprogenitor cells as well as reduced apoptosis of osteoblast, leading to anabolic effects on bone. So, sclerostin by inhibiting this pathway, hinders bone formation. Sclerostin is secreted almost exclusively by osteocytes in adults and its levels are increased by calcitonin and decreased by parathormone, mechanical loading and cytokines.

## AIMS AND OBJECTIVES

The objective of our study was to evaluate serum sclerostin levels in a cohort of T2DM patients and to analyze its relationships with bone turnover markers, BMD and glycated hemoglobin (HbA1c).

## MATERIAL AND METHODS

The study was an observational, cross-sectional study. It was conducted in 50 male type 2 diabetes patients who were attending Medicine OPD of Jawaharlal Nehru Medical College and Hospital or Rajiv Gandhi Centre for Diabetes and Endocrinology, Aligarh, Uttar Pradesh. The study had Institutional Ethics Committee permission, and the procedures followed in the study were in accordance with institutional guidelines. All the participants were enrolled in the study after obtaining informed consent.

The study included only male patients, between 40 and 60 years of age, who were type 2 diabetic as per the American Diabetes Association (ADA) 2014 guideline. The patients having other co-existing diseases which affect bones like Paget disease, rheumatoid arthritis, hyperparathyroidism, hypercortisolism, renal bone disease, malignancy, liver dysfunction, hematological disorder, etc. were excluded from the study. The participant should not have received drugs which alter bone metabolism like calcium supplementation, vitamin D preparation, calcitonin, thiazide, steroids, anticonvulsant, at the time or prior to enrollment in the study.

All the participants were assessed as per a pre-designed proforma. After history, physical examination and routine laboratory investigations, they underwent specific investigations for bone metabolism and turnover like serum calcium, serum phosphate, bone-specific alkaline phosphatase (BSAP) and 25-hydroxyvitamin D [25(OH)D] assay. The serum level of sclerostin was measured by Sandwich enzyme-linked immunosorbent assay (ELISA) technique. The BMD of subjects at lumbar spine L2-L4, was assayed by DEXA scan. The measurements were compared to the normal range for bone density in a healthy young adult of same gender and ethnicity (T-score), with normal range between -1 to +1, T-score between -1 to -2.5 denoting osteopenia and T-score of <2.5 implying osteoporosis.

### Statistical Analysis

The data for continuous variables was expressed as mean ± SD and categorical variables were expressed as numbers or percentages. The association between continuous variables was described by Pearson's correlation coefficients. Statistical analysis was performed using SPSS version 10. Statistical significance was set at $p < 0.05$.

## OBSERVATION AND RESULTS

All the subjects in the study were males in the age group of 40-60 years, with mean age of 47.63 ± 6.88 years. The mean value of serum calcium in the study was 8.75 ± 0.348 mg/dL and that of serum phosphorus was 3.35 ± 0.6 mg/dL. The serum level of BSAP was 28.8 ± 9.2 U/L. 25(OH)D was also estimated in all the 50 subjects enrolled in the study with the mean value of 24.66 ± 3.18 pg/mL. The mean BMD was observed as 1.239 gm/cm$^2$ with SD of 0.0619. The mean value for serum sclerostin was 79.84 ± 20.04 pmol/L (Table 1).

Most of the participants had poorly controlled diabetes with 15 (30%) having HbA1c 6.5-8%, 26 (52%) having HbA1c 8.1-10% and 9 subjects (18%) having HbA1c more than 10% (Fig. 1). On correlating the HbA1c level with serum sclerostin levels, the correlation coefficient r was 0.846 with a p value of <0.001, indicating that poor glycemic control may contribute to increased sclerostin levels which has antianabolic effect on bone metabolism (Fig. 2).

The BMD of the subjects were correlated with sclerostin level and a negative correlation was observed ($r = –0.70$), which was significant ($p < 0.001$) (Fig. 3). BSAP is a marker for positive bone growth and was observed to be negatively correlated with serum sclerostin levels ($r = –0.225$, $p < 0.004$) (Fig. 4). In the study, on correlating the levels of 25(OH)D, it was seen that it


**IJCP SUTRA 427:** Identify your risk factors: and bring these to your doctor's attention, especially if you've had a previous fracture or have specific diseases and/or are taking medications that affect bone health.

**Table 1.** The Values of Glycemic Indices and Bone Turnover Markers

| Parameters | Mean | SD |
|---|---|---|
| Sclerostin (pmol/L) | 79.84 | 20.04 |
| Blood sugar fasting (mg/dL) | 154.98 | 43.66 |
| Blood sugar postprandial (mg/dL) | 209.7 | 52.08 |
| HbA1c (%) | 8.93 | 1.73 |
| 25(OH)D (pg/mL) | 24.66 | 3.18 |
| BSAP (U/L) | 28.8 | 9.2 |
| BMD (gm/cm$^2$) | 1.239 | 0.0619 |
| Serum calcium (mg/dL) | 8.75 | 0.348 |
| Serum phosphate (mg/dL) | 3.35 | 0.6 |

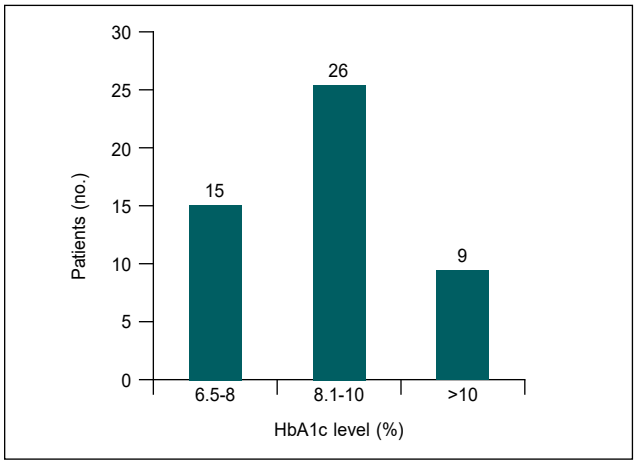


**Figure 1.** Distribution of HbA1c levels in subjects.

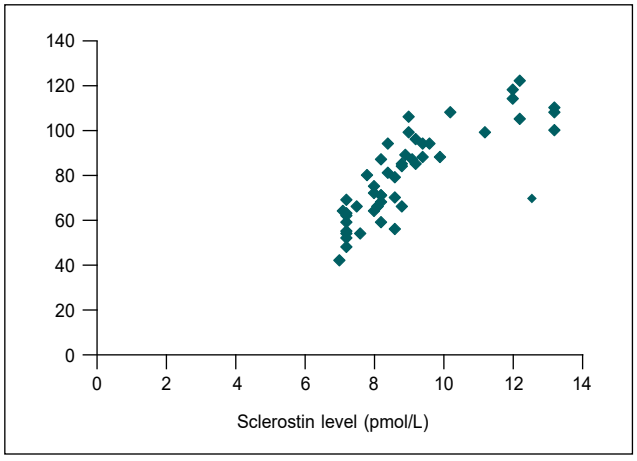


**Figure 2.** Relationship between HbA1c and serum sclerostin.

was negatively correlated with serum sclerostin levels ($r = –0.638$, $p < 0.001$) (Fig. 5). Table 2 summarizes the correlation between the markers of glycemic control and bone turnover with sclerostin level.

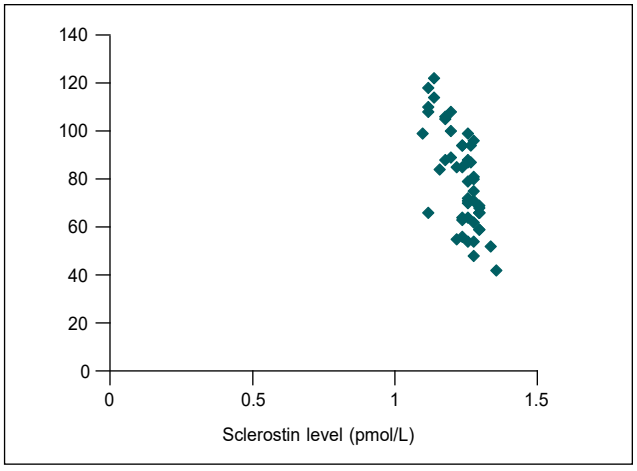


**Figure 3.** Relationship between serum sclerostin level and bone mineral density.

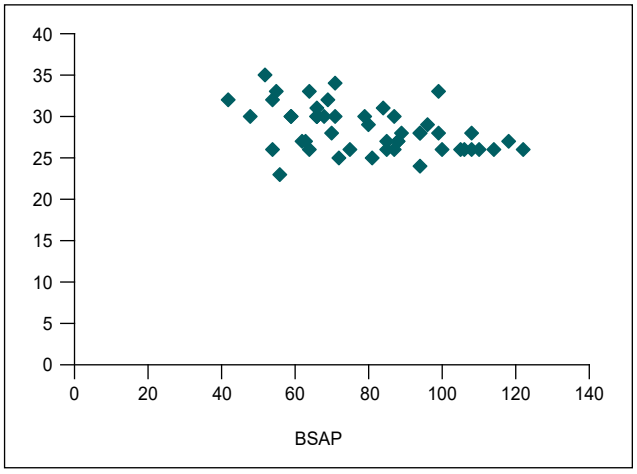


**Figure 4.** Relationship between serum sclerostin and BSAP.

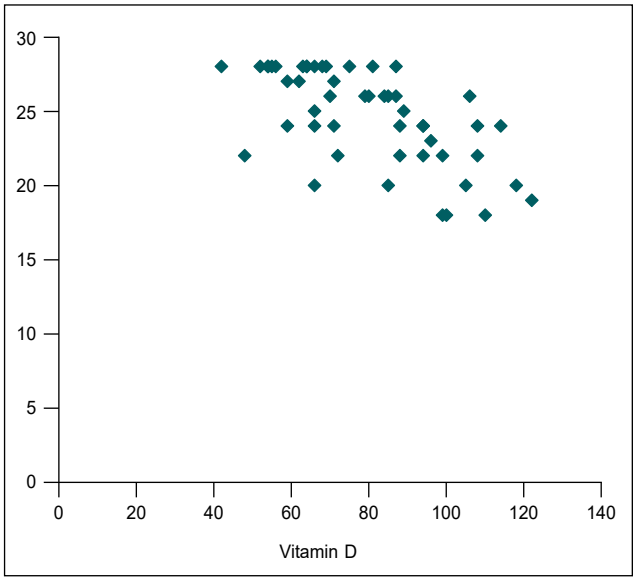


**Figure 5.** Relationship between serum sclerostin and 25(OH)D level.

**Table 2.** Correlation Between the Markers of Glycemic Control and Bone Turnover with Sclerostin Level

| Variables | BS (F) | BS (PP) | HbA1c | Vit. D | BMD | Calcium | BSAP | Phosphate |
|---|---|---|---|---|---|---|---|---|
| Correlation coff ('r' value) | +0.66 | 0.713 | 0.846 | –0.638 | –0.701 | –0.459 | –0.225 | –0.35 |
| P value | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | 0.01 | <0.004 | 0.685 |

BS = Blood sugar; F = Fasting; PP = Postprandial.

## DISCUSSION

The role of sclerostin has been evaluated and compared with other markers of bone turnover in different subgroups of patients like hemodialysis dependant chronic kidney disease (CKD) patients, immobilized patients, etc. Our study aimed to add to the existing knowledge by evaluating the sclerostin levels in type 2 diabetes patients and correlating its level with glycemic indices and markers of bone metabolism.

The mean level of serum sclerostin in our study was 79.84 ± 20.04 pmol/L, which was more than the normal levels observed in previous studies. In a study conducted by Mödder et al, in a population-based sample, the mean sclerostin level in healthy adult male was 33.3 ± 1.0 pmol/L. The higher levels may be partly be attributed to the age of our patients as serum sclerostin levels are observed to increase with age.

In our study, the serum levels of sclerostin were positively correlated with HbA1c levels ($r = 0.846$, $p < 0.001$). Similar association has been demonstrated by García-Martín et al. They postulated that it may be attributed to direct effect of hyperglycemia on bone cells and indirectly by formation of advanced glycation end products. Also the low physical activity in diabetic patients may lead to elevation in serum sclerostin levels. The result of immobilization on sclerostin has been observed by Gaudio et al.

The BMD in our study population was observed to have negative correlation with serum sclerostin level ($r = –0.701$, $p < 0.001$). This is expected observation since sclerostin inhibits osteoblastic activity. This is in accordance with the data derived from patients of sclerostosis and Van Buchem's disease and in mice over-expressing sclerostin. But is in contrast to the results observed in hemodialysis patients where sclerostin levels correlated positively with BMD. Ardawi et al also found negative correlation between the two parameters in pre- and postmenopausal females.

In the study population, the serum levels were correlated with the levels of BSAP and the correlation coefficient was $r = –0.225$ with a significant p value of <0.004. This is conceptually correct as sclerostin has an inhibitory effect on bone turnover. Our results are consistent with those reported by Mödder et al where bone alkaline phosphatase (B-ALP) and sclerostin levels were inversely associated in elderly females.

Our study also evaluated the relation between the levels of sclerostin and 25(OH)D and observed a negative correlation between the two variables ($r = –0.638$, $p < 0.001$). Ardawi et al also identified an inverse association between serum 25(OH)D and sclerostin levels in healthy postmenopausal women. This negative correlation prompted Dawson-Hughes et al to conduct an interventional study to evaluate the role of supplemental calcium and vitamin D on serum sclerostin levels.

## CONCLUSION

In our study, we have demonstrated increased level of serum sclerostin in type 2 diabetes patients and correlated it with HbA1c, BMD, BSAP and 25(OH)D. Sclerostin may be a contributing factor in poor osteogenesis and increased bone fragility in these patients by inhibiting Wnt pathway. But our study is limited by the small size of our sample, selection bias and the cross-sectional nature of our study. Thus, further studies are needed to evaluate the role of sclerostin as a marker of bone biology in all patients, including diabetics and using it as a target for therapeutic intervention.

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**IJCP SUTRA 429:** Feeling extra tired even after a good night's sleep. People with heart failure may limit activities they like to do or take naps to avoid feeling tired.

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■■■■

CHAT WITH DR KK

**Na Baba Na, Ek Bottle Nahi**

# Role of β-blockers in Prevention of Hepatopulmonary Syndrome in Chronic Liver Disease: An Observation

ASHISH GAUTAM*, PRABHAT AGRAWAL*, ASHWINI NIGAM*


## ABSTRACT

**Aim:** Study was initiated to study the presence of hepatopulmonary syndrome (HPS) in chronic liver disease patients, and role of β-blockers in its occurrence. **Methods:** Patients admitted in Dept. of Medicine and patients attending the Medicine OPD were examined and investigated for presence of HDS irrespective of its typical clinical features as explained in the literature. Patients having ascites or pleural effusion were managed by means of paracentesis and pleural tap first and then included in the study. Patients having any other primary pulmonary disease like bronchial asthma or chronic obstructive pulmonary disease were excluded from the study. Arterial blood gas analysis and contrast-enhanced echocardiography was done to confirm presence of arterial hypoxemia and pulmonary shunt, the diagnostic criteria. **Results:** During 1 year study, total 125 patients were enrolled in the study after appropriate selection criteria. Twenty-eight out of 125 patients were not taking propranolol. Propranolol is contraindicated in these patients for one or two reasons. Four out of these 28 patients developed HPS. One out of 97 patients who were on propranolol developed HPS. Total five patients were confirmed having HPS. The Fisher's exact test statistic value is 0.008887. The result is significant at $p < 0.01$. **Conclusion:** Patients of cirrhosis with portal hypertension on treatment with propranolol were having significantly lower chances of development of HPS then those without propranolol. Propranolol may have preventive role for development of HPS.


**Keywords:** Hepatopulmonary syndrome, β-blockers, chronic liver disease

Hepatopulmonary syndrome (HPS) and portopulmonary syndrome are two rare, but fatal extrahepatic complications of chronic liver disease and portal hypertension. Till date, no definitive treatment options are available for managing these complications. Few studies claim liver transplantation as the definitive treatment. Flückiger in 1884 for the first time recognized this clinical entity as complication of liver cirrhosis. Liver disease, with presence of arterial hypoxemia evident on arterial blood gas (ABG) analysis, and intrapulmonary vascular shunt as evident on contrast-enhanced echocardiography or use of technetium-99m–labeled macro aggregated albumin for lung scanning with quantitative brain uptake makes the triad of HPS. Clinical presentations are nonspecific and may include dyspnea on exertion or rest, presence of spider angiomas, clubbing, cyanosis and severe arterial hypoxemia. This study was conducted with the aim to evaluate patients of chronic liver disease for presence of HPS. Diagnostic criteria for HPS are given in Table 1.[1] Retrospective data regarding diagnosis and treatment were collected and evaluated for treatment given so far for management of cirrhosis.

## METHODS

One hundred twenty-five patients with liver disease of varied etiologies were enrolled in the study after

**Table 1.** Diagnostic Criteria for the Hepatopulmonary Syndrome[1]

| | |
|---|---|
| Oxygenation defect | Partial pressure of oxygen <80 mmHg or alveolar-arterial oxygen gradient ≥15 mmHg, while breathing ambient air |
| Pulmonary vascular dilatation | Positive findings on contrast-enhanced echocardiography or abnormal uptake in the brain (>6%) with radioactive lung-perfusion scanning |
| Liver disease | Portal hypertension (most common) with or without cirrhosis |

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appropriate selection criteria. Patients with any evidence of primary respiratory or cardiac disease were excluded. Cirrhosis and portal hypertension was confirmed by history, clinical examination, pathological investigations and radiology.

Patients were further evaluated for presence of platypnea, cyanosis, clubbing and angiomas; the typical associations of HPS. Irrespective of the grade of cirrhosis and presence of signs and symptoms all selected patients were evaluated for pulmonary shunt. For this a transthoracic contrast echocardiography was done using agitated saline. Visibility of micro-bubbles in the left atrium between 3-6 cardiac cycles after they were seen in right-atrium indicated micro-bubble passage through an abnormally dilated vascular bed. A due consent was taken from patients for this examination.

An ABG analysis was done in these patients. ABG was done in both resting supine position and in sitting upright position after 5 minutes. As per the diagnostic criteria in Table 1, cut-off value for considering HPS were resting $PO_2$ <80 mmHg and/or $\Delta PO_2$ i.e., $PO_2$ (A-a) ≥15 mmHg. We used resting $PO_2$ in our study. Using these criteria five patients were diagnosed to have HPS. Out of 125 patients, 97 were using propranolol, whereas 28 were not using propranolol as it was contraindicated in them due to one or more side effects in them. Propranolol is a drug used in portal hypertension as prophylaxis for secondary variceal bleeding. Four out of 28 developed HPS, whereas only one out of 97 developed HPS. The Fisher's exact test statistic value is 0.008887. The result is significant at $p < 0.01$.

## RESULTS

Out of 125 patients, five patients fulfilled the diagnostic criteria for presence of HPS. The mean age of patients was 52.6 years with standard deviation (SD) = 10.6. Eighty-four were male and 41 were females. Cause of chronic liver disease were alcoholic liver disease 56 (44.8%), chronic hepatitis B 38 (30.4%), chronic hepatitis C 14 (11.2%), noncirrhotic portal fibrosis 5 (4.0%); others and undetermined causes 12 (9.6%) (Table 2). Others included one case of autoimmune hepatitis. On the basis of examination and investigation, patients were categorized into Child's grade: A = 12, B = 20 and C = 93. On retrospective evaluation of medical records, it was found that 28 out of 125 patients were not taking propranolol or any other β-blocker. They all had one or two contraindications for using β-blocker. β-blockers are among preferred drugs used to reduce portal hypertension. Patients were categorized further in Group A (β-blocker using group) n = 97, and Group B (β-blocker contraindicated group) n = 28. In Group A, one out of 97 was diagnosed to have HPS. In Group B, four out of 28 patients were diagnosed to have HPS (Table 3).

The Fisher's exact test statistic value is 0.008887. The result is significant at $p < 0.01$. Causes of contraindications for β-blocker use were sinus bradycardia, clinical postural hypotension, diabetes, prolonged PR interval.

**Table 2.** Clinical Characteristics of 125 Study Patients

| Parameters | No. of patients |
|---|---|
| **Sex** | |
| Male | 84 |
| Female | 41 |
| **Clinical features** | |
| Platypnea | 5 |
| Cyanosis | 12 |
| Clubbing | 42 |
| Angiomas | 3 |
| **Causes of CLD** | |
| Alcohol | 56 |
| Hepatitis B | 38 |
| Hepatitis C | 14 |
| NCPF | 5 |
| Others | 12 |
| **Reason for β-blocker contraindications** | |
| Sinus bradycardia | 21 |
| Postural hypotension | 18 |
| Diabetes | 2 |
| Prolonged PR interval | 3 |

CLD = Chronic liver disease; NCPF = Noncirrhotic portal fibrosis.

**Table 3.** Characteristics of Five Patients with HPS

| | No. of patients |
|---|---|
| **Sex** | |
| Male | 4 |
| Female | 1 |
| **Clinical features** | |
| Platypnea | 3 |
| Cyanosis | 5 |
| Clubbing | 5 |
| Angiomas | 0 |
| **Mean $PaO_2$** | **78%** |

## DISCUSSION

Cirrhosis leads to a hyperdynamic state of circulation especially in presence of acute or chronic hepatocellular failure.[2] Peripheral vasodilatation and reduced peripheral vascular resistance manifests with peripheral flushing, erythema, decreased blood pressure and bounding pulse. Cardiac output is increased to compensate for above. The numerous functionally inactive arteriovenous fistulas open up due to this profound vasodilatation. HPS is manifestation of similar mechanism in liver cirrhosis, which develops when the pulmonary venous shunt is at its extreme.[3] Cyanosis and reduced oxygen saturation is a frequent finding in decompensated cirrhosis.[4] Various medications are tried in HPS with variable effectiveness but most do not seems to be effective in its reversal. Pentoxyphyllin[5] and methylene blue[6] till date are found effective up to a certain extent in HPS reversal.

β-blockers are among the preferred drugs for patients with portal hypertension. They are given in titrated doses to prevent primary and secondary bleeding from esophageal varices. β-blockers were clearly declared ineffective in management of HPS.[7] Still, there are few hopes in theory favoring them to use in HPS. A case report published in 1994 by Saunders et al, in which a patient improved from HPS proved by serial exercise testing.[8] This patient was on β-blocker for some time after which he showed signs of improvement. Although author itself was not able to describe the role of β-blocker in improvement from HPS still comparing the data from our study with this case may open the new ways of thoughts in using β-blockers as prophylaxis or may be for treatment of HPS.

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### ICD for Primary Prevention

- Patients with a prior myocardial infarction (at least 40 days ago) and left ventricular ejection fraction (LVEF) ≤30%.
- Patients with a cardiomyopathy, New York Heart Association (NYHA) functional class II to III and left LVEF ≤35%.
- Patients with nonischemic cardiomyopathy generally require optimal medical therapy for 3 months with documentation of persistent LVEF ≤35% at that time.
- Patients should be evaluated at least 3 months after revascularization (coronary artery bypass graft surgery [CABG] or stent placement).
- Some patients with heart failure who are candidates for an implantable cardioverter defibrillator (ICD) also have intraventricular conduction delay (≥120 ms). They are candidates for cardiac resynchronization therapy (CRT) with a biventricular pacemaker.
- CRT in patients with NYHA class III or IV heart failure (HF) (most class III) despite appropriate medical therapy, LVEF ≤35% and QRS duration ≥120-140 ms to reduce symptoms, reduce hospitalizations and improve survival.

# DERMACON INTERNATIONAL 2019 INDIA

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## KEY HIGHLIGHTS

- The 47th Annual conference of IADVL, with an international outreach program and with a theme of "Indian mission with global vision" will bring together.
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- Well planned courses & workshops on dermatosurgery, aesthetic dermatology, lasers and other procedural dermatology.

## CONFERENCE & CME REGISTRATION FEES

| | SLAB 2<br>1st May to 31st Aug 2018 | | SLAB 3<br>1st Sept to 15th Dec 2018 | | SLAB 4 / SPOT REG<br>16th Dec onwards | |
|---|---|---|---|---|---|---|
| Delegate Category | Conference Only | CME + Conference | Conference Only | CME + Conference | Conference Only | CME + Conference |
| IADVL Members | ₹ 10000 | ₹ 12700 | ₹ 11500 | ₹ 14500 | ₹ 15000 | ₹ 19000 |
| Post Graduates IADVL members | ₹ 7000 | ₹ 8500 | ₹ 8000 | ₹ 9500 | ₹ 10000 | ₹ 12500 |
| Accompanying Person | ₹ 7000 | ₹ 8500 | ₹ 8000 | ₹ 9500 | ₹ 10000 | ₹ 12500 |
| Workshop Registrations fees | | | | | | |
| Workshops | ₹ 2000 | N/A | ₹ 2500 | N/A | ₹ 3000 | N/A |
| Target Course | ₹ 3000 | N/A | ₹ 3500 | N/A | ₹ 4000 | N/A |

## INTERNATIONAL EVENTS

- 5 Sister Society has been confirmed (South Africa, Singapore, Iran, SriLanka & SARAD) we are expecting more.
- DERMACON International Quiz Competition.
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- DERMACON International Scholarships to Young Dermatologists.
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# The MURCS Association – Mullerian Aplasia, Renal Agenesis, Cervicothoracic Somite Dysplasia

AJAY C TANNA*, PRANAV I PATEL†, JEMIMA BHASKAR‡


## ABSTRACT

The MURCS (Mullerian agenesis, unilateral renal agenesis and cervicothoracic somite deformity) syndrome is a rare disease presenting with normal secondary sexual characters but uterus and upper vagina are absent due to mullerian agenesis. They usually present with primary amenorrhea. This case is unique because her primary diagnosis was chronic kidney disease and she was spotted in the dialysis unit. On thorough examination, her background diagnosis was arrived at. This case illustrates the fact that every patient must be examined in detail clinically.


**Keywords:** Fetal anomalies, renal failure, mullerian agenesis, dialysis, chromosomes

Embryogenesis and fetal development is a crucial period of life. Proper nutrition and care is a must to ensure a good outcome for the fetus. The care begins from the day of conception and any mistake afterwards will take its toll. Lack of care for even a single day can give rise to permanent damage in future. Here we will talk about one such condition in which teratogenicity occurs during end of 4th week of intrauterine life (Fig. 1). Let's see what happens next.

## METHODS AND STATISTICS

A single case study is presented here as a rare case.

## CASE STUDY

An 18-year-old female patient who presented with complaints of generalized weakness, easy fatigability, breathlessness on exertion, generalized anasarca and decrease in urine output was admitted. Patient had no complaints of decrease in appetite, decrease in food intake, difficulty in swallowing, yellow urine or sclera, abdominal distension, chest pain, perspiration, fever, sore throat, cough, cold, burning micturition or bleeding from any site. Patient was asked about menstrual history to rule out heavy bleeding recently or few months back but on the contrary, patient gave history of primary amenorrhea till date. Patient had no similar episodes in past.

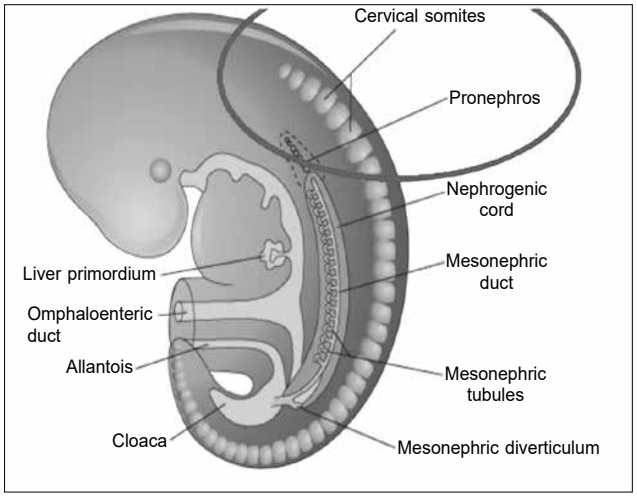


**Figure 1.** 4th week of intrauterine life.

On examination, patient was conscious and oriented to time-place-person. She had short stature, mild tachycardia with hyperdynamic pulse, hypertension, severe pallor without apparent jaundice and generalized edema with periorbital swelling and pitting pedal edema. Lung fields were clear with no heart murmurs. No organomegaly or tenderness observed over abdomen. Per vaginally, patient had small vaginal opening which on further examination was found to be abruptly

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ending in short course. Patient had normal secondary sexual characteristics. Blood picture showed decrease in hemoglobin to 5.3 g/dL with severe microcytic hypochromic anemia with normal bilirubin levels. Urine examination showed albuminuria, hematuria and pyuria. Renal function tests showed creatinine value of 24.5 mg/dL and urea of 287 mg/dL. Ultrasonography of abdomen and pelvic region revealed unilateral single kidney with altered echotexture, absent uterus and absent upper two-third part of vagina, suggestive of mullerian agenesis. Ovaries were normal. To rule out other complications, X-ray of cervicothoracic spine was done which revealed scoliosis. A diagnosis of MURCS association (Mullerian agenesis, unilateral renal agenesis and cervicothoracic somite deformity) was made. Barr body test came negative and further karyotyping done to assess any chromosomal abnormality showed normal chromosome structure of 46, XX. Patient was managed by hemodialysis with blood transfusion and antibiotics for urinary infection, antihypertensive, nutritional supplementation especially iron sucrose and erythropoietin, dietary interventions, etc. Later on, an arteriovenous fistula was inserted for maintenance dialysis. Patient was taught about gradual dilatation technique of vagina and explained about the disease and its prognosis. Echocardiography was done to rule out cardiac anomalies, which was normal.

## DISCUSSION

MURCS association is a syndrome characterized by mullerian aplasia or hypoplasia, unilateral renal agenesis or ectopy and cervicothoracic somite dysplasia which leads to defects in vertebra (e.g., scoliosis in this case), ribs, upper limbs and scapula. Other anomalies can also be seen, such as anorectal, cardiac, pulmonary and ovarian anomalies. The pathophysiology is not clear but it is believed to be an event occurring very early in development around end of 4th week of intrauterine life when the blastemas of pronephric buds and cervicothoracic buds are closely located. Regarding pathogenesis, it is hypothesized that there can be possibility of an unidentified teratogen as there is no chromosomal abnormality or familial transmission. The disease has similarities with 22q11 deletion syndrome and Mayer-Rokitansky-Küster-Hauser syndrome, suggesting a similar pathophysiology. Usually, the patient undergoes normal thelarche but menarche is the stage where the patient seeks help. Secondary sexual characteristics and bodily changes associated with menstruation are normal because ovaries are normal. Infertility, difficult voiding, skeletal abnormality, difficult intercourse, etc. could be the presentation. Per vaginal examination can be difficult. Diagnosis along with screening for all possible anomalies require ultrasonography, X-ray chest and cervicothoracic spine, magnetic resonance imaging (MRI), laparoscopy, pyelography, echocardiography, karyotyping, serum follicle stimulating and luteinizing hormone estimation, testosterone levels, etc. The syndrome is managed by frank perineal dilatation technique and various surgeries for reconstruction of vagina. Conception can happen with assisted reproductive techniques. Having a genetic offspring is possible through a gestational carrier. Psychological counseling is needed for gender identity issues if present. Other anomalies should be corrected e.g., renal replacement therapy for renal anomalies, orthopedic repair of vertebral anomalies, cardio surgery, etc.

## CONCLUSION

As we can see, this association between anomalies in this syndrome requires a combined approach from almost all specialties namely, gynecologist, physician, general surgeon, obstetric specialist, nephrologist, orthopedic surgeon, pathologist, microbiologist, biochemist, endocrinologist, cardiologist, cardio surgeon, pediatrician, psychiatrist, ENT surgeon, etc. Moreover, patient's willingness and effort is also required.

*"I can do things, you cannot;*
*You can do things, I cannot;*
*Together we can do great things."*

Although this may seem like too much of work, at the same time we should not forget our oath because:

*"Helping one person might not change the whole world,*
*But it could change the world for one person."*

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Every citizen of India should have the right to accessible, affordable, quality and safe heart care irrespective of his/her economical background

HEART CARE FOUNDATION OF INDIA
A Not-For-Profit Organisation

# Sameer Malik Heart Care Foundation Fund

An Initiative of Heart Care Foundation of India

E-219, Greater Kailash, Part I, New Delhi - 110048 E-mail: heartcarefoundationfund@gmail.com Helpline Number: +91 - 9958771177

*"No one should die of heart disease just because he/she cannot afford it"*

## About Sameer Malik Heart Care Foundation Fund

"Sameer Malik Heart Care Foundation Fund" it is an initiative of the Heart Care Foundation of India created with an objective to cater to the heart care needs of people.

## Objectives

- Assist heart patients belonging to economically weaker sections of the society in getting affordable and quality treatment.
- Raise awareness about the fundamental right of individuals to medical treatment irrespective of their religion or economical background.
- Sensitize the central and state government about the need for a National Cardiovascular Disease Control Program.
- Encourage and involve key stakeholders such as other NGOs, private institutions and individual to help reduce the number of deaths due to heart disease in the country.
- To promote heart care research in India.
- To promote and train hands-only CPR.

## Activities of the Fund

### Financial Assistance

Financial assistance is given to eligible non emergent heart patients. Apart from its own resources, the fund raises money through donations, aid from individuals, organizations, professional bodies, associations and other philanthropic organizations, etc.

After the sanction of grant, the fund members facilitate the patient in getting his/her heart intervention done at state of art heart hospitals in Delhi NCR like Medanta – The Medicity, National Heart Institute, All India Institute of Medical Sciences (AIIMS), RML Hospital, GB Pant Hospital, Jaipur Golden Hospital, etc. The money is transferred directly to the concerned hospital where surgery is to be done.

### Drug Subsidy

The HCFI Fund has tied up with Helpline Pharmacy in Delhi to facilitate patients with medicines at highly discounted rates (up to 50%) post surgery.

The HCFI Fund has also tied up for providing up to 50% discount on imaging (CT, MR, CT angiography, etc.)

## Who is Eligible?

All heart patients who need pacemakers, valve replacement, bypass surgery, surgery for congenital heart diseases, etc. are eligible to apply for assistance from the Fund. The Application form can be downloaded from the website of the Fund. http://heartcarefoundationfund.heartcarefoundation.org and submitted in the HCFI Fund office.

## Important Notes

- The patient must be a citizen of India with valid Voter ID Card/ Aadhaar Card/Driving License.
- The patient must be needy and underprivileged, to be assessed by Fund Committee.
- The HCFI Fund reserves the right to accept/reject any application for financial assistance without assigning any reasons thereof.
- The review of applications may take 4-6 weeks.
- All applications are judged on merit by a Medical Advisory Board who meet every Tuesday and decide on the acceptance/rejection of applications.
- The HCFI Fund is not responsible for failure of treatment/death of patient during or after the treatment has been rendered to the patient at designated hospitals.
- The HCFI Fund reserves the right to advise/direct the beneficiary to the designated hospital for the treatment.
- The financial assistance granted will be given directly to the treating hospital/medical center.
- The HCFI Fund has the right to print/publish/webcast/web post details of the patient including photos, and other details. (Under taking needs to be given to the HCFI Fund to publish the medical details so that more people can be benefitted).
- The HCFI Fund does not provide assistance for any emergent heart interventions.

## Check List of Documents to be Submitted with Application Form

- Passport size photo of the patient and the family
- A copy of medical records
- Identity proof with proof of residence
- Income proof (preferably given by SDM)
- BPL Card (If Card holder)
- Details of financial assistance taken/applied from other sources (Prime Minister's Relief Fund, National Illness Assistance Fund Ministry of Health Govt of India, Rotary Relief Fund, Delhi Arogya Kosh, Delhi Arogya Nidhi), etc., if anyone.

## Free Diagnostic Facility

The Fund has installed the latest State-of-the-Art 3 D Color Doppler EPIQ 7C Philips at E – 219, Greater Kailash, Part 1, New Delhi.
This machine is used to screen children and adult patients for any heart disease.

## Free Education and Employment Facility

HCFI has tied up with a leading educational institution and an export house in Delhi NCR to adopt and to provide free education and employment opportunities to needy heart patients post surgery. Girls and women will be preferred.

## Laboratory Subsidy

HCFI has also tied up with leading laboratories in Delhi to give up to 50% discounts on all pathological lab tests.

## Help Us to Save Lives

The Foundation seeks support, donations and contributions from individuals, organizations and establishments both private and governmental in its endeavor to reduce the number of deaths due to heart disease in the country. All donations made towards the Heart Care Foundation Fund are exempted from tax under Section 80 G of the IT Act (1961) within India. The Fund is also eligible for overseas donations under FCRA Registration (Reg. No 231650979). The objectives and activities of the trust are charitable within the meaning of 2 (15) of the IT Act 1961.

**Donate Now...**

## About Heart Care Foundation of India

Heart Care Foundation of India was founded in 1986 as a National Charitable Trust with the basic objective of creating awareness about all aspects of health for people from all walks of life incorporating all pathies using low-cost infotainment modules under one roof.

HCFI is the only NGO in the country on whose community-based health awareness events, the Government of India has released two commemorative national stamps (Rs 1 in 1991 on Run For The Heart and Rs 6.50 in 1993 on Heart Care Festival- First Perfect Health Mela). In February 2012, Government of Rajasthan also released one Cancellation stamp for organizing the first mega health camp at Ajmer.

## Objectives

- Preventive Health Care Education
- Perfect Health Mela
- Providing Financial Support for Heart Care Interventions
- Reversal of Sudden Cardiac Death Through CPR-10 Training Workshops
- Research in Heart Care

## Heart Care Foundation Blood Donation Camps

The Heart Care Foundation organizes regular blood donation camps. The blood collected is used for patients undergoing heart surgeries in various institutions across Delhi.

## Committee Members

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This Fund is dedicated to the memory of **Sameer Malik** who was an unfortunate victim of sudden cardiac death at a young age.

- HCFI has associated with Shree Cement Ltd. for newspaper and outdoor publicity campaign
- HCFI also provides Free ambulance services for adopted heart patients
- HCFI has also tied up with Manav Ashray to provide free/highly subsidized accommodation to heart patients & their families visiting Delhi for treatment.

http://heartcarefoundationfund.heartcarefoundation.org

# Study of Prevalence of Hypothyroidism and Effect of Treatment with L-thyroxine in Patients of Chronic Kidney Disease

NS SENGAR*, NIPUN GUPTA†, NANDITA PRABHAT‡


## ABSTRACT

**Objective:** There is scarcity of literature regarding prevalence and severity of thyroid abnormalities in chronic kidney disease (CKD) patients. This study (i) estimated the prevalence of hypothyroidism in CKD patients, (ii) investigated the effect of thyroid hormone replacement therapy (THRT) on changes in estimated glomerular filtration rate (eGFR) in CKD patients. **Material and methods:** This was a descriptive longitudinal study conducted in MLB Medical College, Jhansi over a period of 1 year, on patients with CKD. A total of 120 CKD patients with serum creatinine levels available at least two times in previous 6 months were enrolled, screened for thyroid function and those detected with hypothyroidism were treated with L-thyroxine. Before and after treatment, comparisons were made and for statistical analysis, paired *t*-test was used for association. **Results:** Out of 120 study subjects, maximum patients were in the age group of 51-60 years (36.67%) with 65% being males and 35% females. Twenty-one (17.5%) were found to have hypothyroidism, 18 (15%) had subclinical hypothyroidism and 3 (2.5%) had overt hypothyroidism. The stage-wise distribution of hypothyroidism in CKD patients was 15.6% in stage III, 16.67% in stage IV and 20% in stage V. The rate of decline in eGFR over 6 months was significantly reduced from 3.05 ± 2.02 mL/min/1.73 $m^2$ before the THRT to 1.02 ± 2.5 mL/min/1.73 $m^2$ after giving thyroid hormone replacement ($p < 0.001$). Among the patients given thyroid hormone replacement for 6 months, 61.9% showed slower decline in eGFR, 19% showed unchanged decline, 9.5% patients showed a faster decline in eGFR and 9.5% patients showed an improvement in eGFR after THRT. **Conclusion:** Hypothyroidism (15% subclinical and 2.5% overt) is a relatively common condition in CKD patients. Prevalence of hypothyroidism increased with progressively lower levels of GFR i.e., declining renal function. THRT attenuated the rate of decline in renal function in CKD patients with hypothyroidism, suggesting that THRT may delay reaching end-stage renal disease in these patients.


**Keywords:** Hypothyroidism, chronic kidney disease, estimated glomerular filtration rate, thyroid hormone replacement therapy

Thyroid hormones are important in cellular growth and differentiation, and modulation of physiological functions in all human tissues including the kidney. They also play a role in maintenance of water and electrolyte homeostasis. Therefore, thyroid dysfunction, either hypothyroidism or hyperthyroidism is accompanied by alterations in the metabolism of water and electrolytes, as well as cardiovascular function. On the other hand, the kidney is an important target organ for thyroid hormone actions and for the metabolism and elimination of the thyroid hormones. Derangement in kidney function is associated with abnormalities in the thyroid hormone physiology.[1]

Chronic kidney disease (CKD) affects both hypothalamus-pituitary-thyroidal axis and thyroid hormone peripheral metabolism. The effects of impaired kidney function may lead to hypothyroidism, hyperthyroidism and nonthyroidal illness, which are associated with deranged cardiovascular function, which will adversely affect the prognosis of CKD.[2]

Replacement of thyroid hormone is fundamental to the treatment of primary hypothyroidism. It relieves the symptoms of hypothyroidism and also alleviates the deleterious effects of overt hypothyroidism on the kidney.[3] Even though previous studies have demonstrated that L-thyroxine improves cardiac

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function and dyslipidemia in patients with subclinical hypothyroidism (SCH),[4,5] there is still a lack of consensus in current guidelines on whether to treat SCH patients with thyroid hormone or not.[6] In particular, little is known about the effect of thyroid hormone replacement on the changes in glomerular filtration rate (GFR) in CKD patients with SCH. The direct impact of thyroid hormone treatment on the changes in GFR in the same individuals with SCH could not be evaluated.[7]

In the present study, we compared the changes in GFR before and after thyroid hormone replacement in the same population of adult CKD patients with hypothyroidism. This study was done to simplify the importance of interactions between thyroid functions and kidney disease. This information is essential as it shows a link between two separate conditions. Information obtained from this study will help to increase clinical knowledge and enable clinicians to provide better management for their patients who have thyroid or kidney dysfunction.

## AIMS AND OBJECTIVES

- To estimate the prevalence of hypothyroidism in CKD patients.
- Effect on progression of chronic renal failure after treatment of hypothyroidism in CKD patients.

## MATERIAL AND METHODS

### Study Design

This was a descriptive longitudinal study and patients detected with hypothyroidism were subjected to before and after comparison studies.

### Study Site and Population

This study was conducted on 120 patients of CKD, selected randomly; attending the Nephrology Clinic and admitted in wards of Dept. of Medicine, MLB Medical College, Jhansi, Uttar Pradesh between March 2014 and April 2015. There were no dropouts or deaths during the study.

### Methodology

#### Inclusion Criteria

- Patients with CKD, between 20 and 75 years of age with serum creatinine levels available at least two times in previous 6 months before the start of study.
- Informed consent.

#### Case Definition

Kidney damage for >3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, that can lead to decreased GFR, manifest by either: Pathologic abnormalities *or* markers of kidney damage, including abnormalities in the composition of the blood or urine, abnormalities in imaging tests.

Estimated GFR (eGFR) <60 mL/min/1.73m$^2$ for >3 months, with or without kidney damage.[8] Estimation of eGFR done using the 4-variable Modification of Diet in Renal Disease (MDRD) formula:

$$GFR\ (mL/min/1.73\ m^2) = 175 \times (Standardized\ SCr\ [\mu mol/L])^{-1.154} \times (age\ [years])^{-0.203} \times 1.212\ (if\ black) \times 0.742\ (if\ female)$$

#### Exclusion Criteria

- Decline consent.
- Patients <20 or >75 years of age.
- Patients with heavy proteinuria including nephrotic syndrome or terminal malignancy.
- Patients who experienced acute exacerbation of underlying renal insufficiency due to dehydration, radiocontrast dye, urinary tract obstruction, etc.
- Patients previously being treated for thyroid disease.

**Thyroid Function Test and Definition:** In all patients, serum free tri-iodothyronine (FT3), free thyroxine (FT4) and thyroid-stimulating hormone (TSH) concentrations were measured. These levels were determined by chemiluminescent microparticle immunoassay. The diagnosis of SCH was solely based upon the results of a thyroid function test and was defined as a normal serum FT4, but elevated TSH levels, irrespective of clinical symptoms of hypothyroidism. Normal reference changes FT3 = 2.30-4.20 pg/mL FT4 = 0.89-1.75 ng/dL, TSH = 0.55-4.780 IU/mL.

**Treatment of Hypothyroidism and CKD:** All the patients with SCH took L-thyroxine, initially administered at lowest doses necessary to normalize serum TSH levels, which was 25 µg daily. Patients with overt hypothyroidism were prescribed L-thyroxine at 50 µg daily dose. The dose of L-thyroxine was adjusted every 3 months according to the follow-up levels of TSH. The treatment of CKD was continued as before the start of study: the patients on conservative management were prescribed oral hematinics, calcium supplements and antihypertensives and oral hypoglycemic agents (OHAs)

if required, and the patients who were earlier on hemodialysis were continued with the same.

### Statistical Analysis

Statistical analysis was performed using SPSS trial version. The data was entered into Microsoft Excel Software. Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables as number (percentage). We compared patients clinical and biochemical parameters at following time points: 6 and 3 months before L-thyroxine, time of initiation of thyroid hormone supplement and at 3 and 6 months after L-thyroxine treatment. For association, paired *t*-test was applied and p value <0.001 was considered statistically significant.

## OBSERVATIONS AND RESULTS

The distribution of study subjects was done according to the age (20-75 years) with maximum study subjects in the age group of 51-60 years (36.67%), with 65% being males and 35% females, stage-wise distribution of study subjects (Table 1) showed majority of participants in stage IV (40%) followed by stage III and V (36.67% and 33.33%, respectively). None of the study subjects included was in stage I or II. Among the study subjects, 75% were on conservative management and 25% were on hemodialysis.

The primary disease process, leading to CKD was diabetes mellitus type II (DM II) (36.67%), followed by hypertension (25%), obstructive uropathy (15%), glomerulonephritis (11.67%), cystic diseases (3.33%) and other causes (8.33%). Twenty-one subjects out of 120 study subjects were found to have hypothyroidism (17.5%) out of which 3 were overt hypothyroid (2.5%) and 18 were subclinical hypothyroid (15%) (Table 2).

The distribution of hypothyroidism stage-wise in CKD showed an increasing prevalence of hypothyroidism with decline in eGFR - 15.6% in stage III, 16.67% in stage IV and 20% in stage V (Table 1).

Hypothyroidism was found to be more common in females (19.04%) as compared to males (16.66%) (Table 3). The prevalence of hypothyroidism was 18.88% in patients with conservative management and 13.33% in study subjects on hemodialysis. The rate of decline in eGFR over 6 months was significantly reduced from 3.05 ± 2.02 mL/min/1.73 $m^2$ before the thyroid hormone replacement therapy (THRT) to 1.02 ± 2.5 mL/min/1.73 $m^2$ after giving thyroid hormone replacement ($p < 0.001$) (Tables 4 and 5; Fig. 1).

**Table 1.** Stage-wise Distribution of Hypothyroidism in CKD Patients

| | Stage I | Stage II | Stage III | Stage IV | Stage V |
|---|---|---|---|---|---|
| Total no. of subjects | 0 | 0 | 32 | 48 | 40 |
| No. of hypothyroid subjects | 0 | 0 | 5 | 8 | 8 |
| Percentage of hypothyroidism | 0 | 0 | 15.6 | 16.67 | 20.0 |

**Table 2.** Thyroid Profile in CKD Patients

| | Euthyroid | Overt hypothyroid | Subclinical hypothyroid |
|---|---|---|---|
| No. of subjects | 99 | 3 | 18 |
| Percentage (%) | 82.50 | 2.50 | 15.0 |

**Table 3.** Gender Distribution of Hypothyroidism in CKD Patients

| Gender | Total no. of subjects | No. of hypothyroid subjects | Percentage of hypothyroidism |
|---|---|---|---|
| Male | 78 | 13 | 16.66 |
| Female | 42 | 8 | 19.04 |

**Table 4.** Changes in eGFR Over Time in CKD Patients

| | -6 | -3 | 0 Baseline | +3 | +6 |
|---|---|---|---|---|---|
| eGFR mL/min/1.73 $m^2$ | 25.45 ± 11.15 | 23.92 ± 11.56 | 22.39 ± 11.63 | 21.76 ± 12.14 | 21.35 ± 13.2 |

**Table 5.** Comparison of Rate of Decline in eGFR Before and After THRT

| | 6 months before THRT (-6 to 0 months) | 6 months after THRT (0 to 6 months) | P value |
|---|---|---|---|
| Rate of decline of eGFR in mL/min/1.73 $m^2$ in 6 months | 3.05 ± 2.02 | 1.02 ± 2.5 | <0.001 |


IJCP SUTRA 438: It is important to focus on preventing infections. For instance, be at least 3-feet away from someone who has a cough or cold.

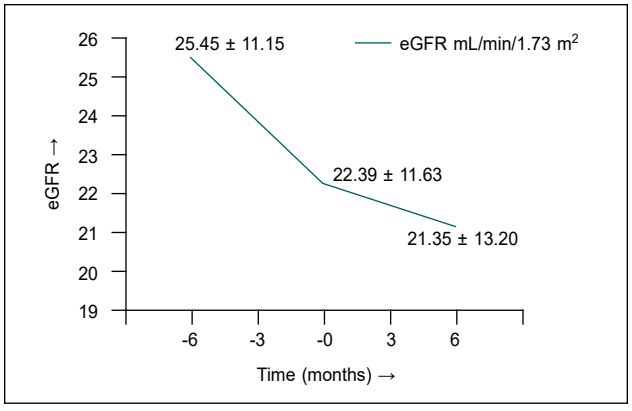


**Figure 1.** Changes in eGFR over time in CKD patients.

## DISCUSSION

The presented study was conducted in Dept. of Medicine, MLB Medical College, Jhansi on 120 subjects from March 2014 to April 2015. The subjects were of CKD, distributed according to the age groups starting from 20 years of age, up to 75 years of age, with maximum study subjects in the group of 51-60 years (36.67%). Of these, 78 (65%) were males and 42 (35%) were females. Classification of CKD into different stages in this study was done as per National Kidney Foundation guidelines, with eGFR using the four-variable MDRD formula.[8] Majority of the participants were CKD stage IV (40%). Number of participants in CKD stage III and V were 26.67% and 33.33%, respectively. None of the participants sampled were in CKD stage I or II. This could be attributed to delay in seeking medical treatment; hence, patients were seen when the disease has progressed to more severe stages. According to the 2003-2006 NHANES (National Health and Nutrition Examination Survey) data of US adults >20 years age, 15.32% is the most recent CKD prevalence with estimated stage-wise prevalence - stage I - 4.1%, stage II - 3.2%, stage III - 6.5% and stage IV + V - 0.6%.[9] Among the 120 patients of CKD included in the study, 90 subjects (75%) were on conservative management and 30 subjects (25%) were on hemodialysis.

Among the primary disease processes leading to CKD, the most common cause was found to be DM II (36.67%), followed by hypertensive nephrosclerosis (25%), glomerulonephritis (11.67%), obstructive uropathy (15%), cystic disease (3.33%) and other causes including human immunodeficiency virus (HIV) infection, pyelonephritis and cardiomyopathies included (8.33%). These results were in concordance with NHANES 2003-2006 data of US, except the percentage prevalence of obstructive uropathy, which was found to be higher in our study subjects of Bundelkhand region.

In our study, the prevalence of hypothyroidism was found to be 17.5% i.e., 21 subjects including 18 subjects of SCH (i.e., 15%) and 3 subjects of overt hypothyroidism (i.e., 2.5%). The stage-wise distribution of hypothyroidism in CKD patients showed the prevalence of hypothyroidism to be 15.6% in stage III, 16.67% in stage IV and 20% in stage V. We concluded that the prevalence of hypothyroidism increased with lower levels of eGFR. This was in concordance with previous study done by Lo et al[10] who used data from NHANES III and revealed the prevalence of hypothyroidism, occurring in 10.9% of patients with stage II CKD, 21% with stage III CKD and 23.1% with stage IV or V CKD. Among these hypothyroidism patients, 56% were considered subclinical. Moreover, Chonchol et al[11] showed that the prevalence of SCH increased from 7% at an eGFR >90 mL/min/1.73 $m^2$ to 17.9% at an eGFR <60 mL/min/1.73 $m^2$ in 3,089 outpatient adults.

In our study, the prevalence of hypothyroidism was found to be more in females (19.04%) as compared to males (16.66%). This was not in concordance with previous studies. Study among 137 subjects concluded at Kenyatta National Hospital, Kenya concluded that there was no statistically significant difference between prevalence of hypothyroidism in males and females. A study conducted by Allawi et al[12] on prevalence of hypothyroidism concluded it to be more in males (20%) as compared to females (6%). In relation to the type of treatment in CKD, the prevalence of hypothyroidism was found to be 18.88% on patients with conservative management and 13.33% in patients on hemodialysis.

At the time of commencement of thyroid hormone therapy in 21 hypothyroid subjects, the baseline characteristics were as shown in Table 6. The overall rate of decline in eGFR over 6 months was significantly blunted from 3.05 ± 2.02 to 1.02 ± 2.5 (mL/min/1.73 $m^2$) ($p < 0.001$) by THRT (Tables 4 and 5). The numbers of patients who had a slower fast or unchanged eGFR decline after THRT were determined, 61.9% patients had a slower decline in eGFR, 19% had unchanged decline, 9.5% had a faster decline and 9.5% patients showed an improvement in eGFR after thyroid replacement.

Among the patients who had a slower decline and improvement in eGFR, 20% (i.e., 3 patients) were of DM II, 53.3% (i.e., 8 patients) had systemic hypertension and 26.7% patients had other etiologies. These results were in concordance with the previous studies conducted.

A study conducted by Shin et al[13] on 113 CKD patients with SCH showed similar results with rates of decline in eGFR significantly attenuated by THRT (-4.31 ± 0.5 vs. -1.08 ± 0.36) ($p < 0.001$), but there was no significant

**Table 6.** Baseline Characteristics of Hypothyroid Patients

| | Total (n = 21) (mean ± SD) |
|---|---|
| Age | 44.1 ± 8.41 |
| Men | 13 |
| Women | 8 |
| DM II | 4 |
| HTN | 11 |
| Obstructive uropathy | 2 |
| Others | 4 |
| SBP | 136.57 ± 19.15 |
| DBP | 82.19 ± 9.44 |
| Thyroid function test | |
| FT3 | 2.33 ± 0.49 |
| FT4 | 0.89 ± 0.32 |
| S. TSH | 9.32 ± 3.52 |
| S. creatinine | 3.56 ± 1.39 |
| eGFR | 22.39 ± 11.63 |
| S. albumin | 3.34 ± 0.42 |

change in serum FT3 and T4 levels. Slower decline in eGFR was seen in 63.7% patients in this study. A similar study by Shin et al[7] conducted previous to the above mentioned study also demonstrated that thyroid hormone replacement preserved renal function, but in that study, the changes in eGFR were just compared between two different study populations, SCH patients with and without THRT.

A study by Hataya et al[14] showed that eGFR increased rapidly over first 6 months after THRT in CKD patients, followed by a plateau. The improvement in eGFR was up to 30% overall.

## CONCLUSION

The present study concluded that thyroid impairment in the form of hypothyroidism is common in CKD patients with SCH being more common and the prevalence of hypothyroidism increases with decline in eGFR levels. Since, thyroid dysfunction can cause significant changes in renal and cardiovascular functions, there is an increasing need to detect hypothyroidism earlier in CKD patients and to initiate early treatment to prevent morbidity and mortality associated. This study emphasized the role of THRT in patients of CKD with subclinical and overt hypothyroidism, as this alleviates the rate of decline in eGFR in these patients and may delay reaching end-stage renal disease in these patients.

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■■■■

# Is It Structural or Metabolic? A Diagnostic Dilemma

E SUMANRAJ*, N VIJAYAKUMAR†, A NANJILKUMARAN†, R UMARANI‡

## ABSTRACT

Osmotic demyelination syndrome (ODS), a disease affecting chronic alcoholic and malnourished patients was described by Adams and colleagues in 1959. It is also known as pontine myelinolysis. Pontine myelinolysis can be subdivided into central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM) depending upon the level of demyelination, within the pons or outside the pons, respectively. Rapid correction of hyponatremia contributes to the pathogenesis of ODS. Whenever a chronic alcoholic and/or malnourished develops confusion, quadriplegia, pseudobulbar palsy and pseudocoma (Locked-in-syndrome) over a period of several days, a high index of suspicion for ODS must be held.

**Keywords:** Osmotic demyelination syndrome, central pontine myelinolysis, extrapontine myelinolysis, hyponatremia

Osmotic demyelination syndrome (ODS), was described by Adams et al in 1959 as a disease affecting alcoholics and malnourished people. The etiology of ODS was not known for a long time but few authors suspected the cause to be either toxin or nutritional deficiency. 'Central pontine' indicates the site of lesion and the term 'myelinolysis' was used to emphasize that myelin was affected preferentially compared to other neuronal elements. Central pontine myelinolysis (CPM) is a noninflammatory, demyelinating condition characterized primarily by the systemic, noninflammatory destruction of myelin sheath in the basis pontis and primarily results from aggressive correction of hyponatremia.

In 1983, Laureno et al suggested rapid correction of hyponatremia as the cause for the condition, based on experimental data on animal model. They suggested that the condition could be prevented by correcting hyponatremia by <10 mmol/L in 24 hours.

Although uncommon, ODS has been reported at a rate of 0.4-0.56% for patients admitted to neurology services and 0.05% of cases admitted in a general hospital. A study found 0.3-1.1% of patients with unsuspected CPM during autopsies, with a greater percentage of CPM noted in patients with liver transplant and chronic liver disease. An autopsy-based study documented a prevalence rate of 0.25-0.5% in the general population and 10% in patients undergoing liver transplantation.

## CASE REPORT

A 63-year-old male presented to the emergency department (ED) with an unsteady gait, giddiness and left-sided weakness. His medical history was significant for hypertension, on irregular treatment and history of consumption of alcohol in the past. He had retrospective history of intravenous (IV) fluid infusion at a private hospital 2 hours prior to the initial presentation to ED.

General physical examination was unremarkable. Neurological examination revealed that the patient was alert, oriented with facial deviation towards right side and power was grade 0/5 both in left upper limb (UL) and lower limb (LL) with NIHSS score of 11. Fundus examination was normal. An initial diagnosis of cerebrovascular accident (CVA) left hemiplegia with left upper motor neuron (UMN) facial palsy was made.

Laboratory investigation showed that the patient had significant hypernatremia (149 mmol/L) at the time of presentation. Computed tomography (CT) of the brain (Fig. 1) performed approximately 3 hours after initial presentation was consistent with features of CVA (right parasagittal posteroparietal cortex).

On next day, 16 hours after initial presentation he developed dysarthria, dysphagia and inability to use his right LL. Motor examination showed decreased tone in left UL and LL, power of grade 0/5 in left UL and LL; grade 2/5 in right LL with exaggerated deep tendon reflexes, left equivocal plantar response (NIHSS

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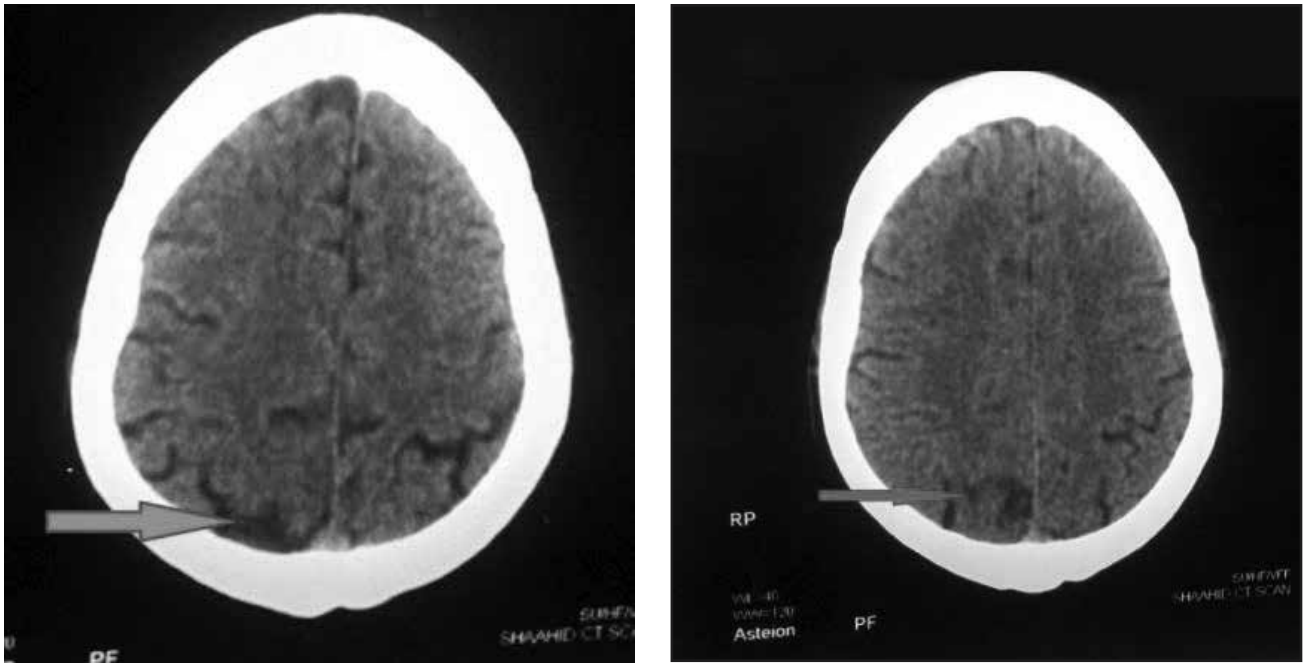


**Figure 1.** CT brain images showing patchy hypodensity at right posteroparietal cortex (*arrow*).

score of 16). Pupils were pinpointed and sluggishly reacting to light. Ocular fundus examination was normal. Patient was shifted to intensive care unit (ICU) and mechanically ventilated. Provisional diagnosis of probable posterior circulation restroke at the level of pons was made. Laboratory investigations revealed normal cell count and renal parameters. However, repeat sodium level was elevated (146 mmol/L).

Magnetic resonance (MR) (Fig. 2) imaging, performed 36 hours after the initial CT, showed well-defined area of diffusion restriction in the lower central pons bilaterally.

Differential diagnosis of pontine infarct, pontine hemorrhage and ODS was made.

In view of IV fluid infusion prior to presentation to our ED and clinical features of ataxia, quadriparesis, dysphagia, dysarthria without ophthalmoplegia and sensory loss suggestive of ODS with two elevated values of sodium and also classical MRI findings of diffusion restriction in the lower central pons bilaterally, diagnosis of ODS was made and treated accordingly. During the course of hospitalization, patient developed VAP for which he was treated and was discharged 3 weeks after admission with residual minimal left hemiparesis.

## DISCUSSION

It is important to differentiate between structural and metabolic causes of neurological deficits, and if structural, the level of lesion has to be localized. Lower cranial nerve palsies and bilateral findings point towards lower pontine lesion, the cause of which may be:

- Pontine infarct
- Pontine hemorrhage
- Osmotic demyelination syndrome (ODS).

### Pontine Infarct

Isolated pontine strokes are relatively frequent, but they can occur as part of the posterior circulation infarction. Ventral infarcts are the most common type of isolated pontine infarction (51-58%). Anteromedial infarct causes hemiparesis or hemiplegia, contralateral ataxia, dysarthria, dysphagia, nystagmus and often ipsilateral facial palsy. Less frequently associated is contralateral loss of proprioception, paresis of the ipsilateral horizontal gaze and internuclear ophthalmoplegia. Anterolateral infarct may produce hemiparesis, ataxia, loss of position sense and loss of vibration sense. Pure motor stroke, ataxic hemiparesis, dysarthria-clumsy hand or sensorimotor stroke are the other forms of manifestations of the anterolateral strokes. Dorsolateral pontine strokes may lead to contralateral hemiparesis, ipsilateral facial weakness, ipsilateral loss of facial pain and temperature sensation, hearing loss and ataxia. Rostral dorsolateral pontine infarct can manifest as ipsilateral Horner's syndrome, contralateral ataxia and contralateral loss of body pain and temperature sensation.

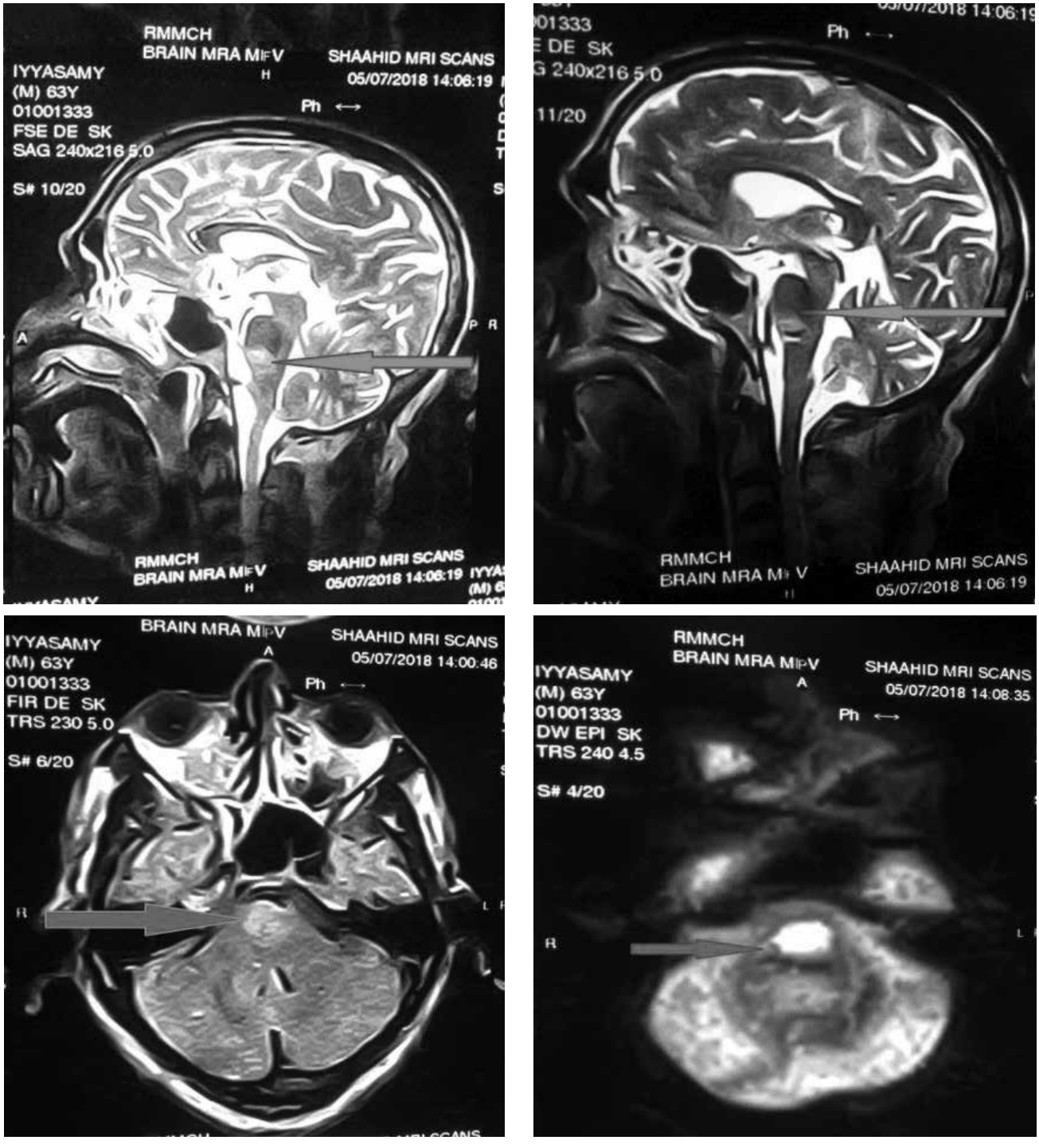


**Figure 2.** MRI brain image showing well-defined area of diffusion restriction in lower central pons bilaterally.

### Pontine Hemorrhage

Classic clinical presentation of pontine hemorrhage is acute onset of coma, tetraparesis, respiratory failure and oculomotor signs, and most patients have diminished sensorium. Prodromal symptoms, such as headache, nausea and vomiting, respiratory dysfunction and dysarthria may be present.

### Osmotic Demyelination Syndrome

ODS is characterized by its subacute sequential presentation, initial encephalopathy or seizures, followed by rapid recovery in relation to electrolyte or osmolality correction, and subsequent clinical deterioration. Clinical manifestations include predominant ataxia (reflecting involvement of pontocerebeller fibers),

dysarthria, dysphagia, quadriparesis and alteration in sensorium. Pupillary and oculomotor signs were less frequently noted. Extrapontine extension results in behavioral abnormalities and movement disorders. The transverse pontocerebellar fibers are most frequently involved, followed by rostrocaudal tracts. Tegmentum and corticospinal tracts are usually spared.

## CONCLUSION

Presence of seizures, predominant ataxia, quadriparesis, pupillary and occulomotor signs with hypernatremia and classical MRI findings of bilateral diffusion restriction are noted in ODS. Behavioral and abnormal movements occur if there is an extrapontine extension. Absence of Horner's syndrome, internuclear ophthalmoplegia and sparing of primary and posterior column sensation favors ODS.

Early diagnosis and early differentiation between structural and metabolic cause of neurological deficits will help avoid inadvertent usage of anticoagulants, antiedema measures, repeated imaging (radiation exposure) and stroke resuscitative interventions. Targeted therapy towards the correction of metabolic parameters will lead to a favorable outcome.

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### Phases of Resuscitation

**Formula of 5**

- **Electrical phase:** First 5 minutes of arrest due to ventricular fibrillation. Immediate DC cardioversion is needed to optimize survival. Performing excellent chest compressions while the defibrillator is readied also improves survival (DC followed by CPR).
- **Hemodynamic phase:** Period from 4 to 10 minutes after sudden cardiac arrest, during which the patient may remain in ventricular fibrillation. Early defibrillation is crucial for survival. Excellent chest compressions should be started as soon as sudden cardiac arrest is diagnosed and continued until just before cardioversion is performed (i.e., charge the defibrillator during active compressions, stopping only briefly to confirm the rhythm and deliver the shock). Resume CPR immediately after the shock is delivered (CPR first and then DC).
- **Metabolic phase:** Period greater than 10 minutes of pulselessness. Treatment is primarily based upon postresuscitative measures, including hypothermia therapy. Patients in this phase generally do not survive, if not quickly converted into a perfusing rhythm.


**IJCP SUTRA 444:** In malaria, chills occur in the afternoon; in filaria, the chills occur in the evening.

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2018

# Enlarged Ovaries Following IVF/ICSI as an Etiology of Obstructive Uropathy Resulting in Acute Renal Failure: A Case Report

PRATIBHA VISHWAKARMA*, PRIYA MOHAN†, KUNDAVI SHANKAR‡, THANGAM R VARMA#

## ABSTRACT

*In vitro* fertilization (IVF) is one of the most comprehensively registered interventions in clinical medicine. IVF is regarded as safe with very few complications. We report a woman who developed acute renal failure due to compression of both ureters from enlarged stimulated ovaries. The condition was diagnosed using magnetic resonance imaging. It was treated with insertion of double-J stents in both ureters and dialysis. Compression of the ureters due to enlarged ovaries should be considered if a patient especially with pre-existing endometriosis develops acute renal failure following IVF.

**Keywords:** Acute renal failure, *in vitro* fertilization, ovarian hyperstimulation syndrome, ultrasound

During the last 35 years, *in vitro* fertilization, (IVF) has become an important treatment option in patients with infertility. Following hormone stimulation, the oocytes are collected from the ovaries transvaginally using ultrasound guidance. The procedure is regarded as safe. The most common complications are hemorrhages, pelvic abscesses and pain. There are also some reports of ureteric damage after puncture by the collecting needle.[1,2] We report a case, where a woman with pre-existing endometriosis developed acute renal failure due to compression of both ureters from enlarged stimulated ovaries.

## CASE REPORT

A 28-year-old woman married for 8 years, with two previous first trimester miscarriages presented to us for treatment of secondary subfertility. She had history of 2 laparoscopies elsewhere suggestive of bilateral tubal block and extensive adhesions between tubes, ovaries and uterus suggestive of stage IV endometriosis. She had regular cycles with a body mass index (BMI) of 20. She had a past history of surgically corrected atrial septal defect at 5 years of age, asymptomatic; since then with good left ventricular ejection fraction. She had ureteric calculi diagnosed on both sides on ultrasound done outside with no renal changes 3 years back, for which she underwent conservative management.

Her follicle-stimulating hormone (FSH) was 12.3 mIU/L and luteinizing hormone (LH) was 14.2 mIU/L, antimullerian hormone (AMH)-1.2 pmol/L with reduced antral follicle count with 2 cm endometriotic cyst on both ovaries. Kidneys were normal. Husband's semen analysis was normal. Hysteroscopy and trial transfer was done as pre-IVF evaluation. She was counseled for therapeutic trial and a flexible antagonist protocol was followed. Recombinant FSH was used for stimulation. Five oocytes were retrieved under ultrasound guidance after 35 hours of human chorionic gonadotropin (hCG) trigger. Three embryos were fertilized and three 8 cell Grade A embryos were transferred without any difficulty.

Six days following embryo transfer, she reported with loin pain and high-grade fever and reduced urinary output. There was no tenderness on abdominal examination. Investigations revealed normal leukocyte count with more than hundred pus cells on routine urine analysis. Renal function test revealed a picture of pre-renal failure with a serum urea of 100 mg/dL and

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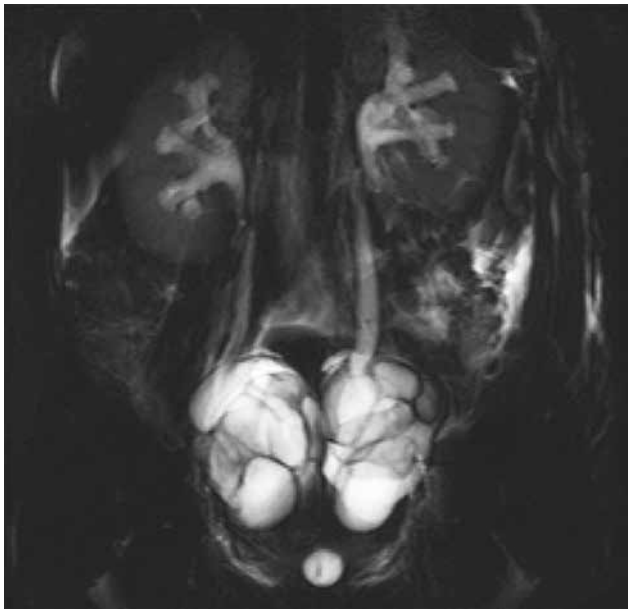

**Figure 1.** Ultrasound showing bilateral stimulated enlarged ovaries compressing both ureters resulting in bilateral hydronephrosis.

creatinine of 7.9 mg/dL. Serum electrolytes showed hyperkalemia. Investigations to rule out other causes of pyrexia were normal. Ultrasound showed bilateral enlarged ovaries measuring right 5 × 6 cm and left 6 × 7 cm and bilateral hydronephrosis (Fig. 1). Magnetic resonance imaging (MRI) scan showed bilateral hydronephrosis and enlarged ovaries, which led to compression of ureters. She was catheterized and her urine output was only 300 mL/24 hours. Nephrologist's and urologist's opinion were taken. Injection carbapenem following sensitivity to Klebsiella and extended-spectrum beta-lactamase (ESBL) growth on culture was started. Patient was transferred to Nephrology department and dialysis was done as her creatinine showed increasing trend and persistent oliguria. Serum creatinine started to decline following dialysis. Double-J (DJ) stent was inserted. The postoperative course was uneventful and her creatinine level showed declining trends. Oral progesterone was continued as luteal support and on Day 16 of embryo transfer, β-hCG was positive. Her β-hCG showed an increasing trend. Renal sonogram was repeated and it was normal. The patient was asymptomatic and urine culture was negative.

At 6 weeks from last menstrual period (LMP), ultrasound showed evidence of echogenic ring and presence of yolk sac with no cardiac activity and fluid collection was seen in the right adnexa suggestive of right ectopic pregnancy. She was posted for an emergency laparoscopy as she was hemodynamically stable, which needed conversion to laparotomy in view of frozen pelvis.

Approximately, 1 liter of blood and clots were removed along with necrotic and hemorrhagic tissue scattered in the abdominal cavity. Right tube was the seat of rupture and salpingectomy was done. Right ovary was stuck to the back of uterus, and left ovary stuck to lateral pelvic wall. Abdomen was washed with saline and a drain was placed. Two units of packed cells were transfused postoperatively. Histopathology confirmed ruptured ectopic gestation in the right tube. She was discharged in a stable condition. DJ stent was removed 6 weeks later.

## DISCUSSION

Transvaginally, ultrasound-guided oocyte retrieval has become the gold standard for IVF therapy. It is considered as a well-tolerated, cost-effective and safe procedure.[3,4] A few cases of ureteral damage due to puncture of the ureter by the collecting needle have been described. In one case, the ureter was compressed by a stimulated ovary in a patient with a transplanted pelvic kidney.[5] The diagnosis of ureteral compression was confirmed by MRI scan, a procedure without ionizing radiation and which should not cause any harm to fertilized embryos.[6] Severe pelvic adhesions may have worsened the situation by limiting the normal movement of the ovaries. Ovarian hyperstimulation syndrome (OHSS) is a common complication in assisted reproductive technologies. In spite of frequent occurrence of abdominal compartment syndrome and oliguria in OHSS, acute renal failure secondary to obstructive uropathy is uncommon in OHSS.[7] Acute renal failure due to a hypovolemic state following production of protein-rich ascites in patients with OHSS has been reported,[8] but in this case, no ascites and only slight hemoconcentration was noted. The most pronounced finding was the huge enlargement of the ovaries and bilateral hydronephrosis.

To date, there have been just two case reports of obstructive uropathy associated with OHSS.[9] The patient was diagnosed earlier as having stage 4 endometriosis and frozen pelvis. Even though the complication risk related to IVF is low, one should be aware of a possible compression or damage to the ureters with subsequent development of acute renal failure. Injury, either by direct puncture or extrinsic compression, compromised ureteral function, but did not completely halt urination—a testimony to the resilient nature of this structure and an intimation of

more frequent, unrecognized injury. We, therefore, suggest that obstructive uropathy should also be considered as a possible etiology in patients with enlarged ovaries who develop oliguria or acute renal failure.

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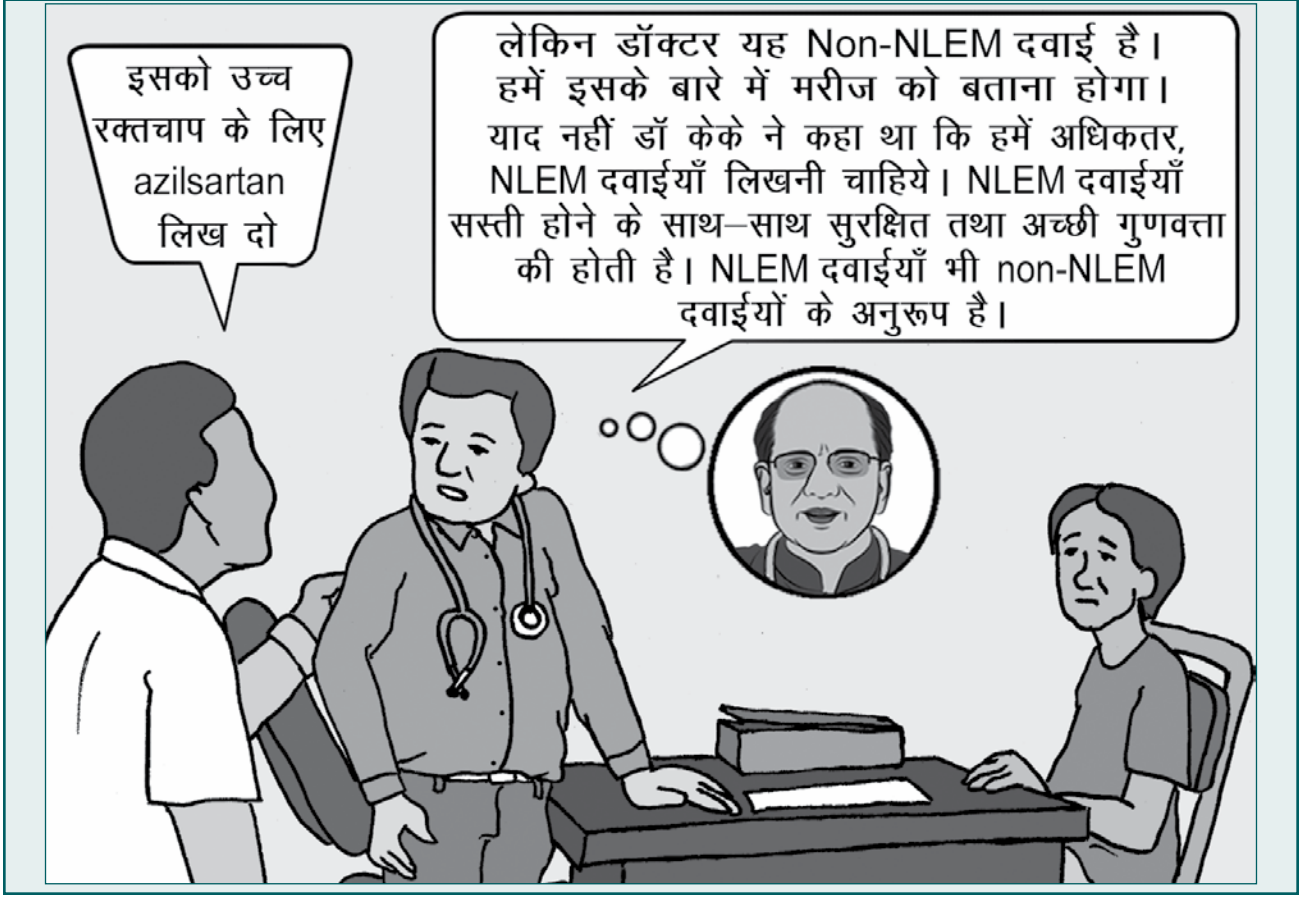
CHAT WITH DR KK

**Lekin "Non-NLEM Drug" Likhee Kyon**



# Cutaneous Larva Migrans

BHAVANA VENKATA NAGABHUSHANA RAO*, CH VNGR RAMANUJAM†

A 34-year-old male patient came to our clinic with an itchy brownish eruption over the dorsum of the right foot of a week's duration. It originated as a small itchy papule and gradually spread like thread over the dorsum of the foot reaching a length of 25 cm (Fig. 1). He was a dog lover; he owns plenty of pet dogs at home. He participates in Dog shows, he got a "the best dog award" for his German shepherd this year. He had no systemic symptoms; pulse, temperatures and blood pressure were normal. He was given albendazole 400 mg orally for 3 days along with antihistamine fexofenadine for 3 days. Itching subsided in 3 days and eruption in 10 days time. He was advised to deworm his pet dogs regularly.

Cutaneous larva migrans is a dermatological lesion that occurs when humans accidentally get infected by dog or cat hookworms *Ancylostoma braziliense* and *Ancylostoma caninum*. It may also be caused by larvae of other non-human parasites. Creeping eruption is a sign that refers to the erythematous migrating cutaneous thread like serpiginous track that is produced by migration of larvae in the skin. Hookworms that are responsible for these kind of lesions are distributed worldwide, but infections are more common in tropical and subtropical countries. Those who are at risk include travelers, children, swimmers, pet lovers and laborers whose activity bring their skin in contact with contaminated soil. Eggs that are passed out from a dog or cat hatch out rhabditiform larvae in 1 or 2 days. In 5-6 days, they become a filariform larvae. When they come in contact with a definite host i.e., dog they penetrate the skin, enter circulation, reach the lungs and ascend to pharynx. They are then swallowed and reach the intestines. Humans may get infected by this filariform larva, they cannot complete their life cycle in humans. They creep within the epidermis and produce an inflammatory track along the migration. Rarely pulmonary eosinophilic syndrome can happen either by direct invasion or due to systemic immunological reaction. Cutaneous larva migrans occurs frequently in the lower extremities. It starts as pruritic papule and spreads as an elevated serpiginous track at the rate of several millimeters a day. It is usually 3 mm broad and 15-20 mm in length and the larva is located 2 cm ahead of the lesion. If exposed to highly contaminated soils multiple eruptions may appear at the same time. Strongyloidiasis can also produce similar eruptions, but they progress fast at a rate of 1 cm in 5 minutes, hence is called larva currens (running larva).

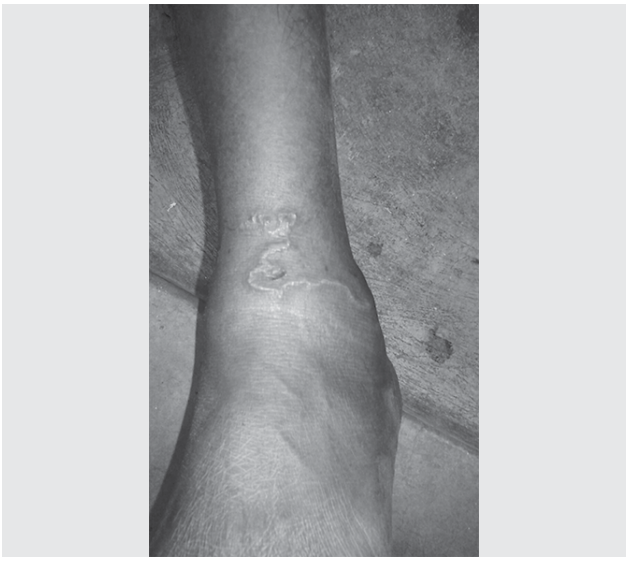


**Figure 1.** Cutaneous 25 cm long lesion on the dorsum of the foot.

Antihelmenthic therapy is useful for early resolution of symptoms and prevents secondary infections. Symptoms disappear 1 week after therapy, pruritus earlier than dermatitis. Ivermectin 200 μg/kg as a single dose or albendazole 400 mg once a day for 3 days, usually suffice, but a weeks therapy with albendazole may be warranted in multiple eruptions. Addition of antihistamines will reduce the intensity of itching. Topical thiabendazole or albendazole has also been reported to halt progress of disease and reduce the itching.

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# Tele3D Imaging and the Scope in India

GORDON J HARRIS

## PLEASE PROVIDE AN OVERVIEW OF THE PROJECT

We opened the 3D Imaging Service in the Radiology Department at Massachusetts General Hospital (MGH) in 1999 to provide image post-processing as a service for aiding radiologists and referring physicians in diagnosis and treatment planning. Our lab was one of the first of its kind and has grown to be one of the largest, processing over 130 exams per day for MGH, our affiliated imaging centers, and our Tele3D client hospitals around the country. Our growth was in parallel with the adoption of multi-slice CT and its expanding use for procedures requiring 3D post-processing, such as CT angiography (CTA). As we grew, it became difficult to keep up with our growth in volume, and increasing needs for extended hours of coverage.

In 2003, in order to provide overnight 3D post-processing, we established a collaboration with a team of radiologists and IT support staff in Bangalore, India, through an agreement with Manipal Hospital and Wipro. Together, we created a 3D lab extension to support our overnight and weekend 3D needs. We went live with the India team in 2004 after 6-9 months of extensive daily training and review of cases led by our 3D Operations Manager, Jennifer McGowan, before we were comfortable that the quality was consistent with our internally processed exams. One of our MGH 3D lab-trained research fellows, Dr Roy D'Souza, joined the Bangalore team in 2004, and helped train other radiologists to process our exams, and continues to lead a team of three radiologists and support staff in Bangalore.

In 2016, we moved the team from Wipro to work under the umbrella of Teleradiology Solutions (TRS) as we felt that alignment with a company focused on radiology remote services would be a better fit for the team there.

Director of 3D Imaging, Massachsuetts General Hospital, Boston

## WHY HAVE YOU CHOSEN INDIA - WHAT IS THE BUSINESS CASE?

After a few years of rapid growth, we faced challenges in meeting our radiologists' and referring physicians' demand for clinical image post-processing in terms of turnaround time, hours of coverage and growing clinical volume while maintaining our high standards for quality, consistency and expertise. It takes us about 9-12 months to train new 3D Technologists in our 40-50 clinical 3D protocols, and our staff were not enthusiastic about the growing demands for them to take night and weekend call.

We were fortunate in having developed this collaboration that enabled us to have a highly skilled team of India-based radiologists perform our 3D exams during our overnight hours in their daytime. We established this to address needs for clinical care. We have radiologists in India performing work that we have 3D Technologists doing at MGH to ensure that the quality is maintained, and it costs us more as an outsourced service on a per case basis than it would to have overnight full-time staff on site. However, given the difficulty in finding and training qualified candidates who want to work overnight, we were unable to solve our issues through staffing on-site.

Thus, this is not the stereotypical overseas outsourcing business case of moving jobs to save expense, but rather, our motivation is to enhance patient care and maintain quality of service. The team in Bangalore is truly an extension of our 3D Lab team. We have bi-weekly calls and daily quality checks, as well as ongoing feedback and training in new protocols. The team has been amazingly cohesive, and most of the India staff have been there for over a decade with little turnover. Our MGH 3D Operations Manager and I visited the team in Bangalore this summer, which was my third visit to meet with the team since we started the India service.

## DOWN THE LINE IN A 5-10 YEAR TIMEFRAME, CAN THE PROCESSING BE TAKEN OVER BY AUTOMATION?

We are in the 20th year of operation of our 3D Imaging Service at MGH. Every year, new technology

comes along that promises to automate different 3D image processing tasks. While these enhancements have impacted our workflow, and some of the more manual tasks have been replaced by more automated processes, it seems that every time some new technique reduces our work in one area, additional new work is requested.

As such, we are now busier than we have ever been and we have trouble keeping up with our workload. Will the advent of new technologies automate some parts of our work and enhance the capabilities of radiologists to provide better diagnosis and quantitative analysis of images? I certainly hope and expect so. Will this mean less work for our 3D lab? Probably not, but it will mean that some of the more mundane and repetitive tasks will likely be replaced by more automation, enabling us to shift our focus to new areas where our expertise can provide added value.

## WHAT IS THE SCOPE FOR PROTOCOL-BASED, TELE3D IMAGING IN INDIA AND IN AREAS SUCH AS MEDICAL TOURISM?

We are exploring ways that we can expand our Tele3D network through our collaboration with our India-based colleagues at Teleradiology Solutions, both in the US and in India and other regions. We have implemented a Tele3D workflow to provide 3D services to teleradiology client sites of TRS, and are preparing to launch this at our first pilot site. Once this is operating, we plan to make this service available to TRS' US-based client hospitals and imaging centers. For India and other regions, we could provide this service in reverse, where daytime cases are processed in India and the MGH team provides coverage during their night-time. While this could be provided for self-pay patients who are either local or traveling for medical tourism, the challenge will be determining how the economics would work for routine clinical 3D exams.

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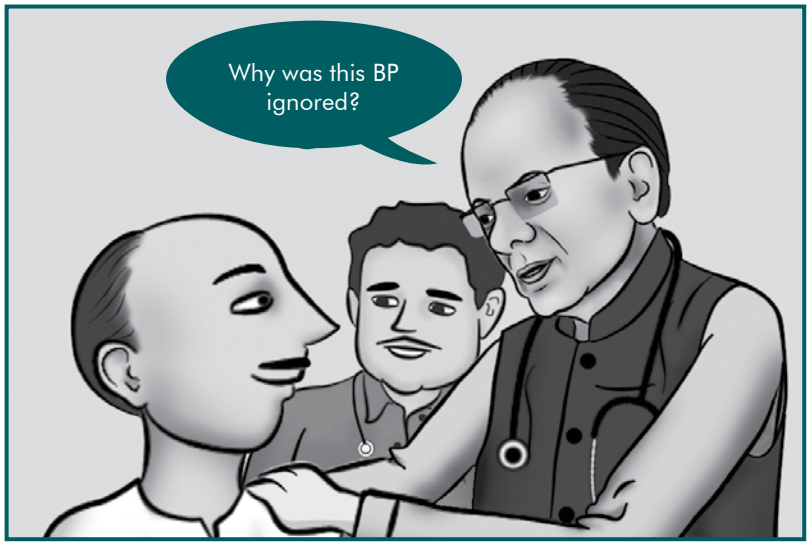
# Make sure

## DURING MEDICAL PRACTICE

**SITUATION:** A hypertensive patient, who also had type 2 diabetes, persistently had mean BP level of 140/90 mmHg.

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**LESSON:** Make sure to remember that hypertension, in association with diabetes, has been found to be significantly correlated with an elevated risk for cardiovascular events. As the association between stroke and BP is stronger in Asians, a target BP of 130/80 mmHg in Asians should be considered.

*Yonsei Med J. 2016;57(6):1307-11.*

# Medtalks with Dr KK Aggarwal

**The probiotic VSL#3 and fecal microbiota transplantation could help induce remission in patients with ulcerative colitis**, according to a systematic review and meta-analysis of randomized controlled trials (Mina Fransawy Alkomos, MD, from New York City Health and Hospitals Corporation and Ain Shams University, Cairo).

**Environmental noise is among the top environmental risks to physical and mental health and well-being,** according to the World Health Organization (WHO) report "Environmental Noise Guidelines for the European Region 2018".

**Erectile dysfunction was reported by 29% of male survivors of childhood cancer** in the first large study that set out to investigate this issue. The study was published as a research letter October 4 in *JAMA Oncology*.

**The Centers for Disease Control and Prevention (CDC) withdrew its Ebola experts** from an outbreak zone in the Democratic Republic of the Congo due to security concerns, according to STAT.

**The Union Health Ministry is creating a group of expert faculty from** government colleges to provide technical assistance to the Board of Governors (BoG) that superseded the Medical Council of India (MCI), particularly in assessing colleges for registration or renewal of licences.

**A simple change in behavior could help prevent recurrent cystitis, a common urinary tract infection (UTI)** in women, according to a randomized controlled study published in *JAMA Internal Medicine* in October 2018. The study showed that drinking more water daily led to fewer episodes of recurrent cystitis and less need for antibiotics.

**Degree of calcification in the abdominal aorta is strongly associated with decline in glomerular filtration rate (GFR)**: Abdominal aorta calcification is associated with a decline in GFR, as per results of a cross-sectional analysis of baseline data from a randomized controlled clinical trial (RENEXC) is conducted to examine the association of abdominal aortic calcification (AAC) with GFR in patients with non-dialysis dependent CKD. The prevalence of AAC was found to be 73% and 47% had severe calcification (AAC score ≥7). The degree of calcification in the abdominal aorta was strongly associated with a decline in GFR, a decrease in plasma albumin, an increase in plasma phosphate, an increase in pulse pressure and cardiac structural changes, such as an increase in left ventricular mass (LVM), left atrial volume (LAV) and left atrial volume index (LAVI). These findings are published Oct. 12 in the journal *Clinical Nephrology*.

According to the National Institute on Drug Abuse, "**A previous substance use disorder is a risk factor for future development of substance use disorder** (SUD)," but "It is also possible that someone who once had an SUD but doesn't currently have one has a balance of risk and protective genetic and environmental factors that could allow for alcohol consumption without developing an alcohol use disorder (AUD)."

**Exposure to sulfur dioxide was associated with preterm birth** as per a systematic review of 41 studies of air pollution and birth outcomes found; exposure to fine particulate matter was associated with low birth weight (LBW), preterm birth and small for gestational age (SGA) births; and exposure to particulate matter ≤10 μm was associated with SGA births (*Environ Int*. 2011;37:498).

**An association between fine particulate matter (2.5 μ) and autism** has been demonstrated in recent epidemiological studies (*Environ Health Perspect*. 2015; 123:264).

**WHO Director-General, Dr Tedros Adhanom Ghebreyesus, has called an Emergency Committee meeting on the Ebola virus outbreak** in the Democratic Republic of the Congo (DRC), which has already claimed around 130 lives. The Emergency Committee, scheduled for Wednesday at WHO headquarters in Geneva, will decide whether the outbreak constitutes a public health emergency of international concern, and what recommendations should be made to manage the spread of the disease.

**This year, more than half of all US states have had confirmed or possible cases of acute flaccid myelitis**, the polio-like illness that can cause paralysis and mostly affects children, according to a new CNN analysis.

**Air Quality Early Warning System for Delhi was launched** by the Union Minister for Earth Sciences and Environment, Dr Harsh Vardhan in Delhi recently. Developed jointly by the scientists at Indian Institute of

Tropical Meteorology (IITM), Pune, India Meteorological Department and National Centre for Medium Range Weather Forecasting (NCMRWF), the System is designed to predict extreme air pollution events and give alerts to take necessary steps as per Graded Response Action Plan (GRAP) of the Government of India. Speaking at the launch, Dr Harsh Vardhan said that the early warning system will help in proactively forewarning, 3-4 days in advance, any large scale air pollution events, which may occur over the Delhi region.

**One drink is 12 ounces of beer, 5 ounces of wine or 1.5 ounces of hard liquor.** And it means having one drink each day of the week, not having seven drinks on Saturday night, sleeping it off Sunday, and begging off until next Saturday night.

**Is there a safe limit for alcohol in a day?** More than 100 studies show that a woman who has one drink per day, compared with a woman who does not drink, has a reduced risk of having a heart attack and the most common kind of stroke. Yet, many of these same studies also show that even a drink a day increases a woman's risk of breast cancer.

**People with diabetes appear to benefit from aspirin, but the risk of bleeding offsets** some of that benefit. For people who don't have diabetes as well as anyone who is age 70 or older - aspirin provides no heart benefit and seems to increase your odds of bleeding.

**One of the biggest exercise errors is using improper technique:** You risk back injury if you arch your back while doing planks or push-ups, and knee injury if you bend too deeply in a lunge or squat. Another mistake is doing the wrong exercise. For instance, running when you have severe back or knee arthritis puts too much pressure on the joint. Lifting too much weight, especially lifting too much too soon, if you're just starting to get back into a routine can lead to muscle tears.

**Toronto-based Myant has announced the launch of a partnership with Mayo Clinic** to bring Mayo Clinic's patented algorithms for heart monitoring and arrhythmia detection to Myant's SKIIN textile computing platform. The agreement gives Myant exclusive license to Mayo Clinic's technology for use in its textile computing or smart clothing projects, including its first generation of SKIIN smart underwear. The collaboration aims to help people at risk of developing Atrial Fibrillation (AFib), and give patients and doctors the ability to proactively monitor heart activity using clothing that detects normal or abnormal heart rhythm.

**Nocturia may be a risk factor for higher nocturnal BP:** Poor sleep quality, particularly from frequent nocturnal urination is strongly associated with nighttime blood pressure (BP) abnormalities, as per results from the Nagahama study published in the *Journal of Hypertension* in November 2018. Systolic BP decreased 8.5% on average. The frequency of urination showed strong and independent association, with smaller nocturnal BP drop in patients with frequent nocturnal urination. Other associations with BP became nonsignificant after adjustment, including the sleep fragmentation index and 3% oxygen desaturation index. Abnormalities in circadian BP variation, particularly increase in nocturnal BP, have been reported to be risk factors for cardiovascular disease.

**Guidelines recommend against routine imaging in patients with early-stage breast cancer** who are at low risk for metastasis, two new studies have found that these guidelines are not being consistently followed. In the first study, the authors report that 30% of patients with early-stage breast cancer underwent staging imaging, despite guidelines recommending against it. The prevalence of inappropriate imaging varied from 26% to 68% among oncologists. The second study found that unnecessary scanning occurred in up to 19% of patients with stage I to II breast cancer. Both papers were presented at the ASCO Quality Care Symposium.

**Preoperative ultrasound imaging of thyroid nodules of concern for malignancy at diagnostic imaging centers rarely** includes lateral neck imaging, according to research presented here at the 2018 Annual Meeting of the American Thyroid Association (ATA). Accepted gold standard of the comprehensive evaluation of suspicious nodules is to include the lateral neck, as well as the thyroid, as critical components of any such ultrasound. This is leading to incomplete surgeries, incomplete evaluation, persistent disease and patient morbidity. It used to be that 20 years ago you would just get a thyroid ultrasound, but then it became clear that a lot of people with papillary thyroid cancer had lymph node involvement and we now know that about a third of patients who have a biopsy-proven thyroid nodule also wind up having lymph node involvement in one or more areas of the neck.

**NITI Aayog to launch guidelines for PPP in treatment of noncommunicable diseases**. The NITI Aayog and MoHFW has worked with State Govts. and representatives from the healthcare industry to develop the Model Concessionaire Agreements (MCA) to supplement efforts for the provision of prevention and treatment services for noncommunicable diseases (Cardiac Sciences, Oncology, and Pulmonary Sciences) at the district hospital particularly especially in tier 2 & 3 cities.

The Guidelines and the MCA will be announced by Dr VK Paul, Member, NITI Aayog, Shri Amitabh Kant, CEO, NITI Aayog and Smt Preeti Sudan, Secretary, Ministry of Health and Family Welfare… (PIB, NITI Aayog, Oct. 16, 2018).

**UN "stands in solidarity with cyclone-hit India and is ready to support the response",** said United Nations Secretary-General António Guterres. He expressed sadness at the loss of lives and devastation caused by Cyclone Titli in India and said that the Organization is ready to provide assistance. According to media reports, at least 25 people have been killed, many more injured, and over 300,000 people evacuated to safer places.

**Modicare to create 10 lakh jobs, says Ayushman Bharat CEO**: The scheme is going to improve the quality of healthcare in public services and also in the private sector, Indu Bhushan, the CEO of Pradhan Mantri Jan Arogya Yojana said while addressing an event organized by industry body Assocham. "The scheme will create considerable employment opportunities ... It will create 10 lakh jobs in health and insurance sector," Bhushan said.

**There are now 62 confirmed reports of acute flaccid myelitis (AFM) across 22 states in the US**: according to the CDC. AFM is an illness similar to polio. As of Sept. 20, the CDC had confirmed 38 cases in 16 states, which aren't required to report AFM cases to the CDC. AFM affects the spinal cord and can cause partial paralysis. It mostly afflicts children and young adults.

**"The outbreak strain of Salmonella was found in live chickens** and in many types of raw chicken products, indicating it might be widespread in the chicken industry," the CDC said in a statement. CDC and public health and regulatory officials in several states are investigating a multistate outbreak of multidrug-resistant Salmonella infections linked to raw chicken products. The US Department of Agriculture's Food Safety and Inspection Service (USDA-FSIS) is monitoring the outbreak.

**The WHO predicts that, without urgent action, the spread of antibiotic-resistant bacteria will lead to** a resurgence in deaths from minor injuries and previously benign infections.

**Ongoing Ebola outbreak in Democratic Republic of Congo does not rise to the level of a Public Health Emergency of International Concern:** In a statement, the Expert Committee convened by the WHO Director-General said, "It was the view of the Committee that a Public Health Emergency of International Concern (PHEIC) should not be declared at this time. But the Committee remains deeply concerned by the outbreak and emphasized that response activities need to be intensified and ongoing vigilance is critical. The Committee also noted the very complex security situation."

**Biopsies of hand tissue could be an early signal of life-threatening cardiac amyloidosis**, suggest Cleveland Clinic researchers who identified amyloid deposits in 10.2% of patients undergoing carpal tunnel release surgery. The study, published online in the *Journal of American College of Cardiology*, contained wide inclusion criteria; all men in their 50s or older and all women in their 60s or older were eligible unless they had known amyloidosis or carpal tunnel syndrome considered to be from trauma or arthritis.

**"As a rule of thumb, you should be concerned when your shortness of breath is out of proportion to** what you would expect for your age or activity level. And definitely take it seriously if you get short of breath when you lie down to sleep, or if you awaken at night with difficulty breathing." Physical exertion and panic are common reasons for shortness of breath.

**Infant mortality in the UK will be 140% higher than other European countries' by 2030**, says a new report by the Royal College of Paediatrics and Child Health, which predicts that if the rate of increase stays the same, the UK's infant mortality will be 140% higher than 15 other European countries within the next 12 years, due to a faster fall of mortality rates elsewhere in Europe. If the mortality rates in the UK starts to decrease again, at the rate seen between 2001 and 2014, it can expect an 80% higher mortality rate than other European countries by 2030 … (*CNN*).

**Do not pick a mushroom that has popped up in your yard from the rainy weather** and eat it, don't do it. The Cleveland Clinic reports about a dozen cases after eating poisonous mushrooms together.

**Dr Swati Bhave has been awarded the All India Women Empowerment Award.** Seven women doctors received this award in the inaugural function of the IMA Women Leaders' Summit held in IMA house New Delhi on 14th October.

**One should consume 2.5 servings of vegetables and 2 servings of fruits daily for a 2000-calorie diet.** They are a rich source of fiber and essential vitamins and minerals, as well as carbohydrates with a low glycemic index. Increased fruit and vegetable intake is associated with decreased risk for mortality, cardiovascular disease and some cancers.

**Recurrent vertigo is a predictor of stroke in hypertensive patients,** as per findings of a study published Oct. 10 in the *Journal of Hypertension*. In the multivariate Cox regression model, the presence of dizziness had no impact on the risk for all-cause mortality, cardiovascular mortality or stroke mortality. However, in an analysis of the different subgroups of dizziness, only vertigo had a prognostic impact. The increased risk was particularly marked on stroke death with a hazard ratio of 2.43 vs. patients without dizziness and 2.22 vs. patients with dizziness excluding vertigo. The study cautions that hypertensive patients with vertigo must be monitored because of the higher stroke mortality.

**Florida reports first pediatric flu fatality:** Several patients including one child have died from influenza as the first week of the 2018-19 flu season drew to a close, according to news and public health department reports.

**World Osteoporosis Day — "Love your Bones"** The most common osteoporotic fractures are spine (vertebral) fractures, a major cause of pain, disability and loss of quality-of-life. Up to 70% of spine fractures remain undiagnosed, leaving sufferers unprotected against the high risk of more fractures. Back pain, height-loss and stooped back are all possible signs of spine fractures.

"**Better Data, Better Lives":** This is the theme for the World Statistics Day, which emphasizes the critical role of high-quality official statistical information in analysis and informed policy decision-making in support of sustainable development. It also reflects the importance of sustainable national statistical capacity to produce reliable and timely statistics and indicators measuring a country's progress.

**Gabapentin tops pregabalin for pain reduction in patients with chronic sciatica**, results of a head-to-head comparison show. But at least one expert has concerns about this conclusion (*JAMA Neurology*, Oct. 15).

**Call to overturn ban on e-cigarettes in Thailand:** The Ends Cigarette Smoke Thailand group, or ECST, has filed a request to the director of Law and Litigation Department in the Office of the Ombudsman Thailand, asking for the ban on e-cigarettes to be reconsidered. The devices were banned on December 12, 2014, by the Ministry of Commerce, which also banned shisha tobacco. According to the Office of the Consumer Protection Board, the sale of e-cigarettes is prohibited. Vendors and smokers can be fined 5,00,000 baht and put in jail for 5 years, while producers or importers could be fined 1 million baht and jailed for up to 10 years… The ESCT believes that making e-cigarettes legal would bring benefits to both sides as the government would receive more tax and dropping the ban would improve Thailand's image after tourists were fined for smoking e-cigarettes, drawing criticism from many quarters. On the slightly positive side, legalizing e-cigarettes would allow the tens of millions of people who smoke cigarettes to use something less harmful, according to research (*Asia Times*).

**A single intravenous (IV) dose of 0.5 mg/kg has a rapid and robust antidepressant effect** according to a dose-ranging study of ketamine as adjunctive therapy for treatment-resistant depression (*Molecular Psychiatry*, Oct. 3).

**Many women who have served in the Armed Forces in the US have experienced sexual assault**, and those victims of assault are more likely to be infertile, a cross-sectional study of infertility in veterans shows (*American Society for Reproductive Medicine 2018 Scientific Congress in Denver*).

**A 2-month weight loss regimen using meal substitutes followed by long-term weight maintenance** through diet and exercise may be an optimal approach to preventing type 2 diabetes through lifestyle, new data suggest. Main results from the Prevention of Diabetes Through Lifestyle Intervention and Population Studies in Europe and Around the World (PREVIEW) study were presented October 5 here at the European Association for the Study of Diabetes (EASD) 2018 Annual Meeting.

"**Now any victim, at any age, can complain the sexual abuse faced by him/her as a child",** says Smt. Maneka Sanjay Gandhi, Minister of Women and Child Development. The Ministry of Women and Child Development, Govt. of India had recently consulted Ministry of Law in view of the overriding provisions of the Protection of Children from Sexual Offences (POCSO) Act, over other criminal laws and provisions of mandatory reporting of such offences. The Ministry of Law after examining the provisions of POCSO Act vis-à-vis provisions of CrPC has advised that there appears no period of limitation mentioned in Section 19 in regard to reporting of the offences under the POCSO Act, 2012. The POCSO Act does not provide for any period of limitation for reporting the child sexual offences.

**A shift toward more plant-based diets can help save the planet:** A study published Oct. 10, 2018 in the journal *Nature*, found that as a result of population growth and the continued consumption of Western diets high in red meats and processed foods, the environmental

pressures of the food system could increase by up to 90% by 2050, "exceeding key planetary boundaries that define a safe operating space for humanity beyond which Earth's vital ecosystems could become unstable," according to study author Marco Springmann of the Oxford Martin Programme on the Future of Food at the University of Oxford. Sustaining a healthier planet will require halving the amount of food loss and waste, and improving farming practices and technologies. But it will also require a shift toward more plant-based diets, according to Springmann.

**You need a joint replacement if (Harvard)**

- You can no longer complete routine daily tasks without help.
- You have significant pain, like pain that keeps you awake at night despite the use of medications, pain that keeps you from being able to walk or bend over, pain that isn't relieved by rest, or pain that isn't helped by nonsurgical approaches.
- Your doctor says that less-complicated surgical procedures are unlikely to help.
- You have osteoarthritis and feel the disease is wearing you down physically, emotionally and mentally.
- You are suffering severe side effects from the medications for your painful knee or hip.
- Tests show advanced arthritis or significant joint damage.

**Nobel Prizes that changed medicine forever: Ivan Pavlov (1904):** "In recognition of his work on the physiology of digestion, through which knowledge on vital aspects of the subject has been transformed and enlarged."

Ivan Pavlov, a Russian physiologist, expanded our knowledge of digestion and identified the role of nervous system in the secretion of gastric juices and their ability to affect movement in the intestinal canal. A master surgeon, he believed that surgery on conscious animals was key to greater physiologic understanding of organ system. His research on digestive systems of dogs won Pavlov the Nobel Prize, although he is most often remembered for his experiments in classical conditioning (*Medscape*).

**Harm Reduction:** People who use drugs are offered only two choices: Get sober or die. Safe injection—that's the message behind the Church of Safe Injection. The "church" is a harm reduction initiative in Portland, Maine—with plans for offshoots in other cities.

Cleveland Clinic researchers have found that **better cardiorespiratory fitness leads to longer life**, with no limit to the benefit of aerobic fitness.

**First time in the world, rhythm ECG screening attempt for 25,000 people**: Heart Care Foundation of India and SanketLife-World's only Pocket 12-lead ECG device will mass screen visitors to the MTNL Perfect Health Mela from 23-27th October at Talkatora Stadium in Delhi. The idea is to detect the prevalence of atrial fibrillation (AF) in the society, which if not detected timely can cause paralysis. An ECG can help detect the arrhythmia at an early stage.

**Agatsa, a start-up based in India, has developed a totally made-in-India product**, "**SanketLife" a pocket-sized lead-less ECG device,** which can measure ECG and stress/HRV levels by using just a thumb-touch. With the help of an algorithm, SanketLife can detect arrhythmia or irregular heart beat or AF at early stage apart from doing a full 12-lead ECG. With SanketLife, a quick ECG can be taken even in a sitting position. The ECG reports are immediately displayed on a mobile screen and can be shared with anyone across the globe using WhatsApp, email or even SMS.

**Fertility rates have declined in the US** and women are giving birth for the first time later and later, according to the CDC. The results came after researchers from the National Center for Health Statistics analyzed birth data compiled by the National Vital Statistics System from 2007 to 2017.

**If you have problems sleeping through the night, you may be at risk for AF**, an irregular heart rate that may cause heart palpitations and is a leading cause of stroke. A study published online by *HeartRhythm* reviewed four studies and found a link between AF and poor sleep.

**Some people's microbiota resists colonization with probiotics**, but others' microbiomes change in response to probiotics, and sometimes in different ways at different points along the gastrointestinal tract.

**Physical activity is inversely associated with all hypertension phenotypes in childre**n: Physical activity is inversely associated with all hypertension phenotypes in children, says the Healthy Growth Study. Increased physical activity was found to be associated with 33–54% lower risk of all hypertension phenotypes. Sedentary behavior was associated with 11-13% higher risk for isolated systolic hypertension (ISH) and systolic and diastolic hypertension (SDH) in boys. Increased moderate-to-vigorous physical activity was associated with 41-65% lower risk of all phenotypes in girls and

ISH and SDH in boys. According to the study, cut-off points of 12,378 steps/day, 47.3 min/day of MVPA and 2.9 h/day sedentary behaviors identify children at increased risk of hypertension (*J Am Soc Hypertens*, Oct. 2018).

**US launches reducing food waste initiative:** The US Department of Agriculture (USDA), the US Environmental Protection Agency (EPA), and the US Food and Drug Administration (FDA) today announced the signing of a joint agency formal agreement under the ***Winning on Reducing Food Waste*** initiative. The agreement is aimed at improving coordination and communication across federal agencies attempting to better educate Americans on the impacts and importance of reducing food loss and waste. In the US, food waste is estimated at between 30 and 40% of the food supply. Wasted food is the single largest category of material placed in municipal landfills and represents nourishment that could have helped feed families in need. Additionally, water, energy and labor used to produce wasted food could have been employed for other purposes.

**Concerns remain about bisphenol A (BPA) safety, despite FDA declaration:** A growing body of research indicates BPA levels in food containers present a public health risk. Despite this evidence, the US FDA continues to assert that BPA is safe for use in food packaging, based on an initial report conducted as part of the Consortium Linking Academic and Regulatory Insights on BPA Toxicity (CLARITY-BPA). The CDC estimates that more than 96% of Americans have BPA in their bodies. The chemical is found in a variety of food containers, including polycarbonate plastic water bottles and can linings.

**Children, who develop inflammatory bowel disease, are at an increased risk of death**, both in childhood and later in life, according to the journal *Gastroenterology*. Inflammatory bowel disease (IBD) is the ongoing inflammation of all or part of the digestive tract.

**Back pain relief:** A 2013 meta-analysis of 10 randomized controlled trials found "strong evidence for short-term effectiveness and moderate evidence for long-term effectiveness of yoga for chronic low-back pain." In fact, since 2007, the American Society of Pain guidelines have urged physicians to consider recommending yoga to patients with long-term pain in the lower back.

**In a first, WHO calls global meet to tackle pollution:** Alarmed at the rising levels of pollution causing growing burden of diseases and deaths, WHO has called health and environment ministers of all countries including India, global leaders and experts from academia and scientific community for the first time to devise a strategy to combat pollution and its impact on health. The high-level three-day meeting, slated from October 30 to November 1 in Geneva, is likely to determine ambitious targets for countries, mainly those where morbidity and mortality is higher.

**People with back pain who did two 90-minute sessions of yoga a week for 24 weeks experienced a 56% reduction in pain**, as reported in the journal *Spine*. They also had less disability and depression than people with back pain who received standard care, such as pain medication. The results also suggested a trend toward the use of less pain medication in those who did yoga. When the researchers followed up with the participants 6 months after the study, 68% of the people in the yoga group were still practicing yoga an average of 3 days a week for an average of 33 minutes per session.

In a 2015 study, **women with rheumatoid arthritis reported improvements in their physical health**, walking ability, pain levels, energy and mood, and had significantly fewer swollen and tender joints, after doing two hour-long yoga classes a week for eight weeks.

**Ovarian cancer is the most common cause of cancer death from gynecologic tumors in the United States.** Worldwide, about 1,00,000 women die of the disease every year.

**Antibiotic-resistant infections kill around 7,00,000 people annually around the world.** Antimicrobials and antibiotics are increasingly misused and overused by the global population.

**Massachusetts Institute of Technology (MIT) chemical engineers have found a way to encapsulate probiotics** in a way that they can be delivered along with antibiotics. As a result, this innovative procedure kills multiple strains of bacteria.

Federal health officials said this past week that **62 cases of AFM have been confirmed in 2018 in US** and 65 more possible cases are being investigated. Experts at the US CDC say they still don't know what causes the syndrome.

**Zika Update: Eight new patients were diagnosed with Zika virus in Jaipur** recently taking the total number of Zika patients in the pink city to 117. Out 117, 98 patients have recovered. Most of the Zika virus cases have been found in Shastri Nagar, Vidhyadhar Nagar, Sindhi Camp and New Sanganer Road. At least 10 of the cases were diagnosed at the Rajput Hostel, which was quarantined and students were held in confinement... (*India Today*).

**Nobel Prizes that changed medicine forever — William Einthoven (1924)**: "For his discovery of the mechanism of the electrocardiogram." Through the advances he made in ECG technology, specifically his invention of the spring galvanometer, William Einthoven provided clinicians with the first reliable means to depict the heart and its functions and illnesses. His instrument recorded five electric potentials of the heart in waves, which Einthoven named P, Q, R, S and T.

**Being unfit should be considered as strong a risk factor as hypertension, diabetes and smoking,** if not stronger than all of them, according to a retrospective study of 1,22,000 people from Cleveland Clinic reported in *JAMA Network Open*. The study suggests that pure workaholics - many of whom are the type of people who never find the time to exercise - are creating worse conditions for themselves than some of the worst health habits and most common fatal conditions known to humankind.

**The UN has launched a strategy to deal with workplace mental health issues and ways to maintain well-being of its staff by** dealing with the stigma attached to it. UN staff struggling with anxiety, depression, post-traumatic stress disorder or other circumstances have reported feeling isolated and ashamed, with no-one to turn to for help, said UN Secretary-General Antonio Guterres. "The UN can and must do better in supporting its staff, and it starts with the new strategy we are setting in motion," said Guterres. Noting that reducing stigma is the top priority, he said the staff would not feel prepared to seek help or disclose their feelings until stigma was overcome. "The strategy also underscores the need to care for each other, and to reach out to colleagues who may be in distress," he added.

**Poor oral health is associated with higher BP:** Poor oral health may interfere with BP control in people diagnosed with hypertension. People with high BP taking medication for their condition are more likely to benefit from the therapy if they have good oral health, according to new research published October 22, 2018 in the journal *Hypertension*. People with periodontal disease were 20% less likely to reach healthy BP ranges, compared with patients in good oral health. Systolic BP in treated patients with severe periodontitis was, on average, 3 mmHg higher than those with good oral health. Individuals with healthier gums have lower BP and responded better to BP-lowering medications.

**"Harit Diwali-Swasth Diwali" campaign** was launched pan-India by Ministry of Environment on Oct. 22 keeping in view the detrimental effects of the firecrackers and also the importance of the Diwali festival. This campaign is merged it with "Green Good Deed" movement launched last year, in which children were advised to celebrate Diwali in an environment-friendly manner by gifting plant sapling to their relatives and friends along with sweets, undertake cleaning of houses, neighborhoods, schools, collect old books and unused notebooks gift to needy children, donate old warm clothing, blankets to night-shelters and other homeless people. The children were encouraged to light up their houses and their schools with candles and diyas.

**'Never give up': UN chief's message for 2018 UN Day**, which falls on 24 October, Secretary-General António Guterres is urging the men and women of the UN, and those they serve, to "never give up" tackling the world's many challenges. He said that, despite the odds and obstacles, and growing inequality: *"We don't give up because we know by reducing inequality we increase hope and opportunity and peace around the world... On United Nations Day, let us reaffirm our commitment. To repair broken trust. To heal our planet. To leave no one behind. To uphold dignity for one and all, as united nations."*

**A higher frequency of eating organic food was associated with a reduced risk for cancer**, according to results from a large population-based observational study published online Oct. 22 in *JAMA Internal Medicine*.

**The American Heart Association (AHA) is celebrating social entrepreneurs by empowering them to identify innovative health solutions** to improve health and well-being in their communities. Through a rigorous 6-to-8-week curriculum funded by the AHA, entrepreneurs gained real-life knowledge in market positioning, brand development, fundraising and other functions to enhance their business models and demonstrate the viability of their projects.

**Severe motion sickness and cybersickness** - a type of motion sickness that stems from exposure to virtual reality - may be considered the same clinical condition, according to the *Journal of Applied Physiology*.

**Eating vegetable nitrates, found mainly in green leafy vegetables and beetroot, could prevent macular degeneration**, a common cause of vision loss in people over age 50. People who ate between 100 and 142 mg of vegetable nitrates each day had a 35% lower risk of developing early age-related macular degeneration (AMD) than people who ate <69 mg of vegetable

nitrates each day. Spinach has approximately 20 mg of nitrate per 100 g, while beetroot has nearly 15 mg of nitrate per 100 g (*J Acad Nutr Dietet*).

**Nobel Prizes that changed medicine forever: Alexander Fleming, Ernst Chain & Howard Florey (1945):** "For the discovery of penicillin and its curative effect in various infectious diseases" the discovery of penicillin was transformational and is perhaps the most well known scientific feat to be rewarded by the Nobel Prize in Physiology or Medicine. Fleming's research on what became known as penicillin provided the foundation for treating bacterial infections. Chain and Florey developed a more stable and purer form of penicillin, which could be used as a reliable pharmaceutical product.

**ADA launches Diabetes Food Hub, a new digital recipe platform for people with diabetes:** The American Diabetes Association (ADA) has launched Diabetes Food Hub, a new digital cooking and recipe destination to help people living with diabetes and their families eat healthfully. Including a collection of tasty recipes approved by ADA's nutrition experts. It provides simple solutions to daily meal planning challenges for people with diabetes. Diabetes Food Hub provides recipes with easy-to-read nutrition guidance, tips for healthy eating, and meal prep inspiration from ADA diabetes experts to help put healthy living within reach for all people.

**10 behaviors for healthy weight loss (Harvard Health)**

1. Know where you are starting.
2. Home in on your goal and make a plan.
3. Identify barriers to your goals and ways to overcome them.
4. Identify current habits that lead to unhealthful eating.
5. Control your portions.
6. Identify hunger and satiety cues (Try to stop eating BEFORE getting full (it takes about 20 minutes for your brain to register "stop eating" signals from your stomach). Foods that can help you feel fuller include high-fiber foods such as vegetables, whole grains, beans and legumes; protein (fish, poultry, eggs) and water).
7. Focus on the positive changes.
8. Go with the 80/20 rule. Stay on track 80% of the time, but leave some room for a few indulgences.
9. Focus on overall health.
10. Eat slowly and mindfully.

**Lead accumulation in shin bone may be associated with resistant high BP**

Cumulative lead burden, as measured by cortical bone in the tibia (shin bone), may be an unrecognized risk factor for drug resistant hypertension, according to new research published Oct. 24 2018 in the *Journal of the American Heart Association*. The risk of resistant hypertension was higher in men with elevated accumulations of lead in the shin bone. Exposure to lead may be due to aging infrastructure such as water pipes.

**Adenovirus outbreak: Health officials continue to investigate after seven people died and at least 11 others have been infected with an adenovirus** at the Wanaque Center for Nursing and Rehabilitation in Haskell, New Jersey, the New Jersey Department of Health said Wednesday. "They range in age from toddlers to young adults," New Jersey Department of Health Commissioner Dr Shereef Elnahal told reporters Wednesday. "The vast majority are under the age of 18. Some have been hospitalized, and some are being cared for at this facility." The outbreak appears to be confined to the facility's respiratory unit, he added… (*CNN*)

**FDA approves baloxavir to treat acute uncomplicated influenza:** Xofluza (baloxavir marboxil) has been approved by the US FDA for the treatment of acute uncomplicated influenza (flu) in patients 12 years of age and older who have been symptomatic for no more than 48 hours.

**Information available with another public authority is not a ground to deny information:** In the matter titled as **"Public information Officer versus V. Chaudhary", W.P.(C) 2025/2014, vide judgment dated 08.10.2018 the Hon'ble High Court of Delhi** has held that whether authentic information is available with another public authority is not a ground to deny the information sought from a public authority.

> *"19. In terms of the RTI Act, all information as available with the public authority is required to be provided to the citizen unless it is exempt from disclosure under Section 8 of the RTI Act or otherwise pertains to the organizations that are excluded from the purview of the RTI Act. Thus, the question whether authentic information is available with another public authority is not a ground to deny the information as sought from a public authority. In this case, the petitioner had sought the status of the properties against which complaints had been sent to MCD. It was his suggestion (although couched as a query) that even though police authorities inform MCD regarding unauthorized construction, they do not take steps to stop the same by accepting illegal gratification.*

*20. The petitioner had duly informed the respondent that a total number of 5313 forms had been sent to the concerned Municipal Corporation. However, the balance information was denied on the ground that it cannot be provided under Section 11 of the Act.*

*21. It is apparent from the above that the petitioner did have the information as sought by the respondent. However, the same was denied to the respondent by referring Section 11 of the RTI Act. A plain reading of Section 11 of the RTI Act indicates that the same does not proscribe furnishing of information. In terms of Section 11(1) of the RTI Act, in cases where the public information officers (PIOs) intend to disclose the information, which relates to or has been supplied by a third party and has been treated as confidential by a third party, it would be necessary for the concerned PIO to give a written notice to the third party. The concerned third party has a right to make a submission either in writing or orally and the concerned PIO is required to keep the same in view while taking a decision regarding disclosure of such information. Thus, Section 11 of the RTI Act cannot be read as a provision proscribing disclosure of information; it is a provision to enable disclosure of third party information subject to certain safeguards. In this view, the decision of the CPIO denying the information by referring Section 11 of the RTI Act is wholly unsustainable.*

*22. The contention of the petitioner that the information as sought by the respondent was third party information, is also unpersuasive. The information as sought by the respondent pertains to unauthorized construction noticed by the police authorities, and in respect of which information had been forwarded to the concerned Municipal Corporation. Such information has neither been provided by any third party nor has been treated as confidential. Undisputedly, the information may relate to third parties inasmuch as it relates to the property of those third parties. However, the information as to unauthorized construction observed by the police authorities cannot be construed as one, which is to be kept confidential in terms of Section 11 of the RTI Act. Subject information that is sought by the respondent is gathered by the police authorities in discharge of their functions and this Court finds no infirmity with the decision of the CIC in directing that the same be provided to the respondent."*

**Teen driver safety: 8 danger zones (CDC)**

1. Driver inexperience
2. Driving with teen passengers
3. Night-time driving
4. Not using seat belts
5. Distracted driving
6. Drowsy driving
7. Reckless driving
8. Impaired driving.

**Cleveland Clinic top 10 medical innovations for 2019**

1. Alternative therapy for pain: Fighting the opioid crisis.
2. The advent of artificial intelligence in healthcare.
3. Expanded window for acute stroke intervention.
4. Advances in immunotherapy for cancer treatment.
5. Patient-specific products achieved with 3D printing, which provide patients the most advanced care, while minimizing the risk of complications at the same time.
6. Virtual and mixed reality for medical education provide simulation training that may enhance traditional medical schooling.
7. Visor for prehospital stroke diagnosis to speed up diagnosis and the time to treatment.
8. Innovation in robotic surgery leading to more precise and effective surgeries with improved surgical outcomes.
9. Mitral and tricuspid valve percutaneous replacement and repair.
10. RNA-based therapies.

**Harm reduction: No Bharat Stage (BS) IV vehicle shall be sold in India from April 1, 2020**, says Supreme Court of India. Recently, a three judge bench headed by Justice Madan B Lokur made it clear that only BS VI compliant vehicle shall be sold in the country from April 1st, 2020. The bench said the need of the hour was to move to a cleaner fuel. The apex court was deciding whether grace period should be given to automobile manufacturers for the sale of BS-VI noncompliant vehicles after April 1, 2020.

The Bharat stage emission standards are standards instituted by the government to regulate output of air pollutants from motor vehicles. The BS-VI emission norm would come into force from April 1, 2020 across the country. The BS IV norms have been enforced across the country since April 2017. In 2016, the Centre had announced that the country would skip the BS-V norms altogether and adopt BS-VI norms by 2020… (*PTI, Oct 23, 2018*).

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# 26th Annual National Conference of Indian Academy of Neurology (IANCON 2018)

## TIME MANAGEMENT FOR NEUROLOGISTS

**Dr (Prof) Man Mohan Mehndiratta, New Delhi**

Time management is essential for a productive and balanced life. Using time management principles helps improve the quality-of-life for an individual by setting priorities and making choices, thus giving the individual a feeling of control and the ability to achieve reasonable goals. Ineffective time management adversely impacts physician career satisfaction. Effective time management requires: Setting short- and long-term goals; setting priorities among competing responsibilities; planning and organizing activities; minimizing exposure to circumstances that result in wasted time. The identification and practice of time management skills will likely improve physician efficiency and career.

## MULTIPLE SCLEROSIS-CHANGING TREATMENT PARADIGM WITH NEWER THERAPIES

**Dr Bassem I Yamout, Beirut**

- Early pathological events in multiple sclerosis (MS) - Axonal transection is irreversible and most abundant in the region of inflammation.
- Early suppression of active inflammation may help to minimize cumulative axonal loss. Early optimized treatment is also essential to prevent progression of MS.
- Exposure to DMDs with a suboptimal effect may lead to development and worsening of disability. Thus, in order to identify patients at risk of poor response and disease progression, it is vital to find out reliable predictors of treatment response.
- Early brain volume loss predicts long-term disability: According to a 10-year retrospective study on the correlation of early whole-brain and central volume loss (n = 261 patients with CIS, RRMS, SPMS or PPMS), rates of both whole-brain and central brain volume loss were significant predictors of 10-year changes in EDSS and MSSS.
- DMTs can be classified under 2 groups: moderate efficacy and high efficacy. Moderate ones can be further categorized as injectables (IFN-beta, peg-IFN-beta-1a, glatiramer acetate) and orals (dimethyle fumarate, teriflunomide, fingolimod, cladribine). On the other hand, high efficacy group can be divided into continuous therapy (natalizumab, ocrelizumab) and noncontinuous therapy (alemtuzumab).
- MS therapy decisions are shared, involving both patient (demographic, lifestyle, emotional and psychological factors, quality-of-life, cognition, fatigue, safety and efficacy, peer perspectives) as well as physicians' (trial data, prognostic factors and disease activity, perceptions of what patients want, cost, logistics and access) perspectives.

## A DIALOGUE WITH DR DINESH NAYAK

**Dr Dinesh Nayak, HOD and Director of Neurology, Gleneagles Global Health City, Chennai**

**What is the recommended dosage of lacosamide?**

The starting dosage of lacosamide is 100 mg/day and the maintenance dose is between 200-400 mg/day. It is prescribed as a twice-daily dose. Lacosamide can be prescribed as an oral administration and also as intravenous route. For titration, lacosamide can be increased at weekly intervals by 100 mg/day till the maintenance dosage is reached.

**What is the pharmacokinetics of lacosamide in epilepsy patients without comorbidities?**

Lacosamide has 100% bioavailability with no interactions with food. There is no known effect of food on the absorption of oral lacosamide, therefore, it can be taken with or without food. Lacosamide is less than 15% bound to plasma proteins with an elimination half-life of 13 hours. It takes 3 days to reach the steady-state plasma concentrations.

**Are there any known drug interactions and food interactions with lacosamide?**

Lacosamide has a low potential for drug-drug interactions. The minimal binding of lacosamide to plasma proteins minimizes the potential for displacement of other drugs. Lacosamide has no interaction or minimal interaction with CYP-450 isoforms, causing minimal effect on the metabolism of other drugs unlikely.

Specific drug-interaction studies involving carbamazepine, valproic acid, omeprazole, metformin, digoxin and an oral contraceptive (ethinyl estradiol and levonorgestrel) also demonstrated no relevant interaction influence on the pharmacokinetics of these drugs or lacosamide.

There is no known effect of food on the absorption of oral lacosamide, therefore, it can be taken with or without food.

**How should lacosamide be withdrawn?**

As with all antiepileptic drugs (AEDs), lacosamide should be withdrawn gradually (over a minimum of 1 week) to minimize the potential of increased seizure frequency in patients with seizure disorders.

**Can lacosamide be used in status epilepticus?**

Status epilepticus is among the most common neurologic emergencies, with a mortality rate of up to 20%. The most important therapeutic goal is fast, effective and well-tolerated cessation of status epilepticus. As per Hofler et al, 2013, according to data from studies of refractory status epilepticus treated with lacosamide, the most often used bolus dose was 200-400 mg over 3-5 minutes. The overall success rate was 56%.[1]

**What is the effect of lacosamide on depression and anxiety symptoms in patients with focal refractory epilepsy?**

Depression is the main psychiatric comorbidity in epilepsy with an estimated prevalence between 20% and 55% and one of the main determinants of quality-of-life. Lacosamide has a positive effect on depressive and anxiety symptoms. The efficacy of lacosamide in seizure control has been demonstrated. However, the antidepressant and anxiolytic effect on mood and anxiety seems to be an independent factor.[2]

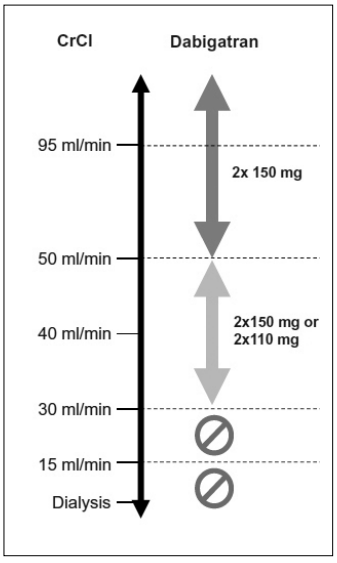
**References:** [1]Höfler J, et al. Epilepsia. 2013;54(3):393-404. [2]Rocamora R, et al. Epilepsy Behav. 2018;79:87-92.

## IN CONVERSATION WITH DR VINIT SURI

**Dr Vinit Suri; Consultant Neurologist**
**Apollo Hospitals, New Delhi**

**What are the advantages and disadvantages of dabigatran in the indications approved?**

Dabigatran is approved for nonvalvular atrial fibrillation, for the treatment of venous thromboembolism and pulmonary embolism and to reduce the risk of recurrent venous thromboembolism and pulmonary embolism. The advantages of use of dabigatran are fixed dosing regimen, no bridging, no INR monitoring and no food interactions and fewer drug interactions. Lastly, it is the only novel oral anticoagulant (NOAC) with an antidote, which makes it 'reversible'. As far as the disadvantages of using dabigatran are concerned, it is difficult to determine the compliance of the patient with the regimen prescribed. Any missed dose may place the patient at increased risk of thromboembolic event and renal monitoring and appropriate dose adjustment is required.




**What all should be considered regarding the dosage and variance of use of dabigatran (150/110/75)?**

Dabigatran is indicated for nonvalvular atrial fibrillation: *For patients with CrCl >30 mL/min:* 150 mg orally, twice-daily; *For patients with CrCl 15-30 mL/min:* 75 mg orally, twice-daily:

- Patients who are not able to tolerate the dose of 150 mg due to side effects can be given 110 mg; however, the recommended dose is 150 mg
- Do not use if CrCl <15 mL/min
- Avoid in pregnancy, breastfeeding or in severe liver disease.

**What are the drug interactions of dabigatran vs. warfarin?**

Treatment with vitamin K antagonists (VKAs) requires careful consideration of multiple food and drug-drug interactions. Despite fewer interactions with the NOAC drugs, physicians should consider the pharmacokinetic interactions of accompanying drugs and comorbidities when prescribing NOACs.

**Can dabigatran be prescribed in patients with renal impairment?**

Studies have reported up to 3-fold increase in drug exposure. In moderate renal impairment, the reported major bleeding rate was comparable between dabigatran 110 mg and 150 mg. A reduced dose may be considered in these patients. The presence of one or more factors known to increase hemorrhagic risk may increase the risk of bleeding. Caution should therefore be exercised.

Close clinical surveillance is recommended. Dabigatran etexilate is contraindicated in cases of severe renal impairment (CrCL <30 mL/min). Patients who develop acute renal failure should discontinue dabigatran etexilate.

**Should dabigatran be withdrawn in any situations?**

*Emergency surgery or urgent procedure*

Dabigatran etexilate should be temporarily discontinued. The specific reversal agent idarucizumab could be useful for the rapid reversal of the anticoagulation effect.

*Elective surgery/intervention*

If possible, dabigatran should be discontinued at least 24 hours before invasive or surgical procedures. In patients at higher risk of bleeding or in major surgery where complete hemostasis may be required, consider stopping dabigatran etexilate 2-4 days before surgery. Clearance of dabigatran in patients with renal insufficiency may take longer.

Dabigatran is contraindicated in patients with severe renal dysfunction (CrCL <30 mL/min) but should this occur then dabigatran etexilate should be stopped at least 5 days before major surgery.

*Acute surgery/intervention*

An acute surgery/intervention should be delayed if possible until at least 12 hours after the last dose. If surgery cannot be delayed, there may be an increase in the risk of bleeding. This risk of bleeding should be weighed against the urgency of intervention.

*Spinal anesthesia/epidural anesthesia/lumbar puncture*

Procedures such as spinal anesthesia may require complete hemostatic function. In patients treated with dabigatran etexilate and who undergo spinal or epidural anesthesia, or in whom lumbar puncture is performed in follow-up to surgery, the formation of spinal or epidural hematomas that may result in long-term or permanent paralysis cannot be excluded.

The risk of spinal or epidural hematoma may be increased in cases of traumatic or repeated puncture and by the prolonged postoperative use of epidural catheters. After removal of a catheter, an interval of at least 2 hours should elapse before the administration of the first dose of dabigatran etexilate. These patients require frequent observation for neurological signs and symptoms.

**How to measure the anticoagulant effect of dabigatran?**

For dabigatran, the aPTT may provide a qualitative assessment of dabigatran level and anticoagulant activity. The relationship between dabigatran and the aPTT is curvilinear. Dabigatran has little effect on the PT and INR at clinically relevant plasma concentrations, which are therefore unsuitable for the assessment of the anticoagulant activity of dabigatran.

**How to deal with dosing errors?**

To avoid dosing errors, patients on NOACs should be encouraged to make use of well-labeled weekly containers, with separate spaces for each dose timing. Importantly; however, dabigatran must not be taken out of its original bottle until immediately before intake.

A forgotten dose may be taken until 50% of the dosing interval has passed. Hence, for NOACs with a BID dosing regimen (i.e., every 12 h), a forgotten dose can be taken up until 6 hours after the scheduled intake. For NOACs with an OD dosing regimen, a forgotten dose can be taken up until 12 hours after the scheduled intake. After this time point, the dose should be skipped and the next scheduled dose should be taken.

***Source:*** Steffel J, et al. Eur Heart J. 2018;39(16):1330-93.

## ROLE OF ROSUVASTATIN IN PREVENTION OF STROKE

**Dr U Meenakshisundaram, Senior Consultant (Neurology), Apollo Hospitals, Chennai**

Statins are known to be effective in primary and secondary prevention of stroke. They have long-term beneficial effects that seem to be mediated by their lipid-lowering potential. Statins can also prevent recurrence or progression during acute stage of stroke on account of their antithrombotic, anti-inflammatory and antioxidative effects.[1]

The Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) trial assessed the effect of statins in reducing vascular events in healthy adults with normal cholesterol level <130 mg/dL and elevated sensitive C-reactive protein (s-CRP). The study had to be terminated early when the benefits of the treatment arm were found to be highly significant for the treatment arm in reducing stroke, myocardial infarction (MI) and the need for revascularization. The rates of the primary end point were 0.77 and 1.36 per 100 person-years of follow-up in the rosuvastatin and placebo groups, respectively, with corresponding rates of 0.18 and 0.34 for stroke, and 0.45 and 0.85 for the combined end point of MI, stroke or death from cardiovascular (CV) causes.[2] The trial provided substantial evidence that starting statin therapy in patients without elevated cholesterol led to a significant reduction in the risk of stroke. In the



**IJCP SUTRA 462:** In low risk patients (no pregnancy, not a newborn/elderly or no comorbidity), with no breathlessness, no testing, hospital admission and/or Tamiflu is required.

JUPITER trial, rosuvastatin reduced the incidence of ischemic stroke by more than half among men and women with low levels of LDL cholesterol who are at risk because of elevated levels of hs-CRP.[3] Therefore, when used in primary prevention among individuals with LDL <130 mg/dL and hs-CRP ≥2 mg/L, rosuvastatin has been shown to significantly reduce first MI, stroke, arterial revascularization, hospitalization for unstable angina and CV death in whites as well as non-whites.[4] In post hoc analyses of the JUPITER trial requested by European health authorities, among primary prevention patients with elevated hs-CRP having high global CV risk (10-year Framingham risk score >20% or SCORE risk ≥5%), but low LDL cholesterol levels, rosuvastatin significantly reduced major CV events. During 1.8-year median follow-up (maximum 5 years) of patients with Framingham risk >20%, the rate of MI/stroke/CV death was 9.4 and 18.2 per 1,000 person-years in rosuvastatin and placebo groups, respectively.[5] In the HOPE-3 trial, significantly fewer subjects in the rosuvastatin group had strokes, as compared to the placebo group. Fewer ischemic strokes occurred in the rosuvastatin group than in the placebo group (41 vs. 77).[6]

Rosuvastatin has also been used successfully in secondary prevention. A meta-analysis revealed that rosuvastatin is better than atorvastatin in the prevention of major CV events when statins are used in the secondary prevention of CV diseases.[7] A randomized, double-blind, multicenter trial compared rosuvastatin 20 mg and placebo in statin-naïve stroke patients. Hemorrhagic infarction or parenchymal/subarachnoid hemorrhage on gradient-recalled echo MRI occurred less frequently in the rosuvastatin group (6/137, 4.4%) as compared to the placebo group (22/152, 14.5%). Additionally, among 314 patients with at least one dose of study medication, progression or clinical recurrence of stroke was less frequent in the rosuvastatin group (1/155, 0.6% vs. 7/159, 4.4%).[1] Another study revealed that rosuvastatin therapy prevented aortic arch plaque progression in ischemic stroke patients with complicated aortic arch plaques (CAP), and seemed to have long-term clinical benefits. Patients with CAP not taking rosuvastatin had significantly more major adverse cerebrovascular events (MACEs) than those with CAP taking rosuvastatin, and those without CAP. Patients with CAP taking rosuvastatin also showed significant improvement in CAP diameter with improved lipid profiles.[8] Large atheromatous aortic plaques (AAPs) are known to be associated with ischemic stroke. It was shown in the EPISTEME trial that treatment with rosuvastatin for 6 months induced AAP stabilization with considerable LDL cholesterol reduction in patients with ischemic stroke.[9]

**References:** [1]Heo JH, et al. J Stroke. 2016;18(1):87-95. [2]Ridker PM, et al. N Engl J Med. 2008;359(21):2195-207. [3]Everett BM, et al. Circulation. 2010;121(1):143-50. [4]Albert MA, et al. Am Heart J. 2011;162(1):106-14.e2. [5]Koenig W, et al. Eur Heart J. 2011;32(1):75-83. [6]Yusuf S, et al. N Engl J Med. 2016;374:2021-31. [7]Zhong P, et al. Drug Des Devel Ther. 2017;11:2517-26. [8]Kaneko K, et al. Neurol Res. 2017;39(2):133-41. [9]Ueno Y, et al. Atherosclerosis. 2015;239(2):476-82.

## CERVICOGENIC HEADACHE: DOES IT EXIST?

**Dr Sumit Singh, Gurugram**

- Yes, it does exist.
- Cervicogenic headache - Pain confined to, or originating in the cervical region. It may radiate to the other side or the head or the shoulder region.
- Multiple sources of headache may be present within the same patient.
- Convergence of upper cervical segment nociceptive afferents in the trigeminocervical complex - Anatomical basis for both headache and neck pain to frequently co-exist.
- Both Neurologists and Pain Specialists should reconcile these intersections and address the multiple sources of pain in those headache patients who present with both headache and neck pain.
- Team of experts working together is the solution.
- Oversimplification of the diagnosis to migraine alone or cervicogenic headache alone may leave the patient with inadequate treatment.

## SECONDARY CAUSES OF PERIPHERAL DEMYELINATION

**Dr Tapas Kumar Banerjee, Kolkata**

- The causes of secondary demyelinating neuropathy include paraproteinemia related disorders, lymphoma, sarcoidosis, certain infections and drugs.
- IgM paraproteinemia is an important cause of demyelinating polyneuropathy, usually not responsive to conventional treatment.
- Biologic therapy with monoclonal antibodies, namely, rituximab, ocrelizumab, ofatumumab, etc. have been of benefit and have changed the outcome of these previously untreatable diseases.

■■■■

# News and Views

### Air Quality Early Warning System for Delhi Launched

Air Quality Early Warning System for Delhi was launched recently by the Union Minister for Earth Sciences and Environment, Dr Harsh Vardhan. The System is designed to predict extreme air pollution events and give alerts to take necessary steps as per Graded Response Action Plan (GRAP) of the Government of India. The air pollution system has been developed jointly by the scientists at Indian Institute of Tropical Meteorology (IITM), Pune, India Meteorological Department and National Centre for Medium Range Weather Forecasting (NCMRWF).

Speaking at the launch, Dr Harsh Vardhan said that the early warning system will help in proactively forewarning, 3-4 days in advance, any large scale air pollution events which may occur over the Delhi region… (*PIB, Ministry of Earth Science, October 15, 2018*).

### Zika Update: 72 Zika Cases Detected in Jaipur

As the number of people infected with Zika virus rose to 72 in Rajasthan, the Union Health Ministry has asked states to check mosquito breeding and intensify vector control strategies to contain the spread of the disease. Sanjeeva Kumar, Additional Secretary (Health), Ministry of Health and Family Welfare held a meeting with various state representatives through video conferencing. He asked them to implement the guidelines as prescribed under the National Vector Borne Disease Control Programme for effective control of Zika.

"States have been asked to intensify vector control strategies which include anti-larvae activities and fogging, and also follow the guidelines as prescribed under the National Vector Borne Disease Control Programme for effective control of Zika virus disease," a health ministry official said… (*ET Health-PTI, Oct. 16, 2018*).

### Cancer Survivors are at Risk for Heart Failure During and After Pregnancy

Young women previously treated for cancer with chemotherapy or radiation therapy with a prior history of cardiotoxicity are more likely to develop clinical congestive heart failure (CHF) during and after pregnancy, according to a study published Oct. 15, 2018 in the *Journal of the American College of Cardiology*.

### Shorter IV Antibiotic Course Effective for Infants with Uncomplicated, Late-onset GBS Bacteremia

Shortened IV antibiotic courses are safe and effective for infants with uncomplicated, late-onset Group B Streptococcus (GBS) bacteremia, with low rates of disease recurrence and treatment failure. Three patients (1.8%) in the shortened IV duration group experienced GBS recurrence vs. 14 patients (2.3%) in the prolonged IV duration group. These findings from a retrospective study are reported online Oct. 11, 2018 in the journal *Pediatrics*.

### Empagliflozin Improves Glycemic Control in Type 1 Diabetes but Increases Risk of Diabetic Ketoacidosis

Results from the Empagliflozin as Adjunctive to Insulin Therapy (EASE) program presented October 4 at the recent European Association for the Study of Diabetes (EASD) 2018 Annual Meeting in Berlin show that while empagliflozin improved glycemic control and weight in type 1 diabetes without increasing hypoglycemia, it also increased the risk for diabetic ketoacidosis (DKA).

### Most People cannot Differentiate Between OCD and OCPD, Say Study

According to new research published in *Community Mental Health Journal*, the general public has trouble understanding differences between obsessive-compulsive disorder (OCD) and obsessive-compulsive personality disorder (OCPD). Binghamton University PhD student Elyse Stewart, lead author said, "Individuals who have OCD experience extreme distress related to unwanted intrusive thoughts or feelings. They engage in a compulsion (some behavior or mental act) to reduce this distress. Individuals with OCPD are characterized by a preoccupation with perfectionism and orderliness that can interfere with their ability to be flexible in different situations."

### Health Minister Reviews Activities for Prevention and Control of Zika Seasonal Influenza

Union Minister for Health and Family Welfare, Shri JP Nadda, held a high level meeting to review the activities for prevention and control of Zika virus and seasonal influenza. He reassured the states for all support from the Union Government. For control of Zika virus in Rajasthan, the Health Minister emphasized on the need

for continuous monitoring. He stated that the Union Health Ministry is in regular contact with the State officials. Secretary (Health) is monitoring the situation on a daily basis in regular coordination with the State Health Secretary.

Shri Nadda stressed on the need for undertaking exhaustive control measures including intensive fogging for next month in order to ensure vector control in the area. He also stressed on strengthening surveillance to facilitate the early identification of cases. The Union Health Minister urged the people to not panic and cooperate with the health officials in controlling the breeding of the vectors. He further said that there was no shortage of medicines and testing kits and required support will be provided to the State. He stated that awareness is the key in controlling the vector borne diseases and no stone should be left unturned to reach out to the people… (*PIB, Ministry of Health and Family Welfare, 16th Oct. 2018*).

### Youth Road Safety Learners Licence Programme Launched

Shri Mansukh L Mandaviya, Minister of State for Road Transport and Highways and Chemical and Fertilizer launched the Youth Road Safety Learners Licence programme in New Delhi. The program is a PPP initiative to be run in collaboration with Diageo India and the Institute of Road Traffic Education (IRTE), and attempts to bring a formal and structured training program for young, first-time drivers as they apply for learner's license.

Launching this first-of-its-kind training program in the country, Shri Mansukh L Mandaviya said, road safety is of prime importance for the Government as recent times have seen an alarming rise in road fatalities especially among the youth. Rash driving, drunken driving, lack of adequate safety measures like not wearing helmets are some of the major factors resulting in high road accidents. He said, the government is committed to making its vision of safer roads and cities a reality. This program will help the Government achieve its target of reducing road accidents by 50 percent by 2020… (*PIB, Ministry of Road Transport & Highways, 15th Oct., 2018*)

### Inducing Labor at 39 Weeks of Gestation is Safe and Beneficial Option

Analysis of data from five randomized controlled trials and published in the journal *Ultrasound in Obstetrics & Gynecology* found that elective induction of labor in uncomplicated singleton pregnancy from 39 weeks' gestation is not associated with higher rates of complications and, in fact, may reduce the risk of cesarean section, hypertensive disease of pregnancy, and need for respiratory support in newborns.

### Psoriasis Patients with Hypertension are at Greater Risk of CV Interventions

Psoriasis is associated with a greater risk for cardiovascular (CV) interventions in patients with hypertension compared to hypertensive patients without psoriasis, suggests a study published Oct. 16, 2018 in the *Journal of Dermatology*. The study suggests that more intense assessments for CV interventions may be necessary in patients with concurrent hypertension and psoriasis vis-à-vis general hypertension patients.

### A Majority of Older Patients are Open to Deprescribing their Medications

Findings of a survey published Oct. 15, 2018 in *JAMA Internal Medicine* show that 92% of older adults would be willing to stop taking 1 or more of their medications if their physician said this was possible and 66.6% wanted to reduce the number of medicines that they were taking.

### Young Patients Show No Deterioration Ongoing Brain Development Initially After Onset of Schizophrenia

According to a study published online October 3, 2018 in *JAMA Psychiatry*, during the initial 1 to 2 years after illness onset, young individuals with schizophrenia showed deficits in dorsolateral prefrontal cortex activation and cognitive control, with developmental trajectories comparable to those of healthy controls. Younger age at onset was not associated with reduced cognition or activation.

### Talazoparib Approved for Patients with Advanced BRCA-positive Breast Cancer

The FDA has approved talazoparib (Talzenna) for the treatment of locally advanced or metastatic breast cancer patients with a germline BRCA mutation. Talazoparib, a poly-ADP ribose polymerase (PARP) inhibitor, is indicated for patients who have received no more than three prior cytotoxic chemotherapy regimens, including an anthracycline and a taxane (if not contraindicated) either in the neoadjuvant, adjuvant or metastatic setting.

### Many Children who Appear Healthy may have Metabolic Problems

In a study reported Oct. 17, 2018 in *Acta Paediatrica*, more than a quarter of otherwise healthy 6-year-old children may have metabolic risk factors that put

them at increased risk for cardiovascular disease (CVD). Among 212 children in the study, 26% showed abnormal metabolic profiles, including insulin resistance, a sign of type 2 diabetes. Insulin resistance was present in 28% of those with overweight or obesity and 5% of those with normal weight.

### Nocturnal Seizures may Increase Risk of Sudden Unexplained Death in Severe Epilepsy

People who died of sudden unexplained death in epilepsy (SUDEP) were more likely to have nocturnal convulsive seizures in general and a higher frequency of nocturnal convulsive seizures, as per a new study published online in *Neurology* on September 21. Monitoring patients with severe epilepsy in residential care facilities during the night reduced SUDEP rate.

### Initial Intensive Weight Loss may Prevent Type 2 Diabetes in Persons with Prediabetes

A 2-month weight loss regimen using meal substitutes followed by long-term weight maintenance through diet and exercise may be an optimal approach to preventing type 2 diabetes through lifestyle in adults with prediabetes. These findings from the Prevention of Diabetes Through Lifestyle Intervention and Population Studies in Europe and Around the World (PREVIEW) study were presented October 5 here at the recent European Association for the Study of Diabetes (EASD) 2018 Annual Meeting in Berlin, Germany.

### *C. difficile* Spores Survive High Temperatures of Hospital Laundering

Washing contaminated hospital bed sheets in a commercial washing machine with industrial detergent at high disinfecting temperatures failed to remove all traces of *Clostridium difficile*, a bacteria that causes infectious diarrhea, suggesting that linens could be a source of infection among patients and even other hospitals, according to a study published October 16, 2018 in *Infection Control & Hospital Epidemiology*.

### Patients with Early-stage Breast Cancer Still Undergo Routine Imaging Despite Guidelines Recommending Otherwise

Guidelines recommend against routine imaging in patients with early-stage breast cancer who are at low risk for metastasis, two new studies have found that these guidelines are not being consistently followed. In the first study, the authors report that 30% of patients with early-stage breast cancer underwent staging imaging, despite guidelines recommending against it. The prevalence of inappropriate imaging varied from 26% to 68% among oncologists. The second study found that unnecessary scanning occurred in up to 19% of patients with stage I to II breast cancer. Both papers were presented at the ASCO Quality Care Symposium.

### Global Health Organizations Commit to New Ways of Working Together for Greater Impact

Eleven heads of the world's leading health and development organizations signed a landmark commitment on Tuesday to find new ways of working together to accelerate progress towards achieving the United Nations' Sustainable Development Goals (SDGs).

Coordinated by the World Health Organization (WHO), the initiative unites the work of 11 organizations, with others set to join in the next phase. The commitment follows a request from Chancellor Angela Merkel of Germany, President Nana Addo Dankwa Akufo-Addo of Ghana, and Prime Minister Erna Solberg of Norway, with support from United Nations Secretary-General Antonio Guterres, to develop a global action plan to define how global actors can better collaborate to accelerate progress towards the health-related targets of the 2030 Sustainable Development Agenda.

"Healthy people are essential for sustainable development – to ending poverty, promoting peaceful and inclusive societies and protecting the environment. However, despite great strides made against many of the leading causes of death and disease, we must redouble our efforts or we will not reach several of the health-related targets," the organizations announced at the World Health Summit in Berlin. "The Global Action Plan represents an historic commitment to new ways of working together to accelerate progress towards meeting the 2030 goals. We are committed to redefine how our organizations work together to deliver more effective and efficient support to countries and to achieve better health and well-being for all people."

The group has agreed to develop new ways of working together to maximize resources and measure progress in a more transparent and engaging way. The first phase of the plan's development is organized under three strategic approaches: align, accelerate and account.

### A Simple Test may Help Predict Long-term Outcome After Stroke

A simple test taken within a week of a stroke may help predict how well people will have recovered up to 3 years later, according to a study published in

the October 17, 2018 in *Neurology*. that those who had thinking problems within 1 week of the stroke were seven times more like to die during the 3 years of the study than those who did not have thinking problems. Those with thinking problems on the first test were also five times more likely to have problems with their motor skills than those who did not have thinking problems early on.

### Study Identifies Risk Factors for Fulminant *C. difficile* Infection After Cardiac Surgery

A single-center, retrospective cohort study published online Sept. 27, 2018 in *BMC Anesthesiology* has identified type 2 diabetes mellitus, preoperative ventilation, utilization of more than 8 units of red blood cell concentrates or of more than 5 fresh-frozen plasma units and a cross-clamp time >130 minutes as predictors of a fulminant *C. difficile* infection.

### People Who Commute Through Natural Environments Daily Report Better Mental Health

Results from the PHENOTYPE project show that people commuting through natural environments on a daily basis had on average a 2.74 point higher mental health score than those who commuted through natural environments less frequently. This association was even stronger among people who reported active commuting i.e., walking or cycling. Natural environments were defined as all public and private outdoor spaces that contain 'green' and/or 'blue' natural elements such as street trees, forests, city parks and natural parks/reserves, and also included all types of water bodies. These findings are published in *Environment International*.

### Children with Inflammatory Bowel Disease have Higher Risk of Mortality

Children who develop inflammatory bowel disease (IBD) (ulcerative colitis or Crohn's disease) have an increased risk of death, both in childhood and later in life, says a study published online Oct. 17, 2018 in the journal *Gastroenterology*. Children who developed IBD before the age of 18 had a three- to fivefold higher mortality rate than people without IBD, both during childhood and into adulthood.

### Adult-onset Type 1 Diabetes is Frequently Misdiagnosed

According to new research presented October 4, 2018 at the European Association for the Study of Diabetes (EASD) 2018 Annual Meeting in Berlin, onset of type 1 diabetes (T1DM) after age 30 years is common and is frequently misdiagnosed as type 2 diabetes (T2DM) in clinical practice. The study found that 21% of those with insulin-treated diabetes who were diagnosed after the age of 30 had severe insulin deficiency, confirming T1DM. Out of this group, 39% did not receive insulin when they were initially diagnosed, with 46% of those individuals self-reporting that they had T2DM. A rapid progression to insulin dependence was highly predictive of late-onset T1DM with 84% of those with the disease requiring insulin within just 1 year.

### EMA Approves Bevespi Aerosphere as a New Maintenance Bronchodilator Treatment

The European Medicines Agency's (EMA's) Committee for Medicinal Products for Human Use (CHMP) has recommended marketing for the medicinal product Bevespi Aerosphere, intended for the maintenance treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). Bevespi Aerosphere is a fixed dose combination of a long-acting beta-2 receptor agonist (formoterol fumarate dihydrate) and a long-acting muscarinic antagonist (glycopyrronium). It will be available as a suspension for inhalation (7.2 μg/5.0 μg).

### Atrial Fibrillation Progression is Associated with Increased Adverse Events

Results of a survey of the patients with atrial fibrillation (AF) in Fushimi-ku, Kyoto published in the October 2018 issue of the journal *Stroke* show that AF progression was associated with increased risk of clinical adverse events - systemic embolism and ischemic stroke - during arrhythmia progression period from paroxysmal to sustained (persistent or permanent). The risk of adverse events was transiently elevated during progression period and declined to the level equivalent to SAF after the progression.

### Insulin Resistance is Prevalent in Children as Young as Age 6

A significant percentage of 6-year-old children showed abnormal metabolic profiles, including insulin resistance, which increased their risk of CVD in a longitudinal cohort study of healthy children, the results of which were published October 17, 2018 in the journal *Acta Paediatrica*. Fifty-five of the 212 children had one or more risk factors for metabolic syndrome requiring action. Waist circumference was a stronger marker for metabolic alterations than body mass index (BMI).

### Shorter Duration of Sleep Apnea Increases Mortality Risk

Duration of the apnea-hypopnea event is a predictor of mortality in obstructive sleep apnea (OSA). According to the study published online October 19, 2018 in the *American Journal of Respiratory and Critical Care Medicine*, individuals with shorter respiratory events may be predisposed to increased ventilatory instability and/or have augmented autonomic nervous system responses that increase the likelihood of adverse health outcomes.

### Better Cardiorespiratory Fitness Leads to Longer Life

A retrospective study of 1,22,007 patients who underwent exercise treadmill testing at Cleveland Clinic between Jan. 1, 1991, and Dec. 31, 2014, to measure all-cause mortality relating to the benefits of exercise and fitness found that increased cardiorespiratory fitness was directly associated with reduced long-term mortality, with no limit on the positive effects of aerobic fitness. Extreme aerobic fitness was associated with the greatest benefit, particularly in older patients (70 and older) and in those with hypertension. The study is published October 19, 2018 in the *Journal of the American Medical Association Network Open*.

### India to Host UNICEF's Global Meet on Maternal and Child Health

India will be the global host of UNICEF's Partnership for Maternal, Newborn and Child Health stakeholders meeting, including participation from nearly hundred countries, this December, officials said. The Partnership for Maternal, Newborn and Child Health Forum will emphasise the importance of people-centred accountability, bringing forward the voices and lived realities of women, children and adolescents through innovative programming and creative projects.

The Forum will be hosted by Ministry of Health and Family Welfare in collaboration with the Partnership for Maternal, Newborn and Child Health (PMNCH) this December.

The UNICEF said Prime Minister Narendra Modi, former Chile President Michelle Bachelet and the chair of PMNCH would deliver the keynote addresses.. (*Economic Times-PTI, Oct. 20, 2018*).

### Hospitalized Acute MI Patients with Hyperglycemia at Risk of Ventricular Tachycardia

Patients hospitalized with acute myocardial infarction (MI) with hyperglycemia are at increased risk for developing ventricular tachycardia (VT). The study reported October 19, 2018 in Cardiovascular Diabetology suggests that these patients should be carefully monitored early after hospital admission, to reduce their risk of VT.

### Biopsies of Hand Tissue could be an Early Signal of Life-threatening Cardiac Amyloidosis

A new research from the Cleveland Clinic has suggested that biopsies of hand tissue could be an early signal of life-threatening cardiac amyloidosis. They identified amyloid deposits in 10.2% of patients undergoing carpal tunnel release surgery. The study, published online in the *Journal of the American College of Cardiology*, contained wide inclusion criteria; all men in their 50s or older and all women in their 60s or older were eligible unless they had known amyloidosis or carpal tunnel syndrome considered to be from trauma or arthritis.

### Drinking More Water may Help Prevent Recurrent Cystitis

According to a randomized controlled study published in *JAMA Internal Medicine*, published online October 1, 2018, women who drank more water 1.5 L of water daily reduced the episodes of cystitis by 50% and they were also prescribed fewer antibiotics.

### Heart Patients should Move Around Every 20 Minutes to Reduce Mortality Risk

Patients with heart disease should interrupt sedentary time every 20 minutes with a 7-minute bout of light physical activities such as standing up and walking at a casual pace, recommends a study presented at the ongoing Canadian Cardiovascular Congress (CCC) 2018 in Toronto, Canada. As per the study, during each hour of sitting time, heart patients should take three breaks which add up to 21 minutes of light physical activity. This will expend 770 kcal a day, an amount associated with a lower risk of premature death.

### FDA Panel Backs Prucalopride for Chronic Idiopathic Constipation

The Gastrointestinal Drugs Advisory Committee of the US Food and Drug Administration (FDA) voted unanimously (10 yes, 0 no) to recommend prucalopride tablets for the treatment of adults with chronic idiopathic constipation.

### One Lakh Benefitted Under PMJAY in 1 Month of its Launch, Says Health Minister

Nearly a month after the roll out of the Centre's PMJAY health insurance scheme, one lakh people have availed

the benefits of the ambitious program, Union Health Minister JP Nadda said recently.

The Pradhan Mantri Jan Arogya Yojana or PMJAY (previously Ayushman Bharat), touted as the world's largest health insurance program, was launched pan-India by the Prime Minister from Jharkhand on September 23. The scheme is expected to benefit up to 55 crore people, providing them an annual health cover of Rs. 5 lakh for secondary and tertiary care hospitalization through a network of Empanelled Health Care Providers (EHCP). There is no cap on family size and age in the scheme. On October 5, 2 weeks after the launch of the PMJAY, Indu Bhushan, CEO of National Health Agency, said around 38,000 people have availed the benefits of the scheme … (*ET Health-PTI, October 21, 2018*)

### Evaluation of Out-of-office BP is Important for Risk Stratification in Treated Patients with Normal Clinic BP

A systematic review and meta-analysis examining the prognostic value of masked uncontrolled hypertension concluded that the risk of CV events and all-cause mortality is significantly higher in patients with masked uncontrolled hypertension than in those with controlled hypertension, which was independent of follow-up length and types of studied events. No difference between the prognostic information was observed with masked uncontrolled hypertension detected either by ambulatory BP monitoring (ABPM) or home BP measurement. The meta-analysis, published in the October 2018 issue of *Hypertension* suggests that evaluation of out-of-office BP is relevant for risk stratification in treated patients with normal clinic BP.

### EU Panel Recommends Marketing Authorization for First Dengue Vaccine

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has recommended granting a marketing authorization for Dengvaxia (dengue tetravalent vaccine [live, attenuated]), for the prevention of dengue caused by dengue virus serotypes 1, 2, 3 and 4 in people who are between 9 and 45 years old, live in an endemic area and already had a prior dengue virus infection.

### Pilot Study Shows Bioelectronic Medicine Treatment is Effective for Lupus

A bioelectronic medicine device was effective in reducing pain and fatigue in patients with lupus, according to results of a pilot trial to be presented at the American College of Rheumatology/Association of Rheumatology Health Professional's (ACR/ARHP) Annual Meeting in Chicago. Stimulation of the vagus nerve significantly reduced pain and fatigue associated with lupus.

### Combination of Palbociclib and Fulvestrant Prolongs Overall Survival

Among patients with hormone-receptor–positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer who had sensitivity to previous endocrine therapy, treatment with palbociclib-fulvestrant led to longer overall survival compared to treatment with placebo-fulvestrant. These findings are published October 20, 2018 in the *New England Journal of Medicine*.

### Tegaserod Approved for IBS with Constipation in Women with No Heart Disease

The Gastrointestinal Drugs Advisory Committee of the US FDA voted overwhelmingly (11 yes, 1 no) to recommend reintroducing tegaserod maleate (Zelnorm, Sloan Pharma) for the treatment of IBS with constipation (IBS-C) in women without a history of CV ischemic disease and who have no more than one risk factor for CVD.

### Poor Oral Health Linked to Higher BP and Also Worse BP Control

Poor oral health may interfere with BP control in people diagnosed with hypertension. People with high BP taking medication for their condition are more likely to benefit from the therapy if they have good oral health, according to new research published October 22, 2018 in the journal *Hypertension*. In the study, patients with severe periodontitis had systolic pressure that was, on average, 3 mmHg higher than those with good oral health.

### Updated Clinical Report on Healthcare Transitions for Youth and Young Adults

A new clinical report, released jointly by American Academy of Pediatrics (AAP), American Academy of Family Physicians (AAFP) and American College of Physicians (ACP) published online Oct. 22 in the journal *Pediatrics* provides new practice-based quality improvement guidance on key elements of transition from adolescence to adulthood: planning, transfer and integration into adult care. The 2018 report describes an evidence-informed, structured healthcare transition process called the Six Core Elements of Healthcare Transition that guides clinicians in the development of transition services.

### Study Shows Antipsychotics Ineffective for Delirium in Critically Ill Patients in ICU

Critically ill patients in intensive care units (ICUs) did not benefit from two antipsychotic drugs - haloperidol or ziprasidone - used to treat delirium, according to findings from the Modifying the Incidence of Delirium USA (MIND USA) study published online Oct. 22, 2018 in *The New England Journal of Medicine*. The two drugs did not affect delirium, survival, length of ICU or hospital stay or safety.

### Adjunctive Satralizumab Reduces Neuromyelitis Optica Relapses

Findings of a study presented at the 34th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) 2018 in Berlin demonstrate that addition of satralizumab - anti-interleukin-6 receptor monoclonal antibody - to standard treatment for neuromyelitis optica spectrum disorder reduced the relapse rate by 62%.

### People with Short Apneas and Hypopneas at Higher Mortality Risk

How long a person with obstructive sleep apnea (OSA) stops breathing may be a better predictor of mortality risk from OSA than the number of times they stop breathing, according to findings from the Sleep Heart Health Study published online Oct. 19, 2018 in the *American Journal of Respiratory and Critical Care Medicine*. The study participants who had short apneas and hypopneas were at greater risk of dying over a decade of follow-up than those who had long apneas.

### Yoga + CBT Improves Chances of Smoking Cessation

Breath easy, a randomized controlled trial of more than 200 adult smokers showed that those who took part in an 8-week program of smoking-focused cognitive-behavioral therapy (CBT) and twice-a-week sessions of Iyengar yoga had 37% greater odds of achieving smoking abstinence at end of treatment than those who underwent CBT along with general wellness classes. This effect was more evident in heavy smokers. These findings are published online October 6, 2018 in the journal *Nicotine and Tobacco Research*.

### Dupilumab Gets FDA Approval as Add-on Maintenance Therapy For Moderate-to-severe Asthma

The US FDA has approved dupilumab (Dupixent, Sanofi/Regeneron) as "add-on maintenance therapy in patients with moderate-to-severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid-dependent asthma". Dupilumab will be available as an injectable solution in prefilled syringes with 200-mg and 300-mg doses administered every other week.

### Exosomal Alpha-synuclein Differentiates Parkinson's Disease from Multiple System Atrophy

Results of a pilot study presented at the annual American Neurological Association meeting in Atlanta show that fractions of alpha-synuclein in neuronal and oligodendroglial exosomes were different enough to distinguish Parkinson's from multiple system atrophy (MSA) patients with 90% sensitivity and specificity. Both Parkinson's disease (PD) and MSA are characterized by an abnormal deposition of alpha-synuclein aggregates in the brain.

### Childhood Obesity Increases the Risk of Slipped Capital Femoral Epiphysis

Compared to a thin child, children with severe obesity at 5 years old had almost 20 times the subsequent risk of developing slipped capital femoral epiphysis, a debilitating hip disease, according to a study published online Oct. 22, 2018 in the journal Pediatrics. Greater the BMI of the child, greater the risk of slipped capital femoral epiphysis. The study authors recommend that doctors who treat children be aware of slipped capital femoral epiphysis, especially amongst obese children.

### A New Diagnostic Test to Aid Determination of Menopausal Status

The US FDA has permitted marketing of the PicoAMH Elisa diagnostic test as an aid in the determination of a patient's menopausal status. The PicoAMH Elisa test measures the amount of anti-Müllerian hormone (AMH) in the blood. AMH levels represent one indicator available to clinicians to determine whether a woman is approaching or is likely to have reached her final menstrual period. The test is meant to be used only in conjunction with other clinical assessments and laboratory findings.

### FDA Approves Baloxavir to Treat Acute Uncomplicated Influenza

Xofluza (baloxavir marboxil) has been approved by the US FDA for the treatment of acute uncomplicated influenza (flu) in patients 12 years of age and older who have been symptomatic for no more than 48 hours.

■■■■

# Collective Consciousness

KK AGGARWAL

Consciousness is an energized field of information with powers to do everything in the universe. Collective consciousness is the internet of the collective souls of many people in a group.

Collective consciousness is the strongest super power ever available in the universe. As per the Vedic texts, whatever is the intent of collective consciousness will become a reality. Scientifically, collective consciousness is based on the principle of critical mass. Vedic literature has shown it to be 1% of the defined population under study.

The origin of the critical mass comes from 100th monkey phenomenon. The story goes as under: long ago in Japan a monkey called Emo used to eat dirty apples everyday picked up from the ground. One day by accident the apple fell down in a river, the dirt got washed off and he ate the washed apple. Obviously, it tasted delicious. He started washing the apples thereafter every day before eating. His fellow monkeys started following the same. The process of following went on. A time came when the 100th monkey washed the apple and ate it. A strange phenomenon was noticed. All monkeys in and around that state started washing the apple before eating. The no. 100 was the critical mass.

Group Editor-in-Chief, IJCP Group

Once this mass is crossed the information will spread like a wild fire and the intent becomes a universal reality. Vedic literature has also shown if 1% of the public of any area meditates together, the crime rate of that area goes down. It also talks about the role of critical mass in prayers in achieving miracles.

Thus principle of critical mass is often used in designing and organizing an event. In a movie hall of 1,000 people if 10 people clap sitting in different areas everybody will clap. The same is true for hooting at a particular scene. Most politicians use this principle when they organize election rallies. For a gathering of 10,000 they need 100 and for a gathering of 1,000 people they only need 10 supporters who are suppose to sit in different areas and shout or clap on given directions. The Mexican way of hooting or clapping in cricket grounds also follows the same principle. For a ground like Eden Gardens with a capacity of 75,000 people you only require 750 people to control the mood of the people. This is what happens in a recent incident when the Indian team was hooted out by the sentence "No Ganguli no play, No Dada no play". If Greg Chappel or Jagmohan Dalmiya had anticipated this, they would have used the same strategy to produce just the opposite result. They could have posted 1500 people (2% of the population) in the stadium shouting pro–Dravid slogans and the end result of the match could have been different.

Most successful leaders used this technology to lead.

■■■■

## Quitting Tobacco

**Formula of 40**

- Cigarette smoking causes over 40 lakh deaths worldwide each year.
- 40% of all regular smokers can be expected to die from a tobacco-related illness.
- Stopping smoking before age 40 is associated with a larger decline in premature mortality than stopping at a later age.
- Cigarette smoking is estimated to be responsible for 40% of all cardiovascular deaths.
- Those smoking >40 cigarettes per day will lose 6 years (M) and 3 years (F) of life.

**Formula of 10**

- 10% or more of quitters may gain over 10 kg after smoking cessation.

**INSPIRATIONAL STORY**

# Two Monks and a Pretty Lady

Once upon a time a big monk and a little monk were traveling together. They came to the bank of a river and found the bridge was damaged. They had to wade across the river.

There was a pretty lady who was stuck at the damaged bridge and couldn't cross the river.

The big monk offered to carry her across the river on his back to which the lady accepted.

The little monk was shocked by the move of the big monk and was thinking "How can big brother carry a lady when we are supposed to avoid all intimacy with females?" But he kept quiet.

The big monk carried the lady across the river and the small monk followed unhappily. When they crossed the river, the big monk let the lady down and they parted ways with her.

All along the way for several miles, the little monk was very unhappy with the act of the big monk. He was making up all kinds of accusations about big monk in his head. This got him madder and madder. But he still kept quiet. And the big monk had no inclination to explain his situation.

Finally, at a rest point many hours later, the little monk could not stand it any further; he burst out angrily at the big monk. "How can you claim yourself a devout monk, when you seize the first opportunity to touch a female, especially when she is very pretty?"

All your teachings to me make you a big hypocrite.

The big monk looked surprised and said, "I had put down the pretty lady at the river bank many hours ago, how come you are still carrying her along?"

**Moral:** This very old Chinese Zen story reflects the thinking of many people today. We encounter many unpleasant things in our life, they irritate us and they make us angry. But like the little monk, we are not willing to let them go away. There is no point in remaining hurt by the unpleasant event after it is over. Learn to move on in life!

■■■■


Two different perceptions depending upon where you are concentrating-on the white image or the black image.


**IJCP SUTRA 472:** Tamiflu is not given without testing, which costs around Rs. 4,000/-. So if you are a low risk patient, why spend this amount?

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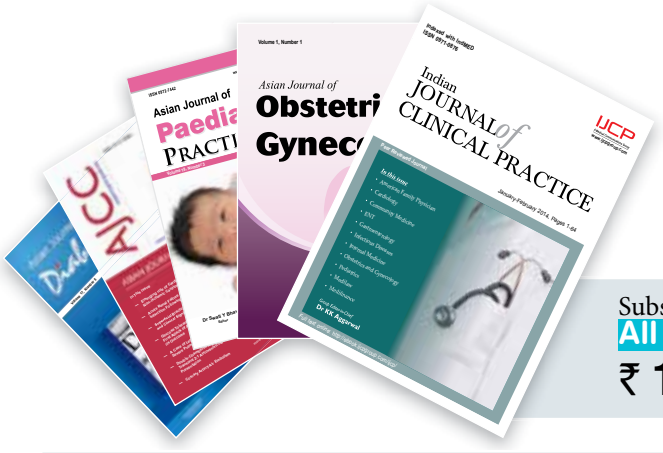

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# Lighter Side of Medicine

HUMOR

## SMELLING AND HEARING

An elderly woman goes to the doctor. She says, "Doc, it's terrible, I pass gas all the time. Fortunately, it's odorless and silent, otherwise I'd be mortified. For example, I've passed gas 10 times just since we've been talking, but it's odorless and silent so you can't tell." The doctor gives her some green pills and tells her to take one a day and come back in a week.

The woman comes back after taking the pills for a week. She says, "Doc, there's been a change but not for the better. I still pass gas all the time, but while it's still silent, now it smells terrible!"

The doctor says, "Well, I'm glad we cleared up your sinus blockage. Now we'll have to work on your hearing."

## OLD AGE SECRET

Grandpa was celebrating his 100th birthday and everybody complimented him on how athletic and well-preserved he appeared.

"Gentlemen, I will tell you the secret of my success," he cackled. "I have been in the open air day after day for some 75 years now."

The celebrants were impressed and asked how he managed to keep up his rigorous fitness regime.

"Well, you see my wife and I were married 75 years ago. On our wedding night, we made a solemn pledge. Whenever we had a fight, the one who was proved wrong would go outside and take a walk."

## STARTING WITH "I".

**Teacher:** Ellen, give me a sentence starting with "I".

**Ellen:** I is…

**Teacher:** No, Ellen. Always say, I am.

**Ellen:** All right. I am the ninth letter of the alphabet.

## GETTING RID OF THE PROBLEM

A farmhand is driving around the farm, checking the fences. After a few minutes he radios his boss and says, "Boss, I've got a problem. I hit a pig on the road and he's stuck in the bull–bars of my truck. He's still wriggling. What should I do?"

"In the back of your truck there's a shotgun. Shoot the pig in the head and when it stops wriggling you can pull it out and throw it in a bush." The farm worker says okay and signs off. About 10 minutes later he radios back. "Boss I did what you said, I shot the pig and dragged it out and threw it in a bush."

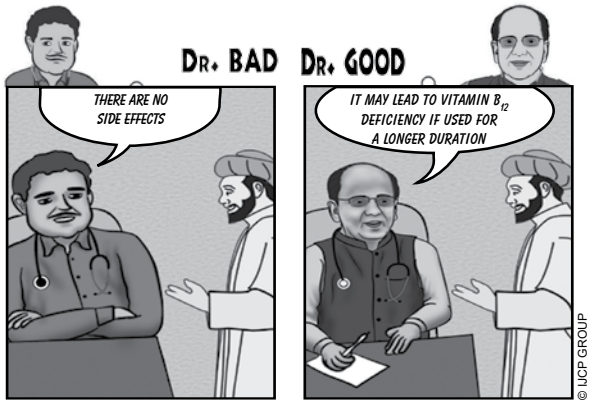
"So what's the problem now?" his Boss snapped.

"The blue light on his motorcycle is still flashing!"

"It was enough to make anybody faint," he said. "My son asked me for the keys to the garage, and instead of driving the car out, he came out with the lawn mower!"

## Dr. Good and Dr. Bad

**SITUATION:** A type 2 diabetic patient who was on metformin therapy was concerned about the side effects of metformin.




**LESSON:** The ADA suggests that long-term use of metformin may be related to vitamin $B_{12}$ deficiency. Therefore, these levels must be monitored periodically in those who are on metformin therapy, specifically those with anemia or peripheral neuropathy.

*Diabetes Care. 2017;40(Suppl 1):S44-S47.*

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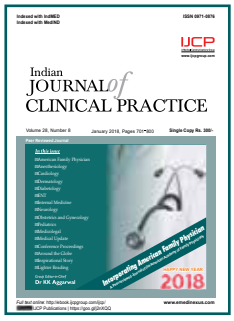

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Padma Shri Awardee
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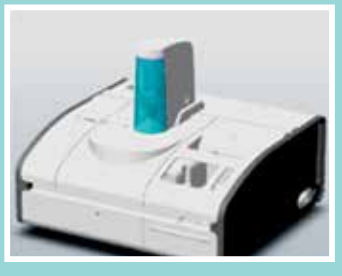

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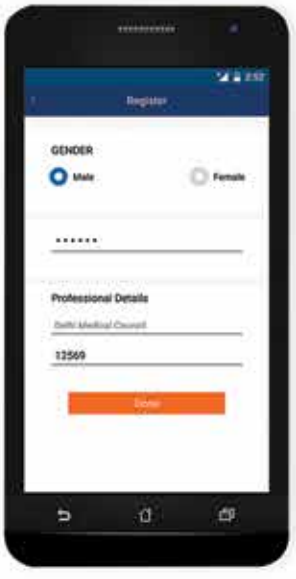


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