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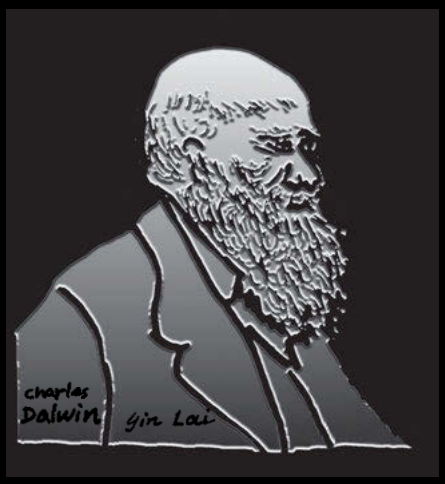

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Our Mission and Purpose

Southern California Clinicians is established by the Medical Staff of Pomona Valley Hospital Medical Center in Pomona, California. It provides a journal for modern California clinicians to publish articles to share their clinical experiences and opinions with other physicians, show their academic achievements in medical practice, and keep a permanent record of valuable case studies and case reports from all departments and all specialities in the modern era.

This journal invites all clinicians in southern California to contribute interesting articles and reviews, including new developments in clinical skills and techniques, or new procedures applied during their medical practice.

In order to maintain the highest quality, accuracy and academic dignity, we reserve the right to peer review all articles. Articles will be reviewed by our editorial board and special consultants.

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Guidelines for Authors

On behalf of the editorial staff of PVHMC's new medical journal *Southern California Clinicians*, I would like to extend an invitation to you to contribute articles for publication. Articles that pertain to your medical practice, any case reports you may have, or past clinical experiences are welcome. Articles for publication in the next journal are due no later than May 31st, 2011.

1) Use a single page to show your full name, your academic degrees and affiliations, and your current address, phone number, fax, e-mail.
2) All articles must be titled.
3) Please submit one typed hard copy and article saved on to CD, double spaced.
4) Length is flexible, from 1 page to 10 pages.
5) You may include a short abstract and conclusion as you wish. Slides, tables, figures, photos or pictures are welcome. Most important is a list of references numbered in the order in which you marked in the text.
6) All articles have to be original, never been published before, reflecting your own experience, knowledge and opinion.
7) All articles, once accepted, will be peer reviewed, corrected or revised and will be sent back to you for your approval.
8) Submit all articles on CD or E-mail to:
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They continue to be the main supporters of
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Thank you all!

Preface for this Edition

Yin H. Lai, M.D.
Editor-in-Chief

This year is already unusual. The entire world is running into economic depression. In the United States, high unemployment rates create more low-income families and the whole nation is suffering from anxiety and frustration.

Then, all health insurance companies are starting new marketing tactics. Rich and young people are buying health insurance with high deductibles and low premiums. Poor and old people are getting more confused. Meanwhile, the government keeps cutting down payments to all medical professions but keeps increasing our responsibilities for high standard-of-quality care. Patients are not seeing their doctors due to loss of cars, no money for gasoline, and inability to pay their co-payments. They wait until they have no choice but to run into urgent care or emergency facilities.

Even so, we medical professionals have to improve our knowledge and skills in order to give top-quality care. Many biological scientists are studying the mechanisms of mutation and evolution at a molecular level. Once we understand how MRSA, VRE and other new bacteria strains keep taking numerous human lives, then, we will be able to stop mutation of antibiotic-resistant strains. How can we stop the aging process to prolong our high quality of life? How can we reduce transplant rejection to a minimum?

Therefore our editorial board has the responsibility to improve our clinicians' knowledge so we can apply high scientific technology to our practice, to help our communities to stay healthy and strong, to improve function of a community and so to keep a healthy and peaceful world.

"學而不思則罔；思 而不學則殆。"
Confucius said: Learning without thinking results being deceived; thinking without learning results in dying !" In this edition, I am very proud to see so many doctors are following Confucius' principle. For example, Dr. Stanley Kim reduces pain from daily sticking on finger tips for blood glucose of numerous diabetic patients by inventing TiniBoy. Dr. Donald Barceloux wrote an internationally well known textbook " Medical Toxicology of Natural substances". Confucius and all of us congratulate on their achievements!

I am so happy to see so many physicians voluntarily serving on our editorial board and contributing such excellent articles. I hope you will enjoy reading the following pages.

Here I want to express my sincere appreciation to all those who donated not only the articles but also money and time to support this medical journal. All our article writers, the entire editorial board, the reviewers, the treasurer and all editorial assistants are all volunteers without compensation. I want to say many thanks to them.

–Yin H. Lai
Editor

TRIGEMINAL NEURALGIA (TN):
An Overview

Ramin AmirNovin, MD

Trigeminal neuralgia (TN) is characterized by a recurrent, unilateral sharp pain in the distribution of one or more branches of the trigeminal nerve. The pain is usually in the distribution of the mandibular or maxillary branches and has a prevalence of 4 per 100,000 people1. Given that the diagnosis is made on a clinical basis, controversy still exits in regard to the best method of diagnosing the disorder 2, 3. In general, facial pain may be due to vascular, neurologic, or dental origins. Many patients with TN originally mistake the pain as dental pain and are hence seen and treated by several dentists, who fail to improve their condition. This is understandable since dental pain is much more common than TN and most dentists will only encounter 3-4 cases of TN in a practicing lifetime15. There is increasing agreement that the pain in TN is caused by the demyelination of the trigeminal nerve, due to either vascular compression, multiple sclerosis, amyloid infiltration, or other sources of trauma4.

Once the diagnosis has been made, the first line therapy is carbamazepine. Seventy percent of patients have good pain control with carbamazepine 5. Of the remaining 30%, almost all have good pain control with the help of other medications, including lamotrigine, phenytoin, gabapentin, oxcarbazepine, topiramate, baclofen, and clonazepam 6, 7. Unfortunately, the mean time to recurrence while on pharmacotherapy is approximately one year 6. Patients with poor pain control by medications are then eligible for surgical interventions. These include Microvascular Decompression (MVD)8 of the trigeminal nerve, Percutaneous Rhizotomies (PR) 9 (with glycerol, alcohol, radiofrequency lesion, or balloon expansion), or Gamma Knife Radiosurgery. Unfortunately, since the pain from TN is very severe, very few patients are willing to be a part of studies on the natural history of this disease. Hence the possibility and rate of spontaneous remission are not well studied.

MVD is a surgical intervention (performed under general anaesthesia) where an incision behind the ear allows for a small 3-5 cm craniotomy to be performed directly at the junction of the transverse and sigmoid sinuses. The cerebellum is retracted exposing the trigeminal nerve. Under the microscope, the nerve is inspected and all the vessels that come in contact with the nerve are mobilized and kept off the nerve with the help of Teflon pledgets. With the advent of newer high resolution MRI protocols, the vascular compression of the trigeminal nerve can be documented well before surgery and hence aids in patient selection. PR is a procedure performed under deep conscious sedation. It involves placement of a needle through the patient's cheek and into the foramen ovale at the skull base. Stimulation of the trigeminal nerve at different depths beyond the foramen is used to find the proper area within the trigeminal ganglion that corresponds to the patient's pain territory. Once the correct area of the nerve is found, the patient is deeply sedated and the nerve is injured using either heat (radiofrequency induced), glycerol, alcohol, or balloon expansion. Gamma Knife Radiotherapy (GK) is performed after the placement of a head frame onto the patient's skull under mild sedation and local anaesthesia. The patient's head (while within the frame) is then scanned using a high resolution MRI protocol. The Brain MRI is then used to stereotaxically target the trigeminal nerve just before its entry into the Meckel's cave. Forty Grays of radiation is applied to a 4 mm target and the brainstem dose is kept less than 12 Grays 16.

MVD, PR, and GK all have a comparable short-term efficacy of approximately 80%. The effects of GK radiotherapy take 1-3 months to be complete while most PR and MVD patients have results within 2 weeks. It is the long-term effects of these therapies that are vastly different. Eighty percent of MVD patients continue to have good pain control at ten years of follow-up. Unfortunately, only 30% of PR patients and 55% of GK patients have good symptomatic control in ten years 9-11, 16. Hence, MVD is currently the mainstay of surgical therapy for refractory TN 1, 12. However, MVD is the most invasive of these procedures with many possible complications, even in experienced hands 13. These include hearing loss (0.5%), diplopia, facial weakness, facial numbness (1%), cerebellar or brain stem infarcts, CSF leaks, meningitis, hydrocephalus, and even death (0.2%) 11-13. The major complications of PR and GK are similar in incidence. They both yield approximately 10% facial numbness and 4-6% painful facial numbness (anaesthesia dolorosa)10,18.

The long-term benefits of MVD probably outweigh the risks in younger patients, but older patients have a higher risk of complication. The risk of CSF leaks, wound infection and dehiscence, and transient confusion are all much higher in the elderly 12. Furthermore, many older patients cannot handle the physiologic stress of general anaesthesia. Unfortunately, the incidence of TN in men increases from 4 to 45.2 in 100,000 people after the age of 80 2. Furthermore, previous studies suggest that the pain becomes more difficult to treat with time 2, 6. Hence, the ability to treat TN in the elderly is an important consideration.

Little literature exists with regards to the best overall approach to the TN patient. Most studies are focused on the effectiveness of individual methods of TN therapy 8, 9, 12, 14. Utilizing MVD for relatively younger patients (less than 70 years old) and PR or GK for older patients (older than 70 years old), might provide the best approach. Such an approach can decrease the overall complication rate of surgical therapies for older patients17. Given the relatively mild nature of GK radiosurgery for the patient, there is a large sub-population of younger patients opting for GK for their medically intractable TN. Fortunately, there is evidence to suggest that MVD is still a relatively safe option for the younger patients whose pain recurs after GK or other previous invasive therapies20,21. Early studies of GK in patients with previous invasive therapies of their TN suggest that it is not as efficacious as in it first application but still a good treatment option. Twenty percent of the patients who undergo salvage GK therapy are pain free at 5 years and another 40% have significant pain control18, 19. Hence,TN that is resistant to one modality of invasive therapy may be either addressed through another modality or a repeat posterior fossa exploration with either MVD or partial rhizotomy, depending on the patient's age and relative health 17-20.

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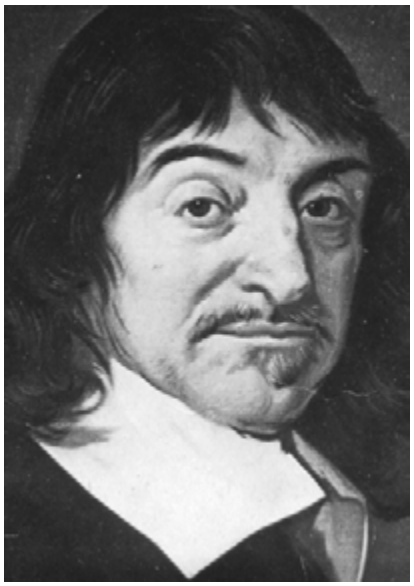

Do you know this man?

The answer will be on page 18.

A STORY OF HYPOGLYCEMIA

By Rubina Aqeel MD FACE

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It was a busy Thursday afternoon. This 20 year old youth had a mental age of 6 years and Diabetes Type I. His blood sugar was difficult to control most of times. But in the last few months, it has become even harder. Mathew's (not real name) blood sugars seemed to be higher in the day. And any time his father increased the dosage of his intermediate acting insulin, he became hypoglycemic at night. Mathew would wake up his father: "Dad, something is not right!" and his sugar was as low as 30. His father and I decided to keep his blood sugars on the higher side for the next few weeks till we figured out what to do. I was just talking to the Dad about how to go about this when Angie knocked on the door, There was a call from the ER. I excused myself and took the call. A young girl had been brought in by paramedics after a seizure. Apparently family members noticed she was acting weird and then she had a seizure. Her blood sugar in the field was 25 mg/dl. After receiving two amps of D50, her blood sugar was 60 mg/dl. After discussion with the ER physician, we decided to continue IV fluids with D10 infusion and I promised to be there as soon as possible. An appointment was made for Marthew, his insulin doses were rechecked and I walked over to the ED.

Jenny (not real name) was 19 years old, awake and alert. She said she had never had any problems before.. She had recently started a new job. The last time she saw a doctor was for a routine pap and birth control pills .That was the only medication she was taking. Physical exam was equally fruitless. On the next day, her blood sugars started to go up. Fasting glucose was over 200 mg/dl. D10 infusion was stopped . C-peptide insulin and Proinsulin levels had been ordered when her blood sugar was low. She was discharged with no cause of the hypoglycemia identified. Dr Williams called me one week later, Jenny was in his office." This girl is continuing to have low blood sugar. I gave her a meter, they are as low as 60, she has to eat all the time and even after eating, her sugar goes up only to a 100mg/dl. You are the endocrinologist, please do something". "Send Jenny to my office right away!" I said. Twenty minutes later, she was in my office and sweating profusely, Fingerstick check showed 55 mg/dl. I gave her glucagon and glucose gel and arranged for admission right away.

Lab work showed that C-peptide and Glucose were normal. Insulin and proinsulin levels were normal as well. Retaking of the history reveals only recurrent hypoglycemia at any time, no predicting factors can be identified. She has no family history of diabetes. She lived with her boyfriend. She was crying, " How can I do my job? They are going to fire me!" D10 infusion was started, Work up included CT scan, MRI and X-rays. Two days went by; Patient was off D10 and was started on regular diet with blood sugars being wonderfully normal. The case manager told me that this patient did not meet criteria for inpatient stay. The patient said with tears: " Please discharge me, I have to go back to my job, or they will hire someone else.". She promised to have all the work done as an outpatient.

She was back in my office two days later; with blood sugar in the 60 to40 mg/dl. She worried about losing her job. " What kind of work do you do?" " I look after a child. They gave me time off from work because the kid's parents were home today." I discussed with Jenny about foods she ate and we talked about modifying her diet. She promises to keep the appointment for CT Scan. I opened the door and we walked out together to the reception desk. Mathew was coming in with his Dad.' Hi Jenny' Mathew gasped. I looked at Mathew's Dad. He was looking askance. Jenny disappeared before scheduling next appointment. Mathew came in and then his dad said that she wanted to go to the DMV. She was the caretaker for Mathew during the day. She had been taught to give Mathew insulin.

I did not see Jenny since then. She was obviously fired from her job. She has not been back to see Dr. Williams either.

Jenny had been taking Mathew's insulin.

A 45 year old Hispanic male was admitted with change in conscious level, having being brought in by paramedics after his wife called 911. Blood sugar in the field was 20 mg/dl. After D50 was given, it went up to 40 mg/dl. He was admitted to telemetry unit and was put on a D10 infusion. Blood sugars were checked every four hours and results were as low as 40 mg/dl. D50 had to be given almost every four hours. After 2 days of this I was asked to see the patient. His name was Jose (not his real name). He started out by telling me that he did not speak English, but he could understand a few words when I tried my bad Spanish. All of the symptoms had started 3 weeks ago, with lethargy, slurring of speech and feeling tired. Symptoms were relieved by eating. There was an immediate effect. He was now eating all the time and had gained 5-10 pounds. 911 was called because he was so lethargic that he could not even swallow. Past history was significant only for dyspepsia for which he had taken Zantac over the counter. There was history of Diabetes in the family. Till the last week he had been working as a mechanic. He had no pain anywhere and no other symptoms. Physical exam was normal except for a blood pressure of 130/90. Work up for hypoglycemia was ordered. Over the next week he had multiple blood tests, CT scans and X Rays. He continued to require D10 infusion. On every occasion I went to see the patient, the wife was at the bedside worried with a lot of questions, but he had no questions. One week went by, I reviewed his chart, all labs were not back yet, I found it strange that he had no questions or concerns and accepted any test ordered without hesitation. The medical students were concerned about his diagnosis. Insulinoma was considered and referral to a tertiary center was planned. I took the nursing supervisor aside and requested we search the bedside table. She was not sure if it was legal. On the day of transfer the Endocrinologist from the tertiary center called me: ". Dr. Aqeel, your patient's urine screen is positive!" Well, it looked like the tertiary center was able to get the drug tests done earlier than me. The patient was confronted, he was very upset and told us he had been taking his wife's medication, which was Glyburide. He asked us not to tell his wife and he promised not to take the medication anymore. A Psych consult was requested, but before he could be seen he left the hospital without telling anyone. The story does not end here.

One month later I was asked to consult on a patient with hypoglycemia in another hospital who had came through the ER. He was now in telemetry, Low and behold it was Jose. At first he failed to recognize me. Since his leaving the other hospital he had been on disability .Again his wife was tearful and full of questions.

"So he did not tell you the diagnosis?" I asked. She said what is going on." He has been taking your medications." She looked at her husband , he looked the other way. She was extremely angry. The patient's hypoglycemia now resolved and we were able to send him home.

Six months later he was admitted to the first hospital again with hypoglycemia. This time he had lost his insurance, his job and even his wife. We rightly made a diagnosis of Fictitious Hypoglycemia. But, before any investigation could be made about how he got the sulfonylurea, he left the hospital.

Fictitious Hypoglycemia

Hypoglycemia is defined as a low plasma glucose. In men 45-50 mg/dl and in women 35-45mg/dl.

The symptoms of hypoglycemia should improve on administration of carbohydrates, confirming the diagnosis. Hypoglycemia is a potentially fatal condition. Fictitious hypoglycemia is a psychiatric disorder in which a patient deliberately causes hypoglycemia by insulin or sulfonylurea abuse. This condition is more common in women. It is also more common in healthy professionals.

Biochemically, Sulfonylurea-induced Hypoglycemia is indistinguishable from Insulinoma.

It is difficult to prove the cause to be insulin in a hypoglycemic patient who has injected insulin on purpose. Insulin levels are difficult to interpret .Insulin antibodies once thought to be useful are now considered non diagnostic.

Assessment of these patients should be carried out in the following stages:

Stage 1:

Documentation of hypoglycemia.

Stage 2:

Draw blood levels for C-peptide, Insulin, Insulin antibodies, Proinsulin, Glucose and Sulfonylurea at the time of symptomatic hypoglycemia. At the same time, an urinary Sulfonylurea level should be checked as well.

Stage 3:

Retaking of history if no cause of Hypoglycemia can be identified.

Stage 4:

Searching of patient's room and belongings

Stage 5:

Confrontation and psychiatric evaluation.

Documentation of hypoglycemia can initially seem very easy. Many times patients will have been treated for symptoms before a blood is drawn. For proper documentation and treatment and for safety purposes, patients may need to be admitted to a telemetry unit.

Blood levels have to be drawn at the appropriate time and without delay, so that treatment of hypoglycemia can be initiated without delay.

Retaking of history is important as some things may not be apparent in the initial history taking. In the second case, the patient initially denied family history of Diabetes.

Searching of the patient's room may seem drastic. Insulin induced hypoglycemia is very difficult to diagnose and it may take more then drastic measures to find the source.

These patients are depressed and they need psychiatric evaluation and care after diagnosis. They could be classified as a type of Munchausen's syndrome. Munchausen's syndrome is a condition which the sufferers describe previous histories that are dramatic but are not true. Such patients may undergo multiple procedures and unnecessary investigations before the untruths are revealed at that point the patient may consult a new doctor or go to another hospital.

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A REVIEW OF HUMAN PAPILLOMA VIRUS AND ITS VACCINES

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In one of the more elegant triumphs of virology, the oncogenetic role of several viruses has been appreciated over the last few decades (1). Ebstein Barr virus has been implicated in Burkitt's lymphoma, same as Hepatitis B and C viruses in hepatocellular carcinoma and Human Herpes Virus 8 in Kaposi's Sarcoma. The commonest potentially preventable infection induced cancer, however, is cervical cancer. This is caused by Human Papilloma Virus(HPV) which has many strains. In summary, HPV types 16 and 18 cause about 70% of cervical cancers and HPV types 6 and 11 cause approximately 90 percent of genital warts. We are now aware that HPV is the most common sexually transmitted infection in the United States. Nevertheless, the sheer magnitude of the numbers is astounding.

The Centers for Disease Control and Prevention estimates that over HALF of all sexually active men and women become infected at some time in their lives. On average, this leads to 11,000 new cases of cervical cancer and 3,700 deaths in the United States each year. Worldwide, cervical cancer is the second most common cancer in women; and is estimated to cause over 470,000 new cases and 233,000 deaths each year. Calculating the attributable fraction of HPV as a causative agent for cancer, Parkin (1) estimated that HPV is responsible for 5.2% of the world cancer burden, making it one of the most important infectious causes of cancer.

The immune response to HPV has been studied in some detail (2). The host immune system usually clears the virus and most infected women do not develop chronic disease. The "high risk" HPV types that induce cervical carcinoma, mainly HPV16 and HPV18, multiply in the superficial layers of the epidermis. These viruses encode two oncogenic proteins E6 and E7, which alter the normal proliferative control of the host cell by interfering with regulatory proteins of the cell cycle. This leads to induction of malignant clones. . Cellular immunity to HPV is implicated as an important factor in cervical carcinogenesis. The antibody response to HPV, on the other hand, has been shown to mediate type-specific protective immunity. This forms the basis for prophylactic vaccination as a means of preventing infection and resultant cancer .

Two recombinant vaccines developed against HPV have been approved by the FDA. I will review relevant clinical aspects of these vaccines for the Primary care doctor.

The Merck vaccine is marketed as GARDASIL. It is a recombinant and therefore non-infectious, quadrivalent vaccine prepared from the highly purified virus-like particles (VLPs) of the major capsid (L1) protein of HPV Types 6, 11, 16, and 18. The evidence for the efficacy of the vaccine is based on data from four studies, one in the United States and three multinational. These enrolled 21,000 women and were placebo controlled trials. Of note, the study period was not long enough for cervical cancer to develop. Instead the prevention of cervical precancerous lesions was believed to be a surrogate marker of cancer prevention.

Glaxo Smith Kline markets another HPV vaccine under the trade name of Cervarix. This is a bivalent vaccine with efficacy against HPV 16 and 18

Studies showed that in women who had not already been infected, Gardasil was nearly 100 percent effective in preventing precancerous cervical lesions, precancerous vaginal and vulvar lesions, and genital warts caused by infection with the HPV types against which the vaccine is directed.

Immunization with HPV vaccines should prevent most cases of cervical cancer due to HPV types included in the vaccine. However, two aspects need to be highlighted. First, females are not protected if they have been infected with the HPV type(s) that cause cancer or warts prior to vaccination. This suggests

that immunization should be administered before any potential exposure. CDC recommends vaccinating at the pre teen stage. Second, Gardasil will not protect against the HPV types not included in the vaccine. Therefore, routine pap screening remain critically important even in the vaccine era.

The studies also looked at whether the vaccine can protect women already infected with some HPV types included in the vaccine from developing diseases related to those viruses. There was no benefit in this particular situation.

Two studies were also performed to measure the immune response to the vaccine among younger females aged 9-15 years. This can be used to predict efficacy of the vaccine in this age group. The antibody responses were found to be equivalent to the 16-26 year age group. The duration of antibody response probably needs more study as does the role of booster doses. Antibody titers decline over time after the third dose, but plateau by 18 months, remaining higher than those after natural infection for several years.

The safety of the vaccine was evaluated in approximately 11,000 individuals who received the product. Most adverse experiences in study participants who received Gardasil included mild or moderate local reactions, such as pain or tenderness at the site of injection. To date, over 16 million doses of Gardasil have been distributed in the United States. As of June 30, 2008, there have been 9,749 VAERS reports of adverse events following Gardasil vaccination. Of these, 94% were classified as reports of non-serious events, and 6% as serious events. Upon review, none of these were related to Gardasil. Cervarix has a similar safety profile (3).

Unresolved aspects of the HPV story include the role of vaccination males who, after all, are the vectors of spread of infection in this situation. Studies are underway but given the low cancer rates from HPV in males, this is a lower priority field of enquiry. Future vaccine strains may have a wider type specificity of HPV strains(analogous to the newer 23 valent Pneumococcal vaccine versus the previous version).

A major point of discussion is over funding for the vaccine. The 3 dose series is expected to cost around $360 and may be prohibitive for lower income Americans. There are concerns that the existence of the vaccine could lead to sexual 'disinhibition'- a euphemism for promiscuity. There is no evidence to support this line of thought. There used to concerns that there would be increased sexual risk taking if penicillin were used to treat syphilis. And that the use of anesthesia in childbirth would lead to increased sex within marriage .Today, HPV vaccination is being discussed along with condom provision and needle exchange programs as a factor that alters social norms.

We can argue these points forever. The undeniable fact is that , for the first time in human history, we have a means to prevent a devastating cancer that has destroyed countless lives. Ask a patient and they will put the debate in perspective for us.

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FOXGLOVE (DIGITALIS PURPUREA L.):
History and Toxicity

By Donald G. Barceloux M.D.

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The paw of the fox inside the flower.

Digitalis Flower (Foxglove)

History

Welsh writings from the 13th century indicate that foxglove was known to herbalist of that time; some medieval herbalist of Germany and England from the 16th and 17th centuries recommended the medical use of purple foxglove (Digitalis purpurea L.). The use of the cardiac glycosides in foxglove specifically for edema secondary to cardiac decompensation (dropsy) was not reported in the modern medical literature until 1785, when William Withering (1741–1799) published the first scientific treatise on foxglove as a diuretic, An Account of the Foxglove, and Some of its Medical Uses: with Practical Remarks on Dropsy, and Other Diseases. This small book contained 207 pages with 169 pages devoted to a description of 219 cases treated with foxglove that were collected over 10 years. These patients had been treated with a variety of diuretics of the time including the dried fleshy bulb of Urginea maritima (i.e., also contains cardiac glycosides), cathartics, calomel (mercury chloride), gum ammoniac (resin extruded from Dorema ammoniacum D. Don after a beetle infestation), ipecac (i.e., a cardiotoxin following chronic use), opium, antimony, bloodletting, and a variety of other remedies. A majority, but not all of these patients received foxglove as an aqueous medication (decoction). Toxic effects noted by Withering in his treatise included nausea, vomiting, confusion, green vision, and slow pulse. By the 8th year of this study (1783), digitalis was added to the Edinburgh Pharmacopoeia.

William Withering was born in the Midlands of England near Birmingham as the only son of an apothecary. After a home education, he was an apprentice to his father for 4 years before entering medical school at the University of Edinburgh in 1762. As a result of his extensive botanical knowledge, William Withering identified purple foxglove as the principal ingredient in the herbal preparation of a local herbalist that was used to treat congestive heart failure (dropsy) in 1775. Erasmus Darwin, the grandfather of Charles Darwin, consulted Withering about the use of foxglove for treating a patient for dropsy in 1776. The patient improved; three years later, Erasmus' eldest son died before completing his doctoral dissertation at Edinburgh. Erasmus posthumously added details of his use of foxglove to his son's dissertation while attributing the use of digitalis to his son rather than Withering. Withering was furious, strongly objecting to Erasmus' claim; these two men subsequently became antagonists with Erasmus publishing his own descriptions of the use of foxglove for dropsy in a publication by the Royal College of Physicians that did not mention Withering.

Withering attributed the effectiveness of foxglove for the treatment of congestive heart failure to diuresis, although he did believe that "this herb had a power over the motion of the heart to a degree yet unobserved in any other medicine…." By 1799, John Ferriar recognized that the diuresis associated with the ingestion of foxglove resulted from the effect of the plant constituents on the heart; however, for almost a century after the publishing of Withering's treatise, diuresis was the primary cardiac use of foxglove. Other uses of this herb included the treatment of delirium tremens, epilepsy, fevers, migraine, tuberculosis, and paralysis associated with "insanity."

In 1930, Dr. Sydney Smith at Burroughs Wellcome in England isolated a similar cardiac glycoside, digoxin from a different foxglove species, Digitalis lanata L. After World War II, the Dutch cultivated this foxglove on a large scale as a source of digoxin; in the United States, digoxin rather than digitoxin from foxglove (Digitalis leaf) became the dominant cardiac glycoside.

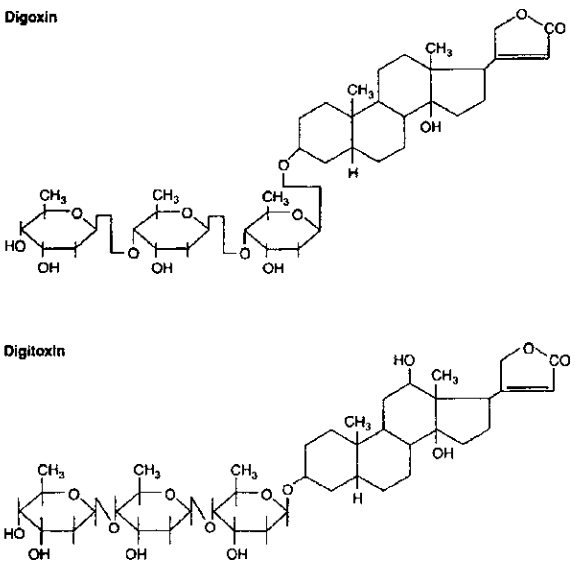
Exposure

There are several species of foxglove in the United States including Digitalis grandiflora Mill. (yellow foxglove), Digitalis lanata (wooly or Grecian foxglove), and Digitalis purpurea L. (purple foxglove). The latter is the common ornamental foxglove present in California. The name Digitalis is an allusion to the German word, fingerhut, which refers to the resemblance of the blossoms to fingers of a glove. This beautiful biennial herb has simple toothed leaves and a tall, central stalk of purple and white tubular flowers that typically appear June to July. The purple foxglove is native to Western Europe, the Mediterranean region, and northwest Africa along with the Grecian foxglove. Misidentification of foxglove for comfrey leaves (Symphytum species) in an herbal tea and for common borage (Borago officinalis L.) in potato dumplings resulted in digitalis poisoning. , Digitalis leaf is obtained for medicinal use by the grinding and milling of D. purpurea leaves; the main botanical source of digoxin is Digitalis lanata Ehrh., which contains primarily digoxin rather than digitoxin (12βhydroxydigoxin). The bitter taste of foxglove usually limits the ingestion of these leaves.

Principal Toxin

Cardenolides are cardioactive steroids with a 5-membered lactone ring. The substitution of a sugar residue for a 3βOH group on the cardenolide produces a cardiac glycoside (digitoxin, digoxin). Each cardiac glycoside is a combination of an aglycone or genin (e.g., digoxigenin, digitoxigenin) and one to four molecules of a sugar (e.g., digitoxose or 2,6-dideoxyhexose). Foxglove contains a number of cardiac glycosides, the most prominent of which is digitoxin. Although the chemical structure of digitoxin (12βhydroxydigoxin) and digoxin are similar, digitoxin is substantially more lipid soluble than digoxin. Consequently, digitoxin has a higher bioavailability, longer elimination half-life, and larger volume of distribution. Figure 1 displays the chemical structures of digitoxin and digoxin.

Fig 1. Chemical Structure of Digitoxin and Digoxin.



D. purpurea contains primary glycosides including purpurea glycoside A, purpurea glycoside B, glucogitaloxin, and digitalinum verum. The plant enzyme, digipurpidase, transforms these primary glycosides into the corresponding secondary glycosides (digitoxin, gitoxin, gitaloxin, and strospeside, respectively). The mean concentration of purpurea glycoside A, purpurea glycoside B, and glucogitaloxin in dry leaf powder from D. purpurea was about 0.74 µg/mg, 0.39 µg/mg, and 1.91 µg/mg, respectively, as measured by high performance liquid chromatography (HPLC).The cardenolide content of foxglove plants varies with a variety of conditions including location, environmental/growing conditions, and strain.

Toxicokinetics

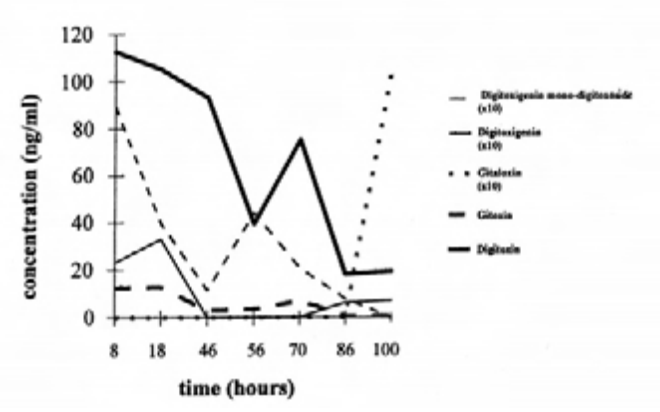


Figure 2: Serum concentrations of major cardiac glycosides in a patient with foxglove intoxication. (From Reference 9)

The cardiac glycosides of D. purpurea are hydrolyzed to digitoxin, gitoxin, and gitalin with only minor amounts of digoxin formed from hepatic metabolism. Hence, D. purpurea toxicity may be prolonged because of the long serum half-life of digitoxin (4–5 days). The serum half-life of digitoxin is about 4 times longer than digoxin. Digitoxin undergoes metabolism to digitoxigenin, digitoxigenin mono-digitoxoside, and gitoxin.

Pathophysiology

Digitoxin and digoxin along with other cardiac glycosides are potent and specific inhibitors of the intrinsic membrane protein Na+K+-ATPase. The molecular target is the βsubunit of sarcolemmal Na+K+-ATPase (sodium pump) that occurs on most eukaryotic cell membranes. This enzyme couples the hydrolysis of high-energy ATP phosphate to membrane ion translocation, resulting in the maintenance of the sodium and potassium gradients. The mechanism of digitalis-induced positive inotropy involves alteration of the balance between intracellular Na+ and Ca++ . Dysrhythmias result from the combination of direct effects on the myocardium and neurally mediated increases in automaticity. No dysrhythmia is pathognomonic of digitalis toxicity; however, the combination of enhanced automaticity and impaired conduction (e.g., AV block with accelerated junction pacemaker resulting in regularization of rapid atrial fibrillation) is highly suggestive. Dysrhythmias not usually associated with digitalis poisoning include supraventricular tachycardia with a rapid ventricular response and Mobitz type II AV block (i.e., site of block below the AV node). Mobitz type I block usually results from intranodal dysfunction.

Clinical Response

Foxglove toxicity resembles oleander and digitoxin poisoning; serious toxicity primarily results from the ingestion of herbal teas steeped in foxglove leaves. Two fatalities resulted from the ingestion of foxglove tea—an elderly woman, who was dead on arrival, and her husband, who died of refractory ventricular fibrillation 17 hours after admission. Gastrointestinal symptoms develop within several hours and are followed by changes in sensorium (e.g., confusion), cardiac conduction defects, bradycardia, hyperkalemia, and ventricular dysrhythmias depending on the severity of the poisoning. Visual disturbances (e.g., yellow haloes) are classic symptoms of Digitalis leaf poisoning; these visual changes do not usually occur following intoxication with pharmaceutical preparations of digoxin. The toxic effects of foxglove are usually prolonged (i.e., days) because of the long half-life of digitoxin compared with digoxin. Ventricular tachycardia, junctional rhythms, and atrial fibrillation with high-grade atrioventricular block persisted 6 days after the ingestion of foxglove tea. In another case report, confusion and visual disturbances lasted 5 days and electrocardiogram (ECG) changes resolved by the 10th day.5

Diagnostic Testing

Elevated serum digitoxin concentrations confirm the ingestion of digitalis-like compounds (in the absence of simultaneous consumption of Digitalis preparations), but digitoxin or digoxin concentrations do not necessarily guide management because of variable cross-reactivity with other cardiac glycosides in foxglove. During serious foxglove intoxication, serum digoxin is usually detectable, but the serum digoxin (or digitoxin) concentration does not correlated to the severity of toxicity. The serum potassium is a good measure of the effect of Digitalis compounds on the sodium/potassium pump. The presence of hyperkalemia indicates serious digitalis poisoning.

Treatment

Management of intoxication with foxglove is similar to the management of oleander and digoxin poisoning. Gut decontamination measures are usually unnecessary. The administration of activated charcoal to alert patients is a therapeutic option, when the patient ingests large amounts of foxglove less than 1 hour prior to presentation; however, there are no clinical data to indicate that activated charcoal improves the outcome of patients with foxglove intoxication. The efficacy of digoxin Fab fragments in foxglove intoxication has not been established. Although the use of digoxin Fab fragments is a therapeutic option, particularly for seriously intoxicated patients, foxglove contain several cardiac glycosides other than digoxin. Some transient improvement in rhythm disturbances in patient with foxglove poisoning may occur following the use of this antidote; however, the use of digoxin-specific Fab fragments does not consistently reversed or shorten by the course of foxglove intoxication.11

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I AM WHO I AM

The answer will be on page 25.

ABOUT BREAST IMAGING

By Patrick Bryan, M.D.

Breast cancer is the second most common cause of cancer death in women, after lung cancer. Over the past 20 years the death rate from breast cancer has dropped by 15%, due mainly to early diagnosis when the cancer is small and is curable.

Mammography

Screening mammography is almost entirely responsible for the improved prognosis for breast cancer. Film-screen mammography has been the standard technique. It produces high-resolution images at relatively low radiation doses. There was concern early on that the radiation exposure from mammography could cause more cancers than it cures, but it has become clear that that is not the case, and it is highly likely that mammography does not cause excess cancer. The main mammographic findings in malignancy are irregular masses, microcalcifications and architectural distortion.

In the last few years, digital mammography has become available and is rapidly replacing film-screen mammography. Digital mammography is superior to film-screen in patients with dense breast parenchyma. Younger women tend to have dense breasts and should have digital mammograms, if available. Dense breasts are at higher risk for developing cancer, which makes it all the more important that the superior digital technology be used to screen them. Tomosynthesis, which has not yet been approved by the FDA, may prove even more useful in detecting cancers in dense breasts.

There has been controversy recently about the recommendation of the U.S. Preventative Services Task Force that routine screening mammography not begin until age 50 and that the intervals between mammograms be two years instead of the present recommendation by the American Cancer Society of annual screening mammography beginning at age 40.

One of the reasons for the controversy is that breast cancer tends to be more aggressive in women in their forties, although it is less common than in later decades. It is estimated that pre-clinical breast cancer has a 16% chance of spreading to lymph nodes in a woman in her 40's vs. 7% for a woman in her 50's, and 5% for a woman in her 60's. It therefore seems reasonable that women in their 40's should have annual mammograms whereas older women might adequately be screened at 2 year intervals. For women over 75, the decision to do screening mammography should be based on overall health and life expectancy.

The downside of screening mammography is considered to be overdiagnosis. To mitigate this downside, biopsy of suspicious lesions should be done by core needle biopsy guided by mammography (stereotactic), by ultrasonography, or by MRI, depending on which modality best identifies the lesion. The preferable image guidance is by ultrasound in the lesion is sonographically visible; stereotactic biopsy is the next most preferable, especially for microcalcifications, and MRI guided biopsy should be reserved for those lesions which are only visible on MRI.

Mammographic features of breast cancers can have great prognostic significance. Tabar and Dean, in a review of thirty years experience with mammography screening state that mammographically detected cancers less than 15mm is diameter are usually curable by surgery alone and do not require chemotherapy or radiation therapy. An exception is tumors with casting-type calcifications, which have a much worse prognosis.

Ultrasound

At one time it was thought that the role of ultrasound was to determine whether a mass was solid or cystic. Major improvements in ultrasound technology over the past two decades have produced scanners with markedly improved resolution and better tissue characterization. Ultrasound evaluation of a mammographically or clinically detected mass can, in addition to determining whether it is cystic or solid, show whether it has features typical of benign masses (smooth margins, orientation parallel to the skin, homogeneous

echogenicity, good through transmission of sound) or features suspicious for malignancy (irregular margins, spiculation, orientation perpendicular to the skin and poor transmission of sound). Ultrasonography is often superior to mammography in patients with dense breasts, and several breast imagers have recommended that ultrasound screening be done in addition to, or even instead of mammography in patients with very dense breasts. Ultrasound, however, is not nearly as good as mammography in detecting microcalcifications.

Ultrasound is the preferred modality for guiding needle biopsies if the mass is clearly visible, as it samples the mass, and causes much less discomfort for the patients as she is lying supine, not prone, and no breast compression is necessary.

MRI

Over the past decade breast MRI has come into widespread use. It was initially used mainly to evaluate breast implants for possible rupture.

In recent years contrast-enhanced MRI is used to detect breast cancer. Specialized breast coils are used and the breasts are scanned prior to administration of gadolinium. A bolus injection of gadolinium is then given and T1 weighted scans are performed at one minute intervals for six minutes. A program of computer aided detection is applied to the data and areas of increased vascularitiy are highlighted in color. A time-intensity curve is generated which shows how quickly a suspicious area takes up the contrast and whether contrast uptake continues throughout the study (benign pattern), or whether it plateaus (equivocal), or there is washout (malignant pattern).

MRI is very sensitive in detecting malignant lesions, but it has a lot of false positives. Lymph nodes and foci of fat necrosis are normally vascular and often have a washout of contrast on the time-intensity curve. MRI can also have false negative results, especially in ductal carcinoma in situ and in lobular carcinoma. Morphologic criteria are applied to a mass as with ultrasound and mammography. If a questionable mass has morphologic features of a lymph node then biopsy need not be done.

Indications for MRI include detection of synchronous tumors in newly diagnosed carcinoma, either in the same breast or in the opposite breast; also to detect tumor recurrence or response to treatment. MRI can be used as a screening tool in patients with dense breast parenchyma, but it is too expensive to use it in the general normal risk population. The American Cancer Society recommends its use in high-risk women (those with greater than 25% lifetime risk of developing breast cancer). This includes women with positive BRCA genes and those with a strong family history of breast or ovarian cancer.

When a suspicious mass is found on MRI it needs to be biopsied. Usually when a suspicious mass is found, the breast is scanned or re-scanned with ultrasound with attention to the area in question. If the mass is found with ultrasonography then ultrasound-guided core needle biopsy is done. If it cannot be seen, then MRI-guided biopsy must be done.

ANSWER

Rene Descartes

This French mathematician, philosophher and physiologist (1596-1650), thought that the pineal gland is the connection of soul and body. His theory of interaction between mind and body had significant contribution to human psychology.

'THE ENEMY OF MY ENEMY IS MY FRIEND':
The Potential of Phage Therapy

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Almost all clinicians would agree that we face an imminent crisis in the treatment of bacterial infections. Resistance has already emerged against every known class of antibiotics, and resistant strains are becoming increasingly common. For example, methicillin-resistant S. aureus (MRSA), vancomycin-resistant enterococcus (VRE), and XDR-TB (extreme drug-resistant tubercle bacillus) are encountered in both hospital and community settings in the U.S. Antibiotics place strong selective pressure on bacteria, leading to the rapid spread of genes encoding drug resistance. Despite our best efforts to optimize antibiotic therapy, many scientists and physicians believe that virulent strains will acquire resistance to all known antibiotics within our lifetime. One promising alternative to antibiotics is 'phage therapy'.

Bacteriophages (literally, 'bacteria-eater') are viruses that infect bacteria. These viruses (also called 'phages') have co-evolved with their bacterial hosts for millions of years. Infection of a bacterium may result in cell death and lysis, or infection may simply decrease the reproductive rate of the host. Phages were discovered independently by a British scientist, Frederick Twort (1915), and a French microbiologist, Felix d'Herelle (1917). One of d'Herelle's first ideas was to use phages to kill pathogenic bacteria and thus treat bacterial infections. However, early efforts in phage therapy were hampered by a lack of understanding of phages, which led to the use of contaminated preparations as well as problems with experimental rigor. When Alexander Fleming discovered penicillin in 1928, the medical

establishment quickly turned toward small molecule antibiotics, with great success, and interest in phage therapy waned in western countries. Phage therapy continued to be practiced elsewhere, although clinical studies of efficacy conforming to western standards were not conducted. However, in light of the current rise of resistance to antibiotics, interest in phage therapy has recently resurged. In this article we discuss questions that clinicians might have regarding phages and their potential use to combat bacterial infections.

How do phages infect bacteria?

Phages vary in the details of the mechanism of infection, but in general they follow a pattern similar to eukaryotic viruses: 1) association of the phage to a cell surface receptor, 2) injection of genetic material into the host cell, 3) replication of phage genome and production of phage proteins, 4) assembly and release of progeny phage, possibly through cell lysis or by extrusion. Lysogenic phages can also integrate into the host chromosome, where they remain latent until environmental conditions trigger release.

Where are phages found in nature?

Phages are very abundant in the environment, typically outnumbering bacteria by a factor of 10 or more (Abedon, 2008). They are generally found wherever bacteria exist (e.g., ocean, soil, feces). Many of the well-studied phages that infect E. coli were isolated from sewage. A study of cholera phage in Bangladesh showed that the presence of Vibrio cholerae phage in environmental water samples was inversely correlated with the incidence of cholera, suggesting that phage may play an important role in regulating the abundance of pathogenic bacteria (Jensen et al., 2006).

Could bacteria evolve resistance to phages?

Phages and bacteria have been evolving together in an evolutionary 'arms race'. While bacteria can evolve resistance to a particular phage, the phage can also evolve to counter bacterial resistance. Recent work demonstrates this arms race during experimental evolution of Pseudomonas fluorescens and its phage Φ2 (Paterson et al., 2010). The potential for evolutionary adaptation is believed to be a major advantage of phage therapy compared with traditional antibiotics, which are modified through the much slower and labor-intensive process of medicinal chemistry.

Are phages bacteriostatic or bacteriocidal?

Lytic phages kill the host cell outright, while other phages reduce the reproductive rate of the bacteria by consuming host resources. (Non-lytic phages could reduce bacterial growth and thus help a patient's immune system clear the infection, although they might not be suitable for immunocompromised patients.) Phages can also be genetically engineered to carry toxic genes for a particular therapeutic application. One ingenious example is the development of phages capable of digesting biofilms (Lu & Collins, 2007), suggesting that phages might be useful for disrupting infections on surfaces. Another strategy is to use the genomes of phages as a source of lytic enzymes that could kill bacteria (Fischetti, 2008), which has shown some success in animal models (Loeffler et al., 2001).

Could phages harm normal bacteria flora or even infect humans?

Because phages are usually highly specific for their bacterial host organism, phage therapy should be, in principle, relatively free from side effects associated with disruption of normal bacterial flora. The possibility for other side effects (e.g., allergic reactions, kidney or liver toxicity) must be evaluated. It is unlikely that phages would evolve to infect humans, given the substantial physiological differences between human and bacterial cells, although this possibility cannot be ruled out. However, it is reassuring that phages already co-exist with bacteria and humans (e.g., in the GI tract).

How might phages be administered?

One straightforward route of administration is topical. There is anecdotal evidence that bandages impregnated with phages were effective against foot ulcers that were refractive to antibiotic therapy (Markoishvili et al., 2002). Treatment of foodstuffs for preventing diarrheal disease is also a straightforward goal; for example, a phage cocktail targeting Listeria has been approved by the FDA for use on ready-to-eat foods (LMP-102, Intralytix). On the other hand, clearance by the human immune system presents a serious challenge to phage therapy for systemic infections, although some research suggests that it may be possible to circumvent this problem by genetically engineering the phage (Merril et al., 1996; Thiel, 2004).

Could phages transfer virulence factors among bacterial pathogens?

Lysogenic phages can transfer genes among host organisms during chromosomal integration. This class of phages is probably unsuitable for phage therapy. Regardless, horizontal transfer of DNA, usually by phages or plasmids, has been a major evolutionary mechanism in bacteria. Because of the existing natural prevalence of this mechanism, many experts believe that the contribution of phage therapy to horizontal gene transfer would be relatively small.

How close is phage therapy to a reality?

Phages are used clinically in former Soviet bloc countries, especially at the Eliava Institute in Tbilisi, Georgia, although rigorous clinical trials have not been performed yet. Several companies have taken an interest in bringing this technology to the U.S. (e.g., Intralytix, Exponential Biotherapies, GangaGen). There may also be regulatory hurdles with phages, especially cocktails, but the FDA approval of LMP-102 demonstrates that these issues can be successfully addressed.

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HEPATIC ARTERY CHEMOEMBOLIZATION

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Introduction

Hepatic artery chemoembolization has been developed to treat the malignant tumor involving the liver, such as carcinoid tumor, hepatocellular carcinoma, or metastatic melanoma of the liver.

The unique vascular perfusion system of the liver makes this treatment modality possible for the liver cancers.

Unlike other organs, the liver is unique because it has two blood supplies—the hepatic artery and the portal vein. The normal liver receives about 75 percent of its blood supply through the portal vein and only 25 percent through the hepatic artery. But when a tumor grows in the liver, it receives more than 95% of its blood supply from the hepatic artery (Fig 1).

Therefore, clamping the hepatic artery will not result in liver necrosis because of the portal venous perfusion to the normal hepatic cells.

Chemoembolization combines hepatic artery embolization with simultaneous infusion of a concentrated dose of chemotherapeutic drugs through a catheter placed by selective hepatic artery catheterization.

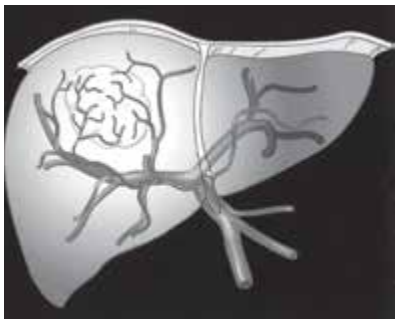

Fig 1.
Dual blood supply to normal liver.

Tumor receives blood exclusively from hepatic artery.

Embolic materials used for this procedure include Gelform, Polyvinyl particles (Ivalon) or Collagen. Also an oily material (Lipiodol) is often used along with the embolic materials for the patients with hepatoma as it has the embolic property and retains in the hepatoma tumor. It is believed that Kupffer cells, the specialized macrophages in the normal liver clear the Lidiodol while the tumor not having the Kupffer cells cannot clear the oily Lipiodol, thus resulting in retention of the Lipiodol in the tumor. The chemotherapeutic drugs mixed with Lipiodol can stay in the hepatoma for a long period of time providing cytotoxic effects in the tumor. The Lipiodol also compromises tumor vascular circulation.

Most patients experience some side effects after chemoembolization. This is called post-embolization syndrome and consists of pain, nausea, vomiting and fever.

Due to the injury to the liver cells associated with embolization, certain metabolic and electrolytes imbalance such as hyperkalemia, hyperphosphatemia or hypomagnesaemia can occur (1).

Pain is the most common side effect and occurs because the blood supply to the treated area is cut off. It can readily be controlled by oral or intravenous medication. Most patients leave the hospital within 2-3 days of the procedure, after their pain and nausea have subsided.

Majority of patients with hepatocellular carcinoma have concurrent liver cirrhosis due to chronic hepatitis or alcoholic liver disease. Therefore, patients with severe hepatic insufficiency (Child-Pugh Score C), portal vein obstruction and renal dysfunction (due to contrast injection during the procedure) are excluded.

Case Study 1

A 66 year-old Caucasian man with a history of chronic hepatitis C and liver cirrhosis developed abdominal discomfort which prompted CT scan of the abdomen. It showed the primary tumor measuring about 9 x 8 cm along with multiple small satellite lesion in the right lobe as well as several enlarged preceliac lymph nodes.

CT guided biopsy of the tumor was done and pathology revealed hepatocellular carcinoma. Past medical history includes TIPS (Transjugular Intrahepatic Portosystemic Shunt) for portal hypertension in 1994 with good clinical improvement of ascites and esophageal varices. Laboratory tests before chemoembolization found that the liver function was not severely compromised; alkaline phosphatase 270 IU/L, SGOT and SGPT 45 and 76 IU/L respectively, albumin 3.7 g/dL, Protime 12.8 seconds with INR 1.25, WBC 4.5 k/uL, hemoglobin 13.2 g/dL, platelet 113k/uL, and Alpha Fetoprotein (AFP) 3.9 Units.

At the radiology suite, he underwent chemoembolization.

Through the femoral artery, the selective right hepatic artery was catheterized.

The mixture of the embolic material (Geloform power), chemotherpeutic drugs, Lipiodol and contrast media were meticulously infused to the tumor bed through the catheter.

For the chemotherapy drugs, cis-Platin 100 mg/ml, Adriamycin 50 mg/ml and Mitomycin 10 mg/ml were used. The procedure continues until the infusion slows down.

After the procedure, he had the immediate post-chemoembolization CT scan (Fig 2).

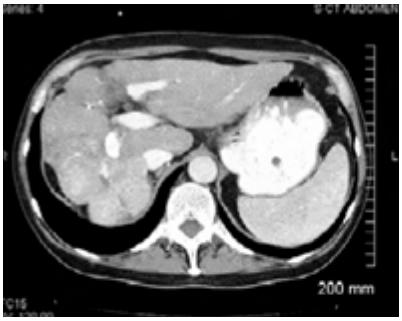

Fig 2.
CT scan immediately after chemoembolization

It showed the Lipiodol retained in the tumor mass, indicating successful chemoembolization.

Before the procedure, prophylactic antibiotic therapy with Metronidazole and Levaquin was started and continued until discharge. He also received morphine for pain relief for a brief period.

About 6 weeks later he had second chemoembolization to treat the tumors not covered by the first treatment. The patient did well enjoying a full life. The CT scan of the abdomen taken 1 year later showed much smaller tumors with the residual Lipiodol (Fig 3).

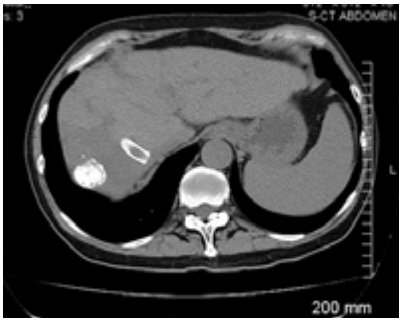

Fig 3.
CT scan 1 year after chemoembolization.

Case Study 2

An 88-year-old Taiwanese man was admitted with extremely severe abdominal pain requiring hourly morphine injection to relieve the pain.

Computer Tomography (CT) scan of the abdomen revealed a 8 cm tumor in the left lobe as well as several small lesions in the right lobe of the liver.

He also has the end stage renal disease (ESRD) on chronic hemodialysis and prostate cancer that is under control with hormone therapy.

The Alpha Fetoprotein (AFP) level was very high at 25,904 Units, and the PSA level moderately elevated at 15 ng/ML. Both hepatitis B and C serology came back negative.

The patient underwent CT-guided needle biopsy of the left liver tumor, and the pathologist reported it as hepatocellular carcinoma.

Because of extremely poor prognosis of non-resectable hepatocellular carcinoma occurring in an elderly man who is undergoing hemodialysis for ESRD, no specific cancer treatment was recommended. However, the patient was suffering from intractable abdominal pain due to the rapidly growing hepatoma.

After a long discussion with the patient's son who is a

physician, he was elected to have chemoembolization for palliation of the severe pain.

He underwent chemembolization in a similar manner as described in the case study 1.

He developed nausea and ileus after the procedure that were resolved before discharge.

By the time he was discharged about a week after the procedure, he no longer required morphine or similar strong narcotics.

Before the procedure, the SGOT and SGPT levels were 65 and 96 IU/L respectively.

The SGOT and SGPT peaked next day after the chemoembolization to 862 and 446 IU/L respectively. The phosphorous levels also went up from 1.6 to 4.3 mg/dL, but the bilirubin and alkaline phosphates levels did not change much.

The hemodialysis continued during his hospitalization, which appeared to help the electrolytes imbalance caused by the chemoembolization.

About one month later, the patient had the follow-up CT scan of the abdomen showing significant shrinkage of the chemoembolized hepatoma.

Discussion

Chemoembolization is most beneficial to patients whose disease is limited to the liver, whether the tumor is primary or metastatic. Cancers that may be treated by chemoembolization include hepatocellular carcinoma , metastatic tumor to the liver from carcinoid tumor, islet cell tumors of the pancreas, ocular melanoma and sarcomas.

For hepatocellular carcinoma, surgical resection remains the gold standard treatment modality. However less than 20% of patients are eligible for the surgery, and only limited number of patients can be candidates for liver transplantation. Liver transplantation has a rather stringent selection criteria; In patients with a single tumor no larger than 5 cm or with up to three tumors, none larger than 3 cm, transplantation resulted in a 4-year overall survival rate of 75% and a 4-year recurrence-free survival rate of 83%. Most transplant centers and the United Network for Organ Sharing (UNOS) have since adopted these criteria, which are now commonly referred to as the "Milan criteria."(2)

The patients in the case study are not candidates for liver transplantation. Chemotherapy is mostly ineffective and cannot improve the survival of the patients with hepatocellular carcinoma.

Therefore, hepatic artery chemoembolization can be a good alternative treatment method.

The 2 most recent prospective randomized trials indicate that chemoembolization significantly prolongs the survival rates of the patients.

Lo et al (3), compared survival outcomes with chemoembolization versus symptomatic management, with 40 patients per group. One-, 2-, and 3- survival rates in the study group were 57%, 31%, and 26% compared with 32%, 11%, and 3% in the control group (p = 0.02) (Fig 4).

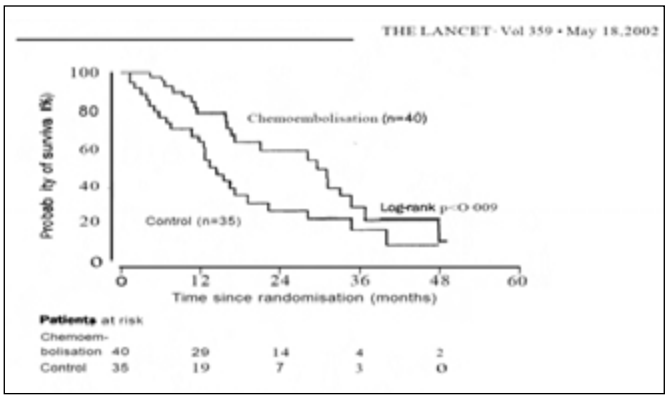

Fig 4. Survival Curves of chemoembolization and controls

Another study, by Llovet et al (4), included 112 patients in three arms and compared outcomes with chemoembolization versus embolization alone versus symptomatic treatment. The trial was stopped when a significant survival benefit was demonstrated with chemoembolization (survival rate,82% at 1 year and 63% at 2 years) versus symptomatic treatment (63% at 1 year and 27% at 2 years; P = 0.009). At that time the trial was halted, there was not a survival benefit identified with embolization alone (75% at 1 year and 50% at 2 years) versus symptomatic treatment, although the difference may have reached significance with continuation of the trial.

Chemoembolization has also been used preoperatively as a neoadjuvant therapy. The potential benefit of neoadjuvant chemoembolization lies in its ability to

cause tumor necrosis, thus making resection technically easier. In addition, chemoembolization may destroy microscopic intrahepatic metastases not included in the resected specimen.

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ANSWER

1) I bet you know my name even if you have never seen me in your life, simply because I am well known.

2) I can give you a shock like an anesthesiologist does.

3) I have a built in factory producing Chlorotoxin, which can treat Rheumaoid Arthritis, Glioma and Multiple Sclerosis.

4) I invite you to visit me at night in Joshua Tree National Park. You can see me with an UV flash light because I do fluoresce.

A PAIN-FREE LANCET WITH A SMALL NEEDLE FOR GLUCOSE MEASUREMENT

Author: Stanley Kim, MD

Abstract

Introduction: A new lancet with an extremely small needle (0.15 mm diameter and 0.75 mm length) mounted on a small pedestal was tested in diabetic patients for blood glucose measurement in a randomized clinical study. Method: Total 37 diabetic patients were enrolled for the study. A pain scale categorized from 0 to 3 was created to measure the intensity of puncture pain which was explained to patients before testing. The patients' fingers were punctured with their own old style lancets and the new lancets sequentially, and puncture pains recorded according to the pain scale. Result: All patients tested with the new lancet reported no pain and recorded the puncture pain as scale 0. Among the total 37 patients tested with their old style lancets, 2 patients (5.40%) reported no pain and recorded the pain as scale 0, thirteen patients (35.14%) recorded as scale 1, 16 patients (43.24%) as scale 2, and 6 patients (16.22%) as scale 3. The average pain scale of the patients who used old style lancets was 1.702 with the standard error 0.133. The chi-square goodness-of-fit test shows that the proportion of the pain scales comes from the claimed distribution with unequal frequencies, and chi-square tests for independence indicate that neither sex nor age of the sample patients is related to the pain scales. The paired t-test to test the existence of any difference in pain levels between the new lancet and the old style lancet showed; $t = 1.702 / 0.133 = 12.796$ with p-value $< .005$($df = 36$). Conclusion: Average pain level from the old style lancet is significantly higher than that from the new lancets. Discussion: Pain-free needle puncture was achieved by limiting the puncture depth less than 0.75 mm with a thin needle with a 0.15 mm diameter. By allowing patients to see the new lancets before testing, psychological pain anticipation was minimized as the very thin and short needle is visually less intimidating. With a pain free puncture, better compliance and improved subsequent glucose may be achieved.

Introduction

Much improvement and innovation have been made in the field of diabetes care in recent years, especially in glucose monitoring technology. However, as lancet technology has not been met with the same innovation, many diabetic patients still suffer from needle puncture pain when measuring their blood sugar levels. Old style lancets with a thick and long needle used to puncture the finger tip for the past 30 years are still being used. Furthermore, both adults and children use the same size lancets as no lancets suitable for diabetic children are available. A typical stainless steel lancet has a diameter of 0.3-0.8 mm and penetrates 0.7-1.3 mm, with depth of penetration directly related to pain (1). Although the extent of tissue injury and pain are less from the puncture by a thinner and shorter needle, the puncture by the very small size needle yields less blood volume that may not be sufficient for the glucose measurement. With modern glucose meters which require a much smaller blood sample for an accurate measurement, diabetic patients no longer need to use lancets with a large size needle. For example, the FreeStyle© glucose monitor (Abbott Laboratory, Abbott Park, Illinois) requires only 0.3 microliters of blood for testing the glucose level (2). The pain from the needle puncture discourages diabetic patients to monitor the blood glucose levels as frequently as recommended, which adversely affects the quality of their health. According to a survey of some 6,600 type 1 diabetic patients, to which 1,895 replied, actual testing frequency was less than that recommended, mainly because of soreness, pain and inconvenience. The difference between the reported recommended and actual frequency of testing was proportional to the number of hospitalization over the prior 2 years (1), which indicates that poor compliance increased complications of diabetes.

A new lancet having an extremely thin and short needle was created and tested in an open randomized clinical

study as to whether it causes less puncture pain when compared with old style lancets while producing enough blood volume for glucose testing.

Methods

A total of 37 diabetic patients (3 patients with type 1 and 34 patients with type 2 diabetes) were enrolled in the study (Table 1). The study was conducted at a medical clinic during the period of April 2nd through September 9, 2008. There are 12 females (32.4%) and 25 males (67.6%), and patients range from 24 to 88 years-old with average age of 66.6.

Patient No	Sex	Age	Brand of Old Lancet	Pain Scale from Old Lancet	Pain Scale from New Lancet
P01	M	62	OneTouch	2	0
P02	M	64	Generic	1	0
P03	M	70	AccuChek	2	0
P04	M	68	Ascensia	3	0
P05	M	68	Ascensia	3	0
P06	F	80	AccuChek	1	0
P07	M	67	Generic	3	0
P08	M	57	FreeStyle	2	0
P09	F	70	OneTouch	2	0
P10	M	63	AccuChek	1	0
P11	M	70	OneTouch	2	0
P12	M	70	OneTouch	2	0
P13	F	75	OneTouch	1	0
P14	M	58	AccuChek	1	0
P15	M	62	OneTouch	3	0
P16	F	80	OneTouch	2	0
P17	F	77	AccuChek	2	0
P18	M	78	BD30G	1	0
P19	F	47	AccuChek	2	0
P20	F	49	OneTouch	1	0
P21	M	24	BD30G	1	0
P22	M	61	AccuChek	2	0
P23	M	83	OneTouch	1	0
P24	M	67	OneTouch	2	0
P25	M	88	AccuChek	0	0
P26	F	58	OneTouch	3	0
P27	M	67	FreeStyle	1	0
P28	M	68	Ascensia	3	0
P29	M	62	FreeStyle	2	0
P30	F	61	OneTouch	2	0
P31	F	84	Generic	2	0
P32	M	63	OneTouch	2	0
P33	F	76	OneTouch	0	0
P34	M	70	OneTouch	1	0
P35	F	66	OneTouch	1	0
P36	M	61	AccuChek	1	0
P37	M	71	AccuChek	2	0

Table 1. Patient Data

Among them, 16 patients are 66 years old or younger, and 21 are older than 66. They all have been testing blood glucose levels at home using typical old style disposable lancets from various makers including the OneTouch®(Life Scan, Milpitas, California), AccuChek softclix®(Roche Diagnostics, Indianapolis, Indiana), FreeStyle®(Abbott Laboratory, Abott Park, Illinois) , Ascencia®(Bayer Health Care LLC, Tarrytown, New York), BD Ultrasoft®(BD, Franklin Lakes, New Jersey). The diameter of those lancet needles ranges from 28 to 30 gauges, and the length is 2.8-3.2 mm.

A new disposable lancet, Tiniboy™ (Health Innovation Ideas, LLC, Upland, California) has a needle size of 38 gauge (0.15 mm in diameter) and 0.75 mm in length. A photograph comparing the new lancet, Tiniboy™ with other lancets is shown in Figure 1.

The OneTouch® lancing device (Life Scan, Milpitas, California) was used as a lancing device for the Tiniboy™ lancet, and the capillary blood glucose level was measured with the OneTouch® glucose monitor (Life Scan, Milpitas, California) that requires at least 1.0 microliter of blood for testing. As a control, patients used their own disposable lancets housed in various lancing devices as the way they normally do at home.

All patients were tested in the fingertip, and the testing sites for the new lancet are comparable to those for the old style lancets.

The finger tip was cleaned with alcohol swab and wiped with sterile gauze, and lancing was performed by a physician. Patients are allowed to see the new lancet before lancing.

The lancing device was opened, and the disposable lancet inserted into the lancet holder. After the lancing device was closed and cocked, it was placed onto the patient's finger tip as usual. Mostly, 3rd and 4th finger tips were selected for testing.

At the first attempt, a penetration depth of level 1 out of 9 was set by adjusting the lancing device. If the first attempt failed to produce enough blood for glucose testing, the second attempt was done with an increase of the penetration depth to level 2 with the same lancet. Likewise, if the second attempt failed, the third attempt was made with another increase to the level 3.

A simple pain scale (Table 2) is created; depending on the intensity of puncture pains, it is categorized from 0 to 3 (0 = no pain, 1 = minimal pain, 2 = mild pain, and 3 = moderate or severe pain). The pain scale is explained to patients before testing. After testing with the new lancet, patients were asked regarding their pain sensations, and their results recorded. Similarly, their pain sensations with their own old style lancets were recorded.

Scale	Intensity of Pain
0	No Pain
1	Minimal Pain
2	Mild Pain
3	Moderate or severe pain

Table 2. Pain Scale

Result

Sampling success at the first attempt was obtained in 19 patients (51%), second attempt sampling success in 17 patients (46%) and the third attempt in 1 patient (3%).

All patients tested with the new lancet reported no pain and recorded the puncture pain as scale 0 (Table 3-a). Among the total 37 patients tested with their old style lancets, 2 patients (5.40%) reported no pain and recorded the pain as scale 0, thirteen patients (35.14%) recorded as scale 1, 16 patients (43.24%) as scale 2, and 6 patients (16.22%) as scale 3 (Table 3-b). The average pain scale of the patients who used old style lancets was 1.702 with the standard error 0.133.

The chi-square goodness-of-fit test (Table 3) showed sufficient evidence at the 5% level of significance that the proportion of the pain scales comes from the claimed distribution with unequal frequencies; chi-square =13.270 with p-value < 0.01.

Chi-square tests for independence (Table 4) were performed to determine whether there is an association between sex and pain scale (Table 4-a) as well as age and pain scale (Table 4-b). Small values of chi-square statistics with large p- values indicate that neither

sex nor age of the sample patients is related to the pain scales (Table 4-c).

The paired t-test to test the existence of any difference in pain levels between the new lancet and the old style lancet showed; t = 1.702 / 0.133 = 12.796 with p-value < .005(df = 36). This concludes that average pain level from the old style lancet is significantly higher than that from the new lancets.

Discussion

Among many difficulties and problems encountered by diabetic patients, daily experience of pain and soreness of the finger cannot be underestimated. Although the pain itself may not be a serious medical condition, it is indirectly associated with dire complications of diabetes. Patients' reluctance of testing blood glucose levels due to fear of puncture pain is a well known cause of the poor compliance among the diabetics. As confirmed in this open randomized clinical study, by reducing the lancet size to the 38 gauge and limiting its penetration depth not more than 0.75 mm, needle puncture pain was virtually eliminated,

and the amount of blood produced by a puncture with this very thin and short needle was at least 1.0 microliter, sufficient for the glucose test when patients

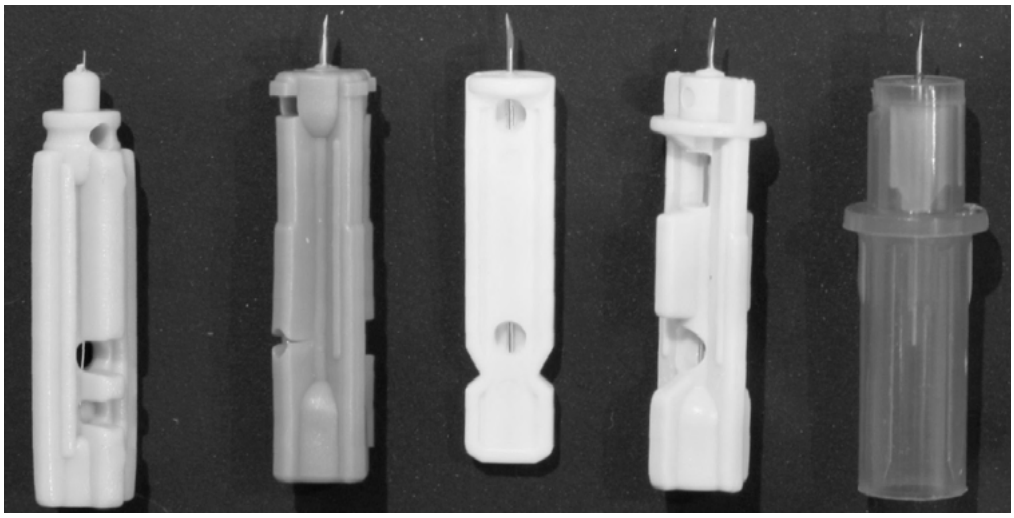

Fig 1.
The new lancet, Tiniboy™ in comparison with other old style lancets.

Table 3. Goodness-of-fit test§

Table 3-a. Percentage of patients according to pain scale with the new lancet

Pain Scale	0	1	2	3
Frequency	37	0	0	0
Percentage	100%	0%	0%	0%

Table 3-b. Percentage of patients according to pain scale with the old style lancets

Pain Scale	0	1	2	3
Frequency	2	13	16	6
Percentage	5.40%	35.14%	43.24%	16.22%

§ The chi-square goodness-of-fit test gives c2 =13.270 with p-value < 0.01. Hence, the null hypothesis was rejected, concluding that the proportion of SCALEs varies with unequal frequencies.

Table 4. Independence test *

*The chi-square independence tests showed very small values of c2 with large p-values. Although the powers of the test are not significantly higher due to relative small sample size in the experiment, it is worth to note that the pain scales are not related to neither age nor sex. The values of contingency coefficient show very weak relationship among SCALE and Sex or Age, and they support the results of chi-square independence tests.

Table 4-a. Sex versus pain scale

Pain Scale	0	1	2	3
Male	1	9	10	5
Female	1	4	6	1

Table 4-b. Age versus pain scale

Pain Scale	0	1	2	3
≤ 66 years	0	7	7	2
> 66 years	2	6	9	4

Table 4-c. Chi-square statistics, p-values and contingency coefficient

Category	Chi-square statistics	p-value	Contingency coefficient
Sex vs. pain scale	1.1661	0.761	0.1748
Age vs. pain scale	2.3610	0.501	0.2449

use a modern glucose monitor. Recent advancement of technology even permits a glucose monitor to measure an accurate blood glucose level with only 0.3 microliter of capillary blood (2).

The reason of this painless needle puncture can be from both biological and psychological.

The Tiniboy™ lancet has an unusually thin and short needle that causes a very shallow and

narrow puncture, probably hitting the capillaries in the superficial dermis sparing the pain nerve fibers below.

Also, anticipation of puncture pain can be minimized by using an extremely small needle, due to the fact that a smaller needle is less intimidating to patients.

The skin consists of the epidermis and the dermis.

Underneath the epidermis which has no blood vessels and negligible pain nerve innervations, the dermis is divided into 2 layers, the papillary layer above and the reticular layer below. Typically, the superficial portion of the papillary layer is arranged into ridge-like structures, the dermal papillae, which contain microvascular and neural components that sustain the epidermis. A vascular plexus, the rete subpapillare, demarcates the lower limit of the papillary dermis (3).

The thickness of the epidermis of the middle fingers in normal persons is about 0.3 mm,

and that of the dermis 1.5 mm (4). The papillary layer has about 0.3-0.4 mm thickness (3).

The Merkel's cells in the epidermis and the Morgagni's corpuscles in the papillary layer are nerve receptors for touch sensation.

Therefore, if a lancet needle penetrates the finger skin at 0.6-0.7 mm depth, it can hit the

rete subpapillae, the superficial vascular structure of the papillary dermis without going

deeper to the reticular dermis where abundant free nerve fibers are present. By penetrating up to the papillary dermis only, the lancet needle may hit the nerve receptors such as Merkel's cells and Morgagni corpuscles, and patients feel something touching instead of unpleasant pain.

The limited penetration depth (maxium 0.75 mm) by the very thin needle (38 gauge) of the Tiniboy™ lancet is conjectured to be the reason why tested patients consistently reported no pain.

The Tiniboy™ lancet's revolutionary structure, employing a small pedestal, enables the functionality of the extremely thin and short needle. Commercially available lancing devices have an exit opening (where the lancet needle protrudes to puncture the skin) of about a 3 mm diameter, with a side wall of about 1 mm-thickness. Therefore, with the use of available lancing devices, a traditional lancet needle shorter than 1 mm cannot hit the skin; as such, currently available lancets have about 3 mm-long lancet needles. However, the Tiniboy™ lancet is structured with a small pedestal of 2.25 mm height and 1.75 mm diameter at the distal end of the lancet body on which a 0.75 mm needle is mounted (Figure 1). When the Tiniboy™ lancet needle penetrates the skin during the lancing procedure, the small pedestal, not the needle, passes through the exit opening. Because the total length of the Tiniboy™ (including the needle, pedestal and lancet body) is commensurate to that of traditional lancets, it can be used interchangingly with old style lancets in conjunction with standard lancing devices.

The length of a needle also influences the thickness of a needle. When the needle is very thin and long, it bends and can even break when it hits a skin, especially hard callused skin. Because of the pedestal's ability to pass through the exit opening of a lancing device, the lancet needle can be shorter than 1 mm, and as a result, the needle is able to be very thin without the risk of bending or breaking.

One can not underestimate the psychological aspect of pain when measuring the intensity of pain. Pain perception is influenced not only by the actual wound size but also by psychological factor. Anticipating pain is perceived as actual pain (5). It is especially true when diabetic patients puncture the finger skin by themselves.

The psychological aspect of pain anticipation was considered as an important factor in measuring the pain intensity in this study.

Therefore, patients in this study were allowed to see the TiniBoy™ lancet before puncturing the skin because the pain anticipation could be less than control lancets, although, in general, it is preferred to design a randomized study as a double blind one.

The goal of this study was to test whether puncture pain can be reduced by the new lancet.

Future study can aim to test whether improved compliance and better blood glucose control can be achieved by measuring hemoglobin A1C in a randomized control trial with this new Tiniboy™ lancet.

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REVIEW OF INTERVENTIONAL PAIN MANAGEMENT

By Bryan X. Lee, M.D.

This article will review the common interventional pain procedures and their indications. It should be noted that I am only reviewing the common interventions and there are many other procedures for different pain conditions that I am unable to list due to space constraints. If your patient is suffering from chronic pain and have seen the usual specialists, please consider a referral to pain management for further pain treatment options.

Low back pain is the most common pain complaint, followed by neck pain. Most pain complaints are for acute pain, which usually resolve in a few weeks with conservative treatments. However, sometimes the pain lingers at which point the patient may need more aggressive treatment, including a referral to pain management. For the chronic pain patients of today, there are multiple treatment options available today that were uncommon or unavailable even 5-10 years ago. Pain management is no longer confined to the simple "nerve block" or "epidural shot" of years past.

Note that the standard of care for interventional pain management has shifted towards procedures performed under fluoroscopic guidance for accuracy and safety. For procedures not conducive to fluoroscopic guidance, nerve stimulation and ultrasound guidance may be used for accuracy and safety. Please note that there are multiple other indications for many of the below listed procedures, but due to the scope of this writing, I am only listing the major indications.

Lumbar Spine Pain ("Low Back Pain")

Lumbar Epidural (Interlaminar) Steroid Injection (LESI): This is the most common "cortisone shot" or "nerve block" for low back pain. It is most effective for patients who have a herniated disc with lumbar radiculopathy (i.e. sciatica). It is also commonly done for lumbar spondylosis, spinal stenosis and degenerative disc disease.

Caudal Epidural Interlaminar Steroid Injection: This injection is a variation of the LESI. Sometimes, it is done on patients with failed back surgery syndrome, in which scar tissue formation in the lumbar spine makes an LESI injection difficult. This injection is done via the sacral hiatus in the tailbone.

Lumbar Transforminal Epidural Injection/Selective Nerve Blocks: These injections selectively target the painful nerve root. It is best for treating lumbar radiculopathy (i.e. sciatica), especially when there is a clearly compromised nerve root. For example, if an L5-S1 herniated disc is encroaching (i.e."pinching") the Left L5 nerve root, then the needle with be guided to the Left L5-S1 neuroforamen under fluoroscope before deposition of the local anesthetic/steroid mixture.

Lumbar Facet Intra-articular or Medial Branch Blocks: These injections are best for patients with lumbar facet syndrome. Lumbar facet pain is usually axial low back pain that sometimes radiates down the buttock to the knee. But, very rarely goes below the knee. Both diagnostic and therapeutic blocks can be done.

Lumbar Facet Radiofrequency Ablation (RFA) or Rhizotomy: This procedure is a variation of the medial branch block, in which the facet medial branch nerves are "destroyed" at a high temperature (e.g. 80 degrees Celsius). This procedure is only performed after diagnostic facet blocks confirm that the low back pain has a strong contributory component from the facets. The relief from RFA can last for months to years.

Sacroiliac Joint Injections: This procedure directly targets pain due to sacroiliitis or sacroiliac joint degeneration. Some studies show that up to 30% of low back pain is due to sacroiliac joint disease, which causes pain localized to the low back and buttock areas. The pain can also radiate to the groins and down the thigh,

but rarely below the knees. The "Patrick's Test" is an easy office maneuver that can help diagnosis sacroiliac pain. Oftentimes, the physician can press the sacroiliac joints and also elicit pain.

Cervical Spine Pain ("Cervicalgia")

Cervical Epidural Steroid Injection: This procedure is commonly performed for cervical radiculopathy, cervical degenerative disc disease or herniated disc, and cervical spinal stenosis. Due to the nature of the procedure, it is most commonly performed under fluoroscopic guidance with contrast dye for accuracy and safety.

Cervical Facet Joint Injections/Medial Branch Blocks: Similar to the lumbar procedures, these procedures target cervical facet pain. Cervical facet syndrome usually involves pain in the neck or cervical spine. It often radiates to the shoulder, but rarely to the arm.

Cervical Facet Radiofrequency Ablation (RFA) or Rhizotomy: This procedure is a variation of the medial branch block, in which the facet medial branch nerves are "destroyed" at a high temperature (e.g. 80 degrees Celsius). This procedure is only performed after diagnostic facet blocks confirm that the neck pain has a strong contributory component from the facets. The relief from RFA can last for months to years.

Cervical Transforminal Epidural Steroid Injection/ Selective Nerve Block: This injection is usually performed for cervical radiculopathy. Because of documented risks including vertebral artery thrombosis and subsequent life threatening complications, it is not as commonly performed by some physicians.

Thoracic Spine Pain

Thoracic Epidural Steroid Injection: As with the Cervical and Lumbar equivalents, this injection is indicated for thoracic radiculopathy, disc disease, and spinal stenosis. Because postherpetic neuralgia occurs usually in the thoracic dermatomes, this injection is also useful for this problem.

Thoracic Facet Joint Injections/Blocks: Again, as with the Cervical and Lumbar equivalents, these injections are usually done for patients with thoracic facet pain, which is usually localized to the thoracic axial spine. It is the least commonly performed facet injection as lumbar and cervical facet pain are more common.

Sympathetic Nerve Blocks:

Stellate Ganglion Block: This is a sympathetic nerve block performed for patients suffering from reflex sympathetic dystrophy (i.e. Chronic Regional Pain Syndrome) of the upper extremity, brachioplexus lesions, and other neuropathic pain conditions of the upper extremity/shoulder.

Lumbar Sympathetic Nerve Block: This is a procedure performed for lower extremity pain, usually due to reflex sympathetic dystrophy (i.e. Chronic Regional Pain Syndrome) of the leg, ankle or foot. It can also be used for other painful lower extremity conditions due to neuropathic etiologies.

Ganglion Impar Nerve Block: This is a sympathetic nerve block done at the Ganglion of Walter, in the coccyx. It can be very effective for coccygodynia and perineal/rectal pain.

Superior Hypogastric Nerve Block: This is a procedure performed commonly for pelvic pain, such as uterine pain, ovarian pain, testicular pain, etc.

Miscellaneous Nerve Blocks

Intercostal Nerve Blocks: These are blocks performed at the intercostals nerves of the ribs, generally for Intercostal Neuralgia, Postherpetic Neuralgia (i.e. shingles pain), and post-thoracotomy syndrome.

Trigeminal Nerve Blocks: These blocks can be performed at one of the 3 trigeminal branches at the trigeminal ganglion. It is effective for trigeminal nerve mediated pain, including trigeminal neuralgia.

Ilioinguinal Nerve Block: This block is often done for inguinal pain, whether due to idiopathic inguinal neuralgia, post-hernia surgical pain, or other neuropathic pain syndrome of the groin.

Genitofemoral Nerve Block: This block is very effective for genital related pain, especially testicular pain.

Lateral Femoral Cutaneous Nerve Block: This procedure is used for patients suffering from anterolateral thigh pain due to lateral femoral nerve irritation (i.e. "Paresthetica Meralgia").

Ankle Blocks: There are 5 nerves in the ankle that innervates various parts of the foot. Depending on the painful area, a patient may get effective relief with a single or multiple nerve blocks.

Advanced Interventions

Spinal Cord Stimulation (SCS): This is a cutting edge procedure most commonly performed for Postlaminectomy Syndrome of the Cervical, Thoracic or Lumbar spine (i.e. "Failed Back Surgery Syndrome"), radiculopathy of the upper or lower extremities, and back and neck pain. It is often performed for patients who have failed common nerve blocks (i.e. "epidural steroid injection") or surgery of the spine. It is also effective for reflex sympathetic dystrophy, angina, and peripheral artery disease. This is a same-day surgery procedure in which electrical leads are placed in the spinal cord to modulate (i.e. "block" or "jumble") the pain signals going to the brain. For example, instead of feeling constant pain the in the leg, such as sciatica, the patient may feel a pleasant tingling sensation in the leg. SCS is based on the Gate Control Theory of pain proposed several decades ago by Ronald Melzack and Patrick Wall. Patients usually undergo a trial of SCS before permanent implantation.

Intrathecal Drug Pump (i.e. "Morphine Pump"): This procedure involves placing an indwelling catheter within the intrathecal space connected to a drug reservoir, usually placed under the abdominal wall. This drug reservoir can have a combination of opioid medication (e.g. morphine, hydromorphone), local anesthetics (e.g. bupivacaine), antispastic agents (e.g. baclofen) and Prialt ("snail venom"). Commonly, intrathecal pumps are placed for patient with pain not controlled with medications by other routes, either due to high dosages or intolerable side effects. The equianalgesic dose between an oral vs intrathecal medication is approximately 300X greater. For example, 300 mg oral morphine is equal to approximately 1 mg intrathecal morphine. Some possible indications for this procedure include terminal cancer pain, intractable pain responsive to opioids, but at extremely high doses or with intolerable side effects. The drug reservoir needs to be filled periodically, usually in weeks to months. The most serious complications tend to be infectious and neurological. This should be a procedure performed after serious consideration by the patient and his/her physician team.

Provocation Discography: This is a diagnostic procedure in which dye is injected into a disc to diagnose discogenic related pain. It is often used by spine surgeons to localize the disc level requiring surgery (e.g. fusion). It is a procedure requiring significant skill on the part of the injectionist.

Percutaneous Discectomy: This is an advanced spine procedure performed by various methods in which a disc is decompressed by a percuteous approach. It is most commonly performed in the lumbar spine for discogenic pain, often after a discogram localizes the causative disc.

These are the common and advanced procedures utilized daily by interventional pain specialists to treat pain patients. As you can see from the representative procedures here, there are a variety of interventions available today that were not common just 5-10 years ago. Pain management is an exciting and growing field with many advances to come in the future.

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THE MISSING DIABETES GUIDELINES FOR ASIAN AMERICANS.

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Introduction:

The prevalence of Type 2 Diabetes is growing in epidemic proportions in the United States, with the last 2007 CDC estimate at 7.8%(1) This disease is associated with high morbidity and mortality (1). Asians represent a large diverse ethnic group in the world, but in the United States, this group only represents less than 5% of the population based on the most recent CDC census (1). There have been very limited studies of diabetes in Asian Americans. Recent trends from international literature report a very high prevalence. From a recent cross-sectional study of diabetes in China, there was an estimated prevalence of 9.7%, higher than years earlier(2). Despite clear evidence of Asians at a high for diabetes, the current American Diabetes Association(ADA) guidelines provide an inadequate diabetes screening approach for Asian Americans(3, 4, 5, 6).

Diabetes: an Asian American epidemic?

Diabetes is increasing at an alarming rate in the United States (1). Incidence of 1.4million people in 2005 reflected a near tripling since the 1980's (1). Diabetes patients suffer severe morbidity such as retinopathy, renal failure, and foot infections (3). Furthermore, they have the cardiac risk equivalent of patients with previous cardiac events (4). Due to these complications, it is imperative to screen diabetes patients early and treat them aggressively.

One of the neglected demographics at high risk for diabetes is the Asian American population. The estimated prevalence of diabetes from the Center of Disease Control (CDC) of non-Hispanic white greater than 20 year of age is 6.6%. For Asians Americans, the prevalence is higher at 7.5%. The California Health Interview Survey also reported a higher diabetes prevalence in Asian Americans compared with causians,6.6% vs. 5%(7).

Obesity: predisposition for diabetes.

With the rise in the prevalence obesity in United States, there was also a parallel increase in type 2 diabetes(1,3). The insulin resistance from obesity predispose patients to relative beta cell failure, and therefore the manifestation of type 2 Diabetes(9,10,11). In order to screen the population for diabetes, the body mass index(BMI) has been used as a tool to alert clinicians to screen for diabetes. Based on the BMI, obesity has been designated by the World Health Organization(WHO) to be the BMI of 30kg/m2 or greater, and overweight between 25kg/m2 and 30kg/m2 (3). This definition unfortunately lacks sensitivity as a screening tool for Asians at risk for diabetes(3,6).

Obesity in Asians in America.

Clinicians may inaccurately presume Asians to have less metabolic risk due to lower a BMI compared with Caucasians. A study using a National US based survey reported that the proportion of Asian Americans with

BMI>30kg/m2 was significantly lower compared with Caucasians, 4.8% versus 21.8%(8). Despite having lower BMI, the age-, sex-, and BMI-adjusted prevalence of diabetes in Asian Americans was ~60% higher than in non-Hispanic whites(6). The WHO expert panel acknowledged this problem in 2002 and reported that "the proportion of Asian people with risk factors for type 2 diabetes and cardiovascular disease is substantial even below the existing WHO BMI cut-off point of 25 kg/m2(6)."

The Thin-Fat Syndrome in Asians.

It is clear that Asians are at a high diabetic risk at a lower BMI(6). The pathology appears not to be about the absolute weight, but the distribution of fat, most notably the percentage of fat in the viscera(9,10,11). For the same BMI of Asian cohorts, there is a 3-5% points higher in percentage body fat compared to Caucasians(13). This has been characterized as the "Thin-Fat" phenotype. Asians generally have a higher percentage of body fat compared with Caucasians of the same age, sex, and BMI. Many studies suggest that Asians are at a higher predisposition for the disposition of visceral fat, which confers a detrimental metabolic effect(9,10,11). In a recent prospective longitudinal study reported by Stevens, she compared the impact of BMI gain and diabetes development between a cohort in the United States and China over 10 years. She found the estimated risk of diabetes per unit increase in BMI over time was significantly higher in the Chinese compared with the Caucasians(13).

The Missing Diabetes Guidelines for Asians Americans

Most major committees and organizations recognize this higher metabolic risk at a lower BMI for Asians(3,6). From the World Health Organization expert consultation meeting in 2002, they concluded that "current WHO BMI cut-off points do not provide an adequate basis for taking action on risks related to overweight and obesity in many populations in Asia(7)." Despite this limitation, the guidelines in the American Diabetes Association(ADA) does not provide a lower BMI index for Asian Americans for the screening for diabetes. They comment on the need to have a lower BMI for ethnic minorities, but do not provide an Asian specific BMI guideline(3).

In order to address this problem, the WHO evaluated the cut off points for overweight and obesity in Asians. The cut off for observed risk ranged from 22kg/m2 to 25kg/m2 and therefore could not be set a one numerical value(6). Because of this limitation, they elected not to change the BMI nomenclature for the Asian population and thus leaving clinicians without an adequate diagnostic label to address this ethnic specific problem.

Conclusion:

Asian Americans are at a higher risk compared with the standard Caucasian population for diabetes in the U.S. Despite having high prevalence of diabetes and metabolic risk, Asian Americans are not provided with proper clinical guidelines for diabetic screening. Healthcare providers and patients need to understand that a substantial percentage of Asian Americans can have diabetes without being identified as being obese or overweight by the current ADA guidelines.

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WHERE YOU LIVE SHOULD NOT DETERMINE IF YOU LIVE

By Dr. Gary Selnow and Dr. Suellen Crano

Dr. Gary Selnow is a professor at the Edelman Institute at San Francisco State University and Director of WiRED International. Selnow is the author/co-author of seven books including Society's Impact on Television, High Tech Campaigns, Electronic Whistle-Stops: The Impact of the Internet on American Politics, and most recently The People, Press and Politics of Croatia.

Selnow was twice a Fulbright Scholar—in Austria, then at the University of Zagreb in Croatia. Selnow coordinated a national communication program for a White House task force and served as a research methodologist for the U.S. Information Agency. He has consulted with the U.S. Department of State and for NBC Television and the National Academy of Sciences. Selnow was a pilot for the U.S. Air Force. He was a regular commentator on Public Radio International's Marketplace program.

Selnow was awarded the 2004 President's Medal at San Francisco State University. He earned his bachelors degree in technical writing at Rutgers University and his masters and doctoral degrees in communication and psychology at Michigan State University.

Suellen Crano, Ph.D.
After earning her Ph.D. in Higher Education Administration/Student Personnel in 1984 from Michigan State University, Dr. Crano served in administrative roles at Texas A&M University, The George Washington University, The University of Arizona, the State of Michigan Department of Higher Management Systems, Wyeth Laboratories, Inc., and most recently, at Western University of Health Sciences. She is a member of the Boards of WiRED International, the Arizona Cancer Center, and the College of Graduate Nursing at Western University of Health Sciences. Not satisfied by underwriting WiRED's VideoVisit program, which enables families to communicate with their children undergoing life-saving medical treatment in western countries, Dr. Crano helped coordinate the launch from a children's cancer ward in the Hospital of Pisa. Her role as a WiRED director enables her to continue a lifelong passion of helping people rebuild devastated lives. She is actively involved in developing materials and relationships for WiRED's educational programs and the International Telemedicine Network. In addition, since becoming a cancer patient herself, Dr. Crano has become an advocate for people with cancer who need assistance.

FORWARDS
Virtual Healing

For many years, Iraqi physicians have been denied access to medical developments taking place outside their country. That has made the practice and the study of medicine more difficult and it has denied medical professionals the opportunity to offer Iraqi patients the latest, and often most successful diagnoses and treatments.

In 2003, WiRED International, a California based not-for-profit organization began supplying Iraqi medical schools and teaching hospitals with computer based medical libraries. WiRED, using computer technology and the Internet, is helping Iraqi doctors recover from 20 years of isolation and censorship under Saddam Hussein, to give Iraq's medical schools quick access to current technical knowledge, electronic research libraries, and video connections with U.S. medical educators. Twenty years of censorship in Iraq effectively isolated Iraqi doctors from advances in medicine. Saddam Hussein blocked e-mail and Internet communication, banned travel to professional conferences, and cut off access to medical journals and textbooks. The result is that Iraqi medicine, once among the best in the world, has

become among the least informed anywhere.

The CDs, hard drive libraries, and the access to many Websites gave Iraqi doctors and medical students an opportunity to read the latest medical journals and catch up on the most recent technical developments. Information is key to the medical profession and the Iraqi medical community has very much appreciated WiRED's assistance with this innovative, effective and most welcomed information support.

This grave need became evident soon after a small group from WiRED International, the NGO,

(Non Governmental Organization) that pioneered computer-based Medical information programs after the Balkan Wars in 1997, entered Iraq on the heels of the coalition forces in 2003. Sponsored by the U.S. State Department, WiRED looked at how they might use information technology to help Iraqi medical schools obtain quick access to current technical information. An American technician and Dr. Gary Selnow, director of WiRED joined with Iraqi doctors and technicians to install electronic libraries in Baghdad-area teaching hospitals. In a single day, WiRED staff converted empty rooms into research libraries called Medical Information Centers (MIC).

A MIC is a collection of interconnected computers that draws technical material from two sources. Where satellite connections are available, MICs provide access to the Internet's rich online resources at the world's leading medical schools and research institutes, the WHO, and U.S. government health agencies. These are valuable databases for any user, but in places where medical journals are few and far between, and where textbooks are older than some medical students, the Internet is a brimming source of technical knowledge.

Where the Internet is not available or affordable, WiRED stocks electronic libraries with as many public-access journals, texts, and research papers as can be loaded onto a computer hard drive. Each MIC is then outfitted with this stand-alone library that can be used without an Internet connection.

WiRED installed the first four MICs in Baghdad in June 2003, and by June 2006 had set up 39 of these centers at hospitals across Iraq. WiRED recently augmented the MICs with videoconferencing equipment at medical schools in Baghdad, Basrah, Erbil, and Mosul. These systems provide direct, high-speed audiovisual communications between Iraqi and American physicians for lectures, seminars, and patient assessments. WiRED's consortium partners at Children'sNational Medical Center in Washington, D.C., the University of California-San Francisco Medical School, and San Francisco State University College of Nursing provide most of the medical content. This is the only

program in Iraq providing Iraqi medical educators with direct links to the outside medical community. These electronic telemedicine bridges, along with the MICs, give Iraqi doctors a chance to break the isolation they've suffered for so many years.

Understanding the potential outcomes of this program is why WiRED treasures words like these from Dr. Kahalid N. Mayah of the Basrah Teaching Hospital: "WiRED may be the best thing done for Iraq. Many nonprofits came to Iraq, some stayed, some went, but your effort to make Iraqi doctors enter to the world of scientific research and information systems was the best thing done." "I just wanted to tell you that our books have been out of date for many years, we have had no reliable source of medical information. The WiRED Centers, with computers, CDs & Internet access provide our first connection to technical data developed by researchers and doctors in other countries. This information obtained at the Medical Information Centers has been a

genuine benefit to me personally and to other Iraqi physicians. Thank you very much for your big help to us Iraqi MD's & hope you may be able to bring us further programs that will help other health staff & not just Iraqi MD's," wrote Dr. Rani Monther at Al-Kindy University for Medicine.

Dr. Manal Oda at Medical City Center (MCC) in Bagdad stated that as an Iraqi MD and a graduate student of medicine in MCC, for many years they have studied and practiced medicine without access to the latest technical information. Early in 2003, WiRED installed several Medical Information Centers at Medical City Center and in other Baghdad locations. These facilities gave them the first chance to review the latest journals and research papers. This material and access to the Internet through WiRED's computers have made a big difference in how many Iraqi doctors learn and practice medicine. They believe that their abilityto serve patients is better because of this information.

WiRED's next project in Iraq is to develop and implement nurses' training programs, as currently, nurses

are no more than glorified housekeepers. When WiRED surveyed physicians about what would most benefit them in their work, the response was a skilled nursing workforce.

All members of WiRED are volunteers. We hope that our work in Iraq, as in all the countries we serve, demonstrates the abiding goodwill of the American people. WiRED seeks to unite medical communities around the world through improved communication. We believe that a universal quest for good health can become the tie that joins people together. To learn more about WiRED and the work it has accomplished, you may access www.wiredinternational.org

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For medical professionals and their patients, isolation is a crippling assault. Medical practice, by its nature, is an integrative activity, involving networks of professionals whose research and experiences collectively form the body of knowledge about healing. Collaboration is valuable in all professions, but in medicine it is especially so. New diagnostics, revised treatments and current techniques, warnings of epidemics on the way, reports of new drugs and devices form a corpus of information that enables physicians to see the full picture and to offer their patients the best possible care. Good doctoring requires good collaboration, and that requires good communication.

Doctors in many poor countries diagnose patients, treat illnesses, and perform surgeries with an understanding of medicine that is years out of date. Through no fault of their own, these doctors rely on scraps of information that come from aging journals and dog-eared textbooks passed around from hand to hand. News about the latest research, medical innovations and clinical practices that, in developed countries stream rapidly to medical schools and hospitals, is slow to reach doctors tucked away in countries where conditions are taxing and communications are poor. As a result, these secluded doctors practice outdated medicine on populations whose lives are already burdened by poverty and isolation. Patients who might be cured remain ill; those who might be saved, can die.

Many times, it isn't a matter of medications or instruments; it's a matter of information and education. It's a matter of doctors sharing in the knowledge abundant elsewhere, so they can diagnose illnesses, prescribe successful treatments, and explain preventions that lead people to good health. Where Western countries benefit from information riches, these remote regions have remained out of sight, out of mind, and out of touch.

Through most of the 1900's, with few available journals and textbooks, obtaining medical updates in remote regions required that professionals from more fortunate and less remote regions get transported. Experts from abroad could visit or if resources for travel were made available, local doctors could visit colleagues outside. At best, this has been a thin and erratic stream of information, and it has never been enough to sustain technical currency. As a consequence, the quality of care in many regions fell farther behind. With the increasing pace of developments in diagnoses and treatments, the gap between rich and poor countries has grown.

Technology, however, and its use in medical education has just begun to change that dramatically as journals and textbooks, along with a host of new educational media, are being made available quickly and at low cost. Moreover, live lectures, case consultations, and other instant forums are easy to schedule on the Internet, so no one has to travel to dangerous or faraway locations.

A non-profit uses IT for medical education in third world and war-torn countries

Starting in the late 1990s, a California based not-for-profit organization pioneered the use of computer technologies for medical education in remote regions. First, it supplied computers and CD-roms to war affected countries in the former-Yugoslavia. Upgrading later to hard drives packed with medical libraries, it brought educational material to Africa, Central America, and Iraq. Most recently, it has converted

to an Internet-based delivery system that provides not only access to medical libraries, but training courses, and other real-time educational services. To date, the organization has established nearly 100 medical education centers in 12 developing countries; it has arranged for a consortium to prepare content; Now this organization is configuring IT tools to deliver educational programs to doctors beyond the "last mile"—in rural areas where Internet service is lacking or limited.

In many locations, the organization sets up Medical Information Centers (MICs) that connect isolated doctors and other health care professionals to electronic medical information. Typically located in hospitals or clinics, these centers supply isolated doctors and other healthcare professionals with:

- Computers, Internet access (where possible), studio cameras for teleconferencing, satellite gear (if necessary), and other technology
- Medical curricula delivered via the latest technologies
- Connections with well-trained experts in developed regions

A volunteer-driven organization, WiRED works in partnership with university and hospital administrators in host countries to secure facility locations and arrange for program content. It contracts with local vendors and technicians to set up the centers. After lining up content specialists in medical schools and research centers, WiRED helps coordinate the delivery of education and information programs and fosters exchanges among participants.

Its work in Iraq, where WiRED has installed 39 MICs, illustrates the concept. Arriving on the heels of the first American troops in 2003, WiRED technicians, working collaboratively with Iraqi doctors and IT specialists, quickly installed e-libraries in nine leading medical schools and teaching hospitals in and around Baghdad. Information-poor physicians became avid users of these facilities as they accessed current journals and textbooks and other resources through CD-roms and the Internet. Over time, the organization added teleconferencing and other programs.

In 2008, a U.S. State Department representative contacted WiRED for assistance with a cholera outbreak in Kirkuk. Insurgents had prevented foreign doctors from entering that city, so WiRED was asked to "build an electronic bridge" to join doctors in Kirkuk with experts on the outside. Within days, the non-profit provided world-class cholera training programs developed by leading infectious disease specialists at the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) in Dhaka. Days later, WiRED arranged teleconferences between doctors in Kirkuk and an international team of experts. The program provided rapid assistance and opened the doors for long-standing collaborations between doctors in Kirkuk and doctors outside.

The benefit of technology is that it helps doctors isolated by economics, politics, and war rejoin their less isolated and more fortunate colleagues. Technology can bring the world's most isolated doctors together with the world's best trained, best outfitted doctors and enable them to talk medicine together. They can discuss experiences and ways to address tough cases. Together they can examine research, promising techniques, and methods of curbing epidemics. And, sometimes, these men and women can just talk about doctoring in places worlds apart. WiRED provides the equipment, the coordination and the contacts to create these forums. These opportunities improve medical science and ease the isolation of doctors serving in regions the world sometimes forgotten.

The International Telemedicine Network

In 2009, WiRED helped organize the International Telemedicine Network (ITN) comprising prestigious medical institutions such as the University of California, San Francisco; George Washington University; Claremont Graduate University, Arizona Cancer Center and ICDDR,B. This consortium provides complete training courses, packaged for easy access through the Internet.

The ITN study modules include readings, videos, animations, PowerPoints, all integrated with narratives and lectures that connect the elements and flesh out details. The best analogy is a college course. A professor prescribes readings and other course material and then brings it all together through discussion. The training modules are complete, ready-to-go courses. Soon, the program will include real-time, interactive follow-up sessions, all conducted on the Internet. Not only can the ITN supply recurrent educational programs, it also can respond rapidly to emergencies, epidemics, and other urgent requests.

The Last Mile

As technology spreads throughout developing regions, doctors in large cities now are finding easier access to medical information. Moreover, large organizations and medical institutions from advanced countries are reaching out to developing regions, so we expect considerable progress during the next decade.

Most of the outreach, however, is to large-population areas and misses the backwaters. Beyond the metro areas, the news is not so encouraging. The likelihood of Internet access diminishes with distance from the cities, and this leaves smaller hospitals and clinics and their doctors off the grid. With time, the Internet will expand in these remote regions, too, but the process is slow.

Currently, WiRED, which, a decade ago, led in the use of technology for medical education in developing regions, is focusing on the "last mile." How can technology bridge that final gap between more abundantly served urban areas and the regions beyond the grid?

Providing Internet connections in these outlying locations is cost prohibitive. So, WiRED is in the process of developing a two-step system that makes medical information and training courses available through portable media. How does it work? First, the International Telemedicine Network and other partner institutions prepare courses packaged in self-contained modules. Each module is distributed through the ITN Web portal, allowing doctors with Internet access to work with them directly. Doctors in the last mile can access them through one of two distribution options: portable drives and iPhones. To download this information, WiRED is establishing a distribution tool on the ITN Web portal it calls the Training Course Filling Station.

This process will enable someone to click a single button to download an entire training module to a thumb drive for delivery to laptops in the field. Similarly, a single click will allow the training module to load on an iPhone, Palm or other portable device. Interactivity enjoyed by Internet users isn't possible, but current technology has provided a means of distributing a rich assortment of high-quality medical information to places still waiting for the Net.

In a matter of 15 years, communication technology has provided a way to link doctors in remote regions with their colleagues outside. The isolation and the lack of access to medical developments are coming to an end. That said, the final step is often the most difficult. The challenge now is to reach into the last mile to help many millions of people whose doctors still remain out of sight, out of mind and out of touch. Where you live should not determine if you live.

"I wanted to tell you that for many years, we have studied and practiced medicine without access to the latest technical information. Early in 2003, WiRED installed several Medical Information Centers at Medical City Center and in other Baghdad locations. These facilities gave us the first chance to review the latest journals and research papers. This material and access to the Internet through WiRED's computers have made a big difference in how many Iraqi doctors learn and practice medicine. Our ability to serve patients is better because of this information."

—Dr. Manal Oda

"With all the money being spent in Iraq, the few funds allocated to these computers and databases have to be one of the best investments in our medical future. Good medical practice needs the best information and these Centers help us access it.

—Dr. Sardar Al-Jaff

"I just wanted to tell you that our books have been out of date for many years, we have had no reliable source of medical information. The WiRED Centers, with computers, CDs and Internet access provide our first connection to technical data developed by researchers and doctors in other countries. This information obtained at the Medical Information Centers has been a genuine benefit to me personally and to other Iraqi physicians."

—Dr. Rani Monther

"To have this new information source will be a great advantage in our work and our studies. At this point, we have just a small collection of books and all of them are several printings behind current volumes," he said. "Now we can use this Medical Information Center to access the latest updated information and to stay in touch with our colleagues in other places."

—Medical student Renee Castillo

Saddam's symbol of power near his palace in Baghdad

WiRED's MIC (Medical Information Center) in Baghdad's Medical City Center.

A Doctor reviewing research data in Basrah, Iraq.

WiRED installed MIC in this medical school as a hub of its CHIC (Community Health Information Center program) Nairobi, Kenya

Traditional Healers, an informal health care system in Kenya, use our CHIC to study health Information.

WiRED installed four MICs here in Mostar, Bosnia. Mostar was once a frontier town of Ottoman Empire.

THE VAP CHOLESTEROL TEST:
What Every Primary Care Physician Should Know

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The Vertical Auto Profile test (VAP) is a relatively new cholesterol test that directly measures subclasses of Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL) and High Density Lipoprotein (HDL), as well as Lipoprotein A. The test was created by Jere Segrest MD, PHD at the University of Alabama and a company called Atherotech was formed in 1999 that subsequently patented the work.

Its been dubbed as one of "Five Tests Worth Paying for" by The Wall Street Journal, and Forbes Magazine hails the Vertical Auto Profile cholesterol test as one of the "Ten Ways to Live Longer." Patients everywhere are talking to their primary care physicians about this innovative test and whether it would be beneficial for their health. It's our obligation as physicians to educate ourselves, as well as our patients, and help make informed decisions about their health with the most up-to-date, evidence based approach as possible. This article helps explain the history and significance of the Vertical Auto Profile Cholesterol test, as well as its strengths and limitations to date. At the conclusion of the article it is the hope of the authors that the physician reader will have the background knowledge and current data to make accurate and useful decisions regarding the use of VAP cholesterol testing and the health of their patients.

One of the biggest differences between traditional lipid panels and the VAP test, is that traditional lipid panels estimate the LDL with the equation LDL = total cholesterol – HDL– (0.20 × triglycerides), while VAP test directly measures the LDL, independent of other lipid parameters. Also, VAP measures many individual subclasses of LDL VLDL and HDL. The Vertical Auto Profile test separates LDL into 3 components: LDL-C, Lp(a), and IDL. It directly measures triglyceride-rich lipids: VLDL (1,2,3 and total), and it measures the HDL subclasses HDL2 and HDL3. Finally, the VAP test measures the pattern density of an individual's LDLs to see if one has predominately large buoyant LDL particles or if one has the more atherogenic small, dense LDL pattern density.

The VAP test has many clinical strengths that the inquisitive physician should be aware of when taking care of their patients. Thus far the VAP test has shown evidence that it may be superior at identifying a far greater number of individuals at risk for cardiovascular incidents. One of the reasons why, is that the conventional lipid panel merely estimates the LDL, and in some instances, the estimate can be fairly inaccurate, especially when HDL levels are very low or triglyceride levels exceed 150 mg/dl. In these circumstances, "LDL cholesterol values may underestimate true lipoprotein-associated risk of CHD; such patients therefore may benefit from using the more sensitive measures of the number of apoB particles or the number of LDL particles…" (Lichtenstein AH). Another added benefit of directly measuring the LDL levels is that the patient need not be fasting to calculate accurate results. This will help increase the sensitivity of test results. A second major strength of the VAP test is that there is supporting evidence that certain sub fractions of the LDL, VLDL and HDL are more strongly associated with an individual's risk of having a cardiovascular incident. For example, a person's LDL may be normal, but if one of the sub fractions, like Lipoprotein A is elevated within the total LDL this may indicate a higher risk for heart disease because increased Lp(a) is a genetic risk factor for CAD. Likewise, HDL2 has been shown to be the "best" cholesterol and when low, is a risk factor for CAD, and VLDL3, the smallest and most dense of the VLDL sub particles has been shown to be the most dangerous. (Ziajka) Not only has the sub particle fraction been used to predict cardiovascular incidents, but also the LDL pattern density that the VAP test measures. It has been shown that individuals with a LDL pattern density predominately of small, dense particles (known as Pattern B), are at a greater risk of developing atherogenic changes than individuals with predominately large, buoyant LDL particles, known as Pattern A. Some sources speculate that the VAP test, as opposed to the traditional lipid panel, may identify up to 40% more individuals at risk for coronary artery disease. (Ziajka)

Another clinical implication of the VAP test has to do with the pharmacologic basis of what drugs work best at targeting the individual subclasses of the LDL, VLDL and HDL. One major study, summarized in the charts below, has shown strong evidence to support that certain drugs of different classes, and even within a given class, are much more effective at lowering or increasing levels of the various subclasses.

Impact on Therapy - Statins

Agent	LDL-C	LDL Size	Lp(a)	HDL_2	$VLDL_2$
Lovastatin	~21–42% Reduction	↑	↑	↑	↑
Pravastatin	~22–34% Reduction	↓ ↔	↔	↑	↓
Simvastatin	~26–47% Reduction	↑	↔	↑ ↑	↓
Fluvastatin	~22–36% Reduction	N/A	N/A	↑	↓
Atorvastatin	~40–60% Reduction	↑	↑ ↑	↓	↓ ↓
Rosuvastatin	~46–55% Reduction	↑	↔	↑ ↑ ↑	↓ ↓

The charts show how many cholesterol medications work on increasing or decreasing the subfractions LDL-C, LpA, HDL2, VLDL3 and LDL size.

Impact on Therapy - Other Agents

Agent	LDL Size	Lp(a)	HDL_2
Gemfibrozil (Lopid)	↔ ↑	↔	↔
Fenofibrate (Tricor)	↑ ↑	↓	↔
Ezetimibe (Zetia)	↑	↔	↓
Colesevelam (Welchol)	↑	↔	↔
Colestyramine (Questran)	↑	↔	↔
Colestipol (Colestid)	↑	↔	↔
Niacin	↑ ↑ ↑	↓↓	↑ ↑ ↑
Omega-3 Fatty Acids	↔	↓	↔

- Using VAP Expanded Lipid Testing from Atherotech to Develop Optimal Patient Treatment Plans
  Paul E. Ziajka, M.D., Ph.D

If research continues to support that certain sub particles carry their own independent risk of cardiovascular disease, and that certain pharmacologics target these individual risk factors, the clinical implications of utilizing VAP testing to prevent cardiovascular incidents in our patients could be profound

The VAP test has a slew of clinical strengths to keep in mind, but there are also current shortcomings and points to consider before we recommend this test on all our patients with potential CV risks. Whenever we order a medical test we need to ask ourselves how the results will change our management of the patient. Based on the results should we start cholesterol lowering meds? And if so at what dose? Will the rate of CV incidents and deaths decrease? And by how much? The answers to these questions appear to be the major shortcomings of this diagnostic test as there are currently no large scale studies that compare dosaging of drugs to VAP risk factors and to the percent change in cardiovascular incidents and patient survival. Although MD Consult and Up To Date, two widely accepted electronic medical resources, generally agreed that VAP testing would be very beneficial at identifying many more patients at risk for CV disease, and both made many references to the profound usefulness of VAP testing in the future, both appear hesitant to suggest such testing at this point. In a major article on MD Consult combining the results of 36 independent articles, MD Consult states its position on the usefulness of VAP testing as follows:

"Such goals based on advanced lipoprotein tests do not yet have sufficient supporting evidence to serve as population guidelines. Although such goals may reduce clinical events, the magnitude of such reduction is unclear, and the cost of such an approach remains to be seen."

- MD Consult- Advanced Lipoprotein Testing: Recommendations Based on Current Evidence- Mar 2009

Similarly, Up to Date gives this assessment of VAP:

"Higher LDL particle number has been associated with cardiovascular disease incidence, but studies have not determined whether any measures of LDL subfractions add incremental benefit to traditional risk factor assessment. Routine use of clinically available LDL subfraction tests to estimate cardiovascular disease risk is premature.

- Up to Date- Systematic review: association of low-density lipoprotein subfractions with cardiovascular outcomes- Apr 2009.

The goal of this article is not to simply recommend for or against the Vertical Auto Profile test, nor provide a list of articles that make those suggestions. Recent evidence does suggest that VAP testing would help identify significant numbers of people at risk for CVD compared to standard lipid panels, and it is clear that our current guidelines fail to identify a significant portion of the population with increased risk for CVD. However, it is also apparent that the results of VAP testing do not yet have data to serve as population guidelines. Medicine is a science, but it is also an art. The primary care physician must consider the scope of this test, taking into account the strengths of its clinical implications as well as its current shortcomings. With this knowledge primary care physicians can then decide if the VAP test is medically appropriate to order, and how the results will change the management of their patients.

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HEALTH CARE REFORM ACT H.R. 3590

The Patient Protection and Affordable Care Act of March 23, 2010

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The Patient Protection and Affordable Care Act, health system reform legislation signed into law by President Obama on March 23, 2010 has many significant benefits for patients, and some insignificant benefits for the physicians.

How health system reform affects patients:

The Patient Protection and Affordable Care Act, H.R. 3590 health system reform legislation signed into law by President Obama on March 23, 2010 has many significant benefits for patients—those who already have health insurance and those who don't. While some benefits take effect in 2010, many others will be phased in over several years to allow the health care system to absorb the changes ahead. Here's a snapshot of those benefits as provided by AMA News:

Patient benefits that take effect in 2010

For patients with private health insurance:

- Your insurer can no longer drop you from your plan if you get sick.
- Children ages 18 and younger can no longer be denied private insurance coverage if they have a pre-existing medical condition. (While some ambiguities have been raised about application of this provision, implementing regulations will clarify that the prohibition on pre-existing condition exclusions for children will begin as planned in September. America's Health Insurance Plans (AHIP) has stated it will fully comply with the regulations.)
- For adults with pre-existing medical conditions who cannot obtain private insurance coverage, a temporary national "high-risk pool" will be established to provide coverage, with financial subsidies to make premiums more affordable, until all insurers are required to cover people with preexisting conditions in 2014.
- Young adults up to age 26 can remain as a dependent on their parents' private health insurance plan.
- Your health insurance benefits can no longer run out because of a long or expensive illness because insurers can no longer impose lifetime financial limits on benefits.
- Preventive services for women, such as mammograms, and immunizations for children must be covered by insurers, with no co-payments or deductibles required. In addition, Medicare patients who will hit the coverage gap known as the "doughnut hole" this year under the prescription drug benefit will receive a $250 rebate from Medicare.

Patient benefits that take effect during the next four years

In the private health insurance market:

- U.S. citizens and legal residents cannot be denied private health insurance coverage for any reason, beginning in 2014. All U.S. citizens and legal residents must obtain health insurance coverage or pay a minor tax penalty (although there are some exemptions). This is to ensure that everyone is in the insurance pool so that no one can get a "free ride" by not having affordable coverage and then going to an emergency room for care.
- State-based health insurance exchanges will begin operating in 2014, where people who do not

have access to employer-based insurance can shop and compare the benefits and costs of private health insurance plans. These exchanges will create insurance pools that will allow people to choose among affordable coverage options. All insurance companies in the exchange must provide at least a minimum benefit package, as well as additional coverage options beyond a basic plan.

- Federal subsidies through tax credits or vouchers will be provided in 2014 to people who cannot afford the full cost to help them purchase coverage through the exchanges.

- Beginning in 2011, states can require insurance companies to submit justification for premium increases and can impose penalties for excessive increases.

For patients enrolled in Medicare or Medicaid:

- You no longer will pay any cost sharing for a number of preventive services, effective Jan. 1, 2011.

- If you are subject to the "doughnut hole" for your Medicare drug coverage, you will receive a 50 percent discount on those prescription drugs beginning Jan. 1, 2011.

- A series of pilot programs will be implemented during the next four years to help find new ways to improve quality and lower the cost of the care you receive from your doctors, hospitals and nursing homes in the Medicare and Medicaid programs.

- Medicaid coverage will be expanded in 2014 to all eligible children, pregnant women, parents and childless adults under age 65 who have incomes at or below 133 percent of the federal poverty level.

How health system reform affects physicians:

American Medical Association has published the following brief summaries of the provisions of the Implementation Timeline Under H.R. 3590 ,The Patient Protection and Affordable Care Act of March 23, 2010

Following is a timeline description of some of the major provisions of the health system reform legislation that the President signed into law on March 23, 2010.

- Extension of medical liability protections under the Federal Tort Claims Act to officers, governing board members, employees and contractors of free clinics.

- Fully funded practice expense Geographic Practice Cost Index (GPCI) floor increase: 2010 and 2011.

- Work GPCI floor extension: Effective for 2010.

- Administrative Simplification: The operating rules development process begins. Health Plans must adopt and implement a set of operating rules for certain electronic transactions within specified time periods on future dates.

- Small business tax credits for employee insurance plans phase-in begin.

- Temporary reinsurance program for employers providing health insurance coverage to retirees over age 55 who are not eligible for Medicare.

- Temporary national high-risk pool to provide immediate access to health coverage for individuals with pre-existing medical conditions.

- Dependent coverage for children up to age 26 in all individual and group policies.

- Prohibit rescissions of coverage in all plans, except in cases of fraud.

- Prohibit lifetime limits on coverage and restrict annual limits in all individua and group health plans.

- Prohibit pre-existing condition exclusions for children in all plans. (While some ambiguities have been raised about application of this provision, implementing regulations will clarify that the prohibition on pre-existing condition exclusions for children will begin as planned in September.

The America's Health Insurance Plans (AHIP) has stated it will fully comply with the regulations.

- This document highlights the implementation timeline for provisions in the H.R. 3590 relating to elements included in American Medical Association Resolution 203 (I-09). A more comprehensive summary document will be forthcoming.

- Require new group and individual health plans to cover certain preventive services and immunizations without cost- sharing.

- Require health plans to report medical loss ratios.

- Establish process for states to review and report increases in health plan premiums, and for plans to justify their increases.

- Establish the Patient-Centered Outcomes Research Institute to contract with appropriate federal agencies or the private sector to conduct comparative effectiveness research (CER).

2011

- Primary care/general surgery Medicare bonus (10 percent over 5 years): Effective January 1, 2011 through December 31, 2015. Primary care bonus applies to primary care physicians (family medicine, internal medicine, geriatric medicine or pediatric medicine) and practitioners (NP, CNS, or PA) for whom primary care services (HCPCS codes 99201-99215; 99304- 99340; and 99341-99350) account for at least 60 percent of Medicare allowed charges over a designated time period.

- Funding for state demonstration programs to evaluate alternative liability reform models authorized for five fiscal years.

- Physician Quality Reporting Initiative (PQRI) bonuses: Effective for 2011 through 2014, with 1 percent bonus in 2011 and 0.5 percent bonus in subsequent years.

- Plans required to provide rebates if medical loss ratios exceed required minimums.

- Secretary of Health and Human Services (HHS) to oversee convening of stakeholders to receive input on an ICD-9-CM to ICD-10 crosswalk by January 1, 2011.

- Coverage for Medicare wellness and preventive care services, incentives for Medicare preventive services established through elimination of coinsurance.

- Coverage for preventive services and eliminate cost-sharing for such services in Medicaid, and require coverage of tobacco cessation services for pregnant women.

- Restrictions on physician ownership of specialty hospitals: New requirements for meeting exception for physician ownership of hospital effective 18 months after enactment. To qualify for the exception the physician ownership or investment and provider agreement must be in place by August 1, 2010 (or December 31, 2010 if the Reconciliation Bill is enacted).

2012

- Practice expense GPCI floor subject to budget neutrality adjustments.

- Medicare claims data release: Effective January 1, 2012.

- Secretary of HHS to solicit input and consider additional electronic transaction standards and operating rules by January 1, 2012.

- Adoption of unique health plan identifier system must occur no later than October 1, 2012 (through rule making).

- Government Accountability Office (GAO) must issue a report on whether new federal policies, standards and guidelines would create causes of action against health care providers.

2013

- Public reporting of physician performance information to begin January 1, 2013.

- Administrative Simplification: Starting December 31, 2013, health plans would be required to file a certification statement with the Secretary of HHS that their data and information systems comply with the most current published standards.

- Administrative Simplification: Operating rules for eligibility and health plan claims status transactions take effect by January 1, 2013.

2014

- Requirement for most individuals to have acceptable coverage or pay a tax penalty; tax credits and cost-sharing subsidies available.

- Health insurance exchanges established in each state for individuals and small businesses; provide choice of

coverage through a multi-state plan.

- Require all qualified health benefits plans to offer at least the essential health benefits package (except grandfathered plans).
- No annual limits on dollar value of coverage.
- Penalties on employers of more than 50 who do not offer coverage and have at least one full-time employee who receives tax credit.
- Require guarantee issue and renewability, limited rate variation, risk adjustment in individual and small group markets, no pre-existing condition exclusions for adults.
- Ensure coverage for individuals participating in clinical trials.
- Limit any waiting periods for coverage to 90 days.
- Expand Medicaid to all individuals under 65 with incomes up to 133 percent of federal poverty level; enhanced payments for primary care physicians in 2013 and 2014.
- Allow states to create a Basic Health Plan.
- Enhanced employer-provided employee wellness programs.
- Administrative Simplification: Operating rules for electronic funds transfers (EFT) and health care payment and remittance advice to take effect by January 1, 2014 (Health care providers, including physicians, must also comply with EFT standard for Medicare payments by January 1, 2014).

2015

- Independent Payment Advisory Board (IPAB): First implementation year of IPAB Medicare cost reduction recommendations.
- PQRI penalties: Effective beginning 2015 (1.5 percent); (2016 and subsequent years, 2 percent).
- Cantwell cost/quality value index: Effective January 1, 2015 (based on 2014 performance).

2016

- Multi-state compacts to allow insurers to sell policies across state lines (regulations by July 1, 2013).
- Administrative Simplification: Operating rules for health claims or equivalent encounter information, enrollment/disenrollment in a health plan, health plan premium payments, and referral certification and authorization transactions to take effect by January 1, 2016.
- Administrative Simplification: Adoption of health claims attachments standard and operating rules to take effect by January 1, 2016.

Sustainable Growth Rate Formula mess:

The US House of Representatives passed on November 2009, a Democratic-sponsored bill H.R. 3961 that would rewrite the controversial sustainable growth rate formula in Medicare and eliminate a 21.2% Medicare pay cut for physicians scheduled for 2010. But the senate squashed the SGR bill. Unlike its House counterpart, the Senate bill would have frozen physician payment rates at their current levels. Senate Democrats maintained that separate healthcare reform legislation would have built on the SGR bill to make Medicare reimbursement more attractive to physicians. Unless the House & Senate pass a bill to permanently fix the SGR to eliminate a 21.2% Medicare pay cut for physicians by June 1, 2010 the physicians stand to loose more than one fifth of their income this year.

Healthcare management in the other countries:

Canada:

Publicly-funded Healthcare system, most of the services provided by private companies.

Population of 30 million, GNP $760 million, Per Capita $24.00 Highest tax bracket: 45%

U.K.:

NHS (National Health Service) Publicly-funded Healthcare system, most of the services are provided by the government. It is a single – payer/single provider system. General Practitioners share the capitation fund proportionately linked to membership. They

depend heavily on preventive care measures. Hospitals and physicians are run by the government.

Population of 60 million, GNP $1544 million, Per Capita $26 K. Highest tax bracket: 45%

Norway:
Norway is a welfare state. They have universal healthcare system. Funded by the tax-payers' money through the government. It is not linked to employer. On per capita basis, Norwegians spend about $ 4800.00/year on Healthcare.

Population of 4.8 million, GNP: $ 257 billion, Per capita $53k. Max. Tax Bracket: 70.9% (marginal tax=50% + wealth tax=1.1% + surtax = 12% + National Insurance tax = 7.8%)

The Healthcare's big picture:

U.S. population of 310 million, GNP: 12,540 billion, per capita 38K, spend an average of $7500/year for health insurance

Currently insured population :

- 186 millions are getting health insurance through employer
- 40 million Americans are insured through Medicare
- 38 million Americans are insured through Medical

Un-insured population:

- Out of 46 million Americans who were without any Healthcare insurance now the 32 million uninsured Americans will be covered under the new HR 3590 Act. But some 14 million undocumented illegal immigrants are left out in the cold without any help for health insurance.

The Cost of the Healthcare Reform Act HR 3590, according to U.S. Department of Health and Human Services, will be over $4.3trillion and comprise 19.5 percent of the gross domestic product (GDP) by 2017. The revenue to cover 296 million Americans will be raised through the following methods:

- Refundable Tax Credit:
  For single: max income <$15K (full credit) / <$30K (partial credit); max credit $2500
- Medicaid/SCHIP Eligibility:
  Everyone up to 200% FPL (Federal Poverty Level) eligible for Medicaid
- Individual Mandate:
  Penalty: 50% of premium; eligible for full premium subsidy up to 100% FPL, partial subsidy capped at 300% FPL
- Employer Mandate: Pay or Play
  Mandate applies to firms with more than 10 employees; penalty for noncompliance is 10% of payroll
- 5.4% Surtax on the 0.3% of earners.
- Cutting Medicare Advantage programs.

Effects on the Physicians, and Hospitals:

The physicians have to brace for the 19% increased work load taking care of the newly insured subscribers, by Medi-Cal/ Medi-Caid getting 70% less reimbursements. Some of the physician practices might not be able to absorb the loss, and thus the older physicians may have to retire early, further decreasing the available manpower. The hospitals will be more or less in the same boat.

Healthcare reform is designed to facilitate or accelerate efforts to improve the delivery of health care services through better information, innovative models of care, or better infrastructure. The time will tell if the HR 3590 Act will accomplish that!

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RESTLESS LEGS SYNDROME

"The Phantom of the Night"

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"From Goulies and Ghosties,
And Three-leggity Beasties,
and things that go bump in the night,
Good Lord deliver us!"

— An Olde Scottish Prayer

Those old Scots must have known something about Restless Legs Syndrome [RLS] to be praying for deliverance from "things that go bump in the night". RLS can be subtle and undiagnosed for decades, or it can painfully obvious to those afflicted and their loved ones. It can occur in the young and old. (See Slide 1). It can occur day or night, and even present itself as insomnia. My goal, in the short space of this article, is to give the reader some knowledge about Restless Legs Syndrome, its presentation, and its treatment.

RLS is characterized by disturbing sensations in the limbs, usually the legs [but can also be arms and shoulders]. The morbidity of RLS can include discomfort, pain, excessive tiredness, sleep disturbance, and/or sleepiness. Sleep disturbance is the primary complaint [95%] and a circadian pattern is typical [worse in the evenings and night]. After a few hours of interrupted sleep the limb discomfort usually abates. Symptoms are increased by anything that decreases level of awareness [ETOH, sleepiness] and can be reduced by movement [sitting up, walking, rubbing legs] or other activities [eating, hot baths, etc.]. It was first described in the 1600's and was given it's moniker by Ekbom in 1945. It occurs in less than 10% of young adults and can approach 30% among the elderly. The age of onset was under 10 years of age in 20% of all RLS suffers. (See Slide 2 and 3).

There is a strong genetic component [Autosomal Dominant], but secondary RLS [Iron Deficiency, Renal Failure, Pregnancy, Neuropathy, Parkinsonism] is also very common. Central dopaminergic dysfunction is at the heart of RLS. Dopamine Agonists [typically Pramipexole or Ropinirole] are the mainstays of treatment once Iron Deficiency has been ruled out.

In the elderly with RLS, the average Ferritin level was 33 mg% ["normal" 15-300 mg %] while in control subjects it was 59 mg%. In Parkinson's Disease [PD], 21% had RLS symptoms and PD preceded the RLS in 69%. In Chronic Renal Failure [CRF], RLS can be seen in 20-25% of the patients and usually correlates with the patient's hemoglobin level. The advent of erythropoietin therapy for anemia in CRF has reduced the frequency of RLS in this population.

Diagnosis of RLS can be accomplished by: Self report logs, diagnostic questionnaire, patient interview, ambulatory monitoring [actigiraphy], and polysomnography if needed. Very often RLS patients will have Periodic Limb Movements of Sleep [PLMS] ongoing through out the night after their limb discomfort has subsided. Some patients will have only PLMS which cause sleep disruption without any sign or report of RLS.

Children can have the same complaints as adults and be diagnosed if, in addition they have 2 of the 3 following findings: #1- Sleep disturbance for age, #2- Parent or Sibling with RLS, #3- Polysomnography with 5 or more PLMS/hour of sleep. Growing Pains and Attention

Deficit Hyperactivity Disorder are in the differential diagnosis of RLS in children. The age of onset can be as early as infancy. Besides the autosomal dominant mode of inheritance in many children with RLS, 72% have a ferritin level less than 50 mg% and 76% of those responded favorably to Iron therapy. Even PLMS in these kids dropped from 28/hr to only 13/hr when Iron therapy was used. In children with ADHD, 36% had increased PLMS, while those with increased PLMS, 44% had ADHD. (See Slide 4, 5, 6, 7)

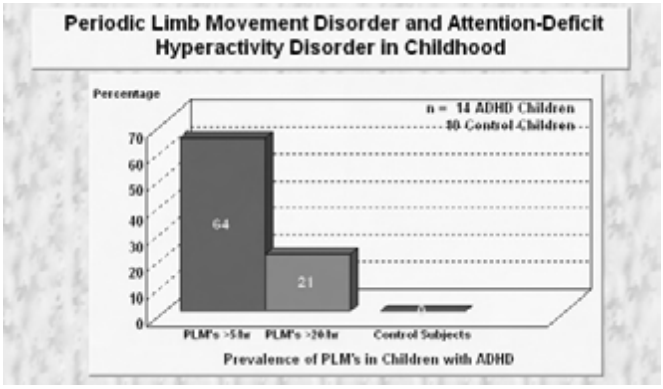
The mainstays of treatment for RLS are Dopamine Agonists such as Mirapex ® and Requip ®. Sinemet ® was used originally but, after one month, symptoms would return requiring an increased dose or a drug holiday to improve the drugs effectiveness. Benzodiazapines [Klonopin ®], Opoids [Vicodin ®, Darvocet ®] or Anticonvulsants [Neurontin ®] will reduce the limb discomfort but don't prevent the limb movements. Even old line agents such as Clonodine or NSAID's have been used with limited benefit.

While treatment can commence with the above agents, a serum ferritin must be drawn and then concomitant therapy with Iron given if the level is less than 50 mg%. Iron therapy has the potential to cure RLS and not just provide for an ongoing medication regime. One caveat is, to list the reason for a ferritin level as "R/O Iron Deficiency Anemia". Curiously, Medicare/Insurance Cos. don't recognize the association of RLS/PLMS with a low ferritin, despite the abundance of literature on this finding.

Other treatment can be employed such as behavioral [exercise, hot baths, and massage], caffeine restriction, and good sleep hygiene. Pregnant women may need lifestyle management and a mild opoid. For intense pain, Neurontin ® should be considered along with a dopamine agonist. (See Slide 8, 9, 10)

I hope this article has been useful and if I can be of further help, please do contact me. Further information and educational material can be obtained from the Restless Legs Syndrome Foundation [www.rls.org] or the National Sleep Foundation [www.sleepfoundation.org].

(below are all slides from 1-10)



Slide 1

Slide 2

Slide 3

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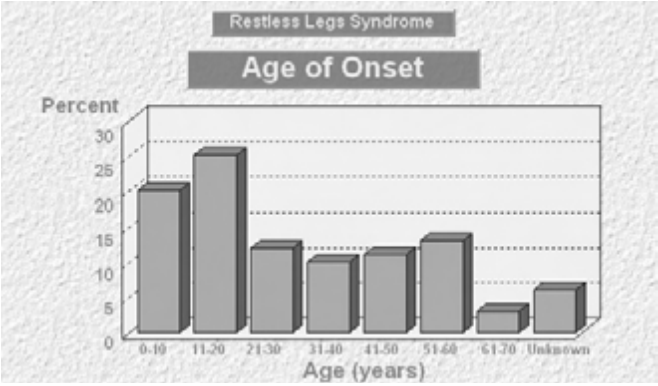

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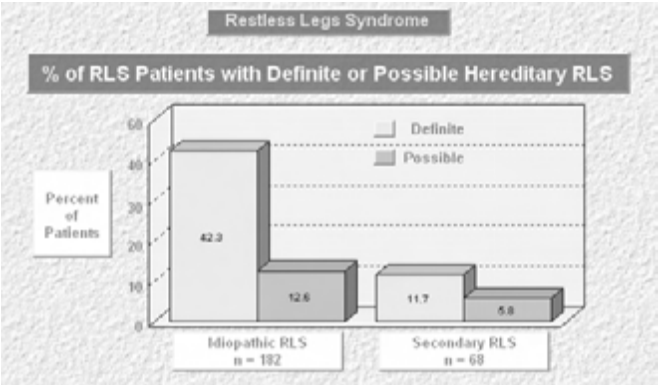

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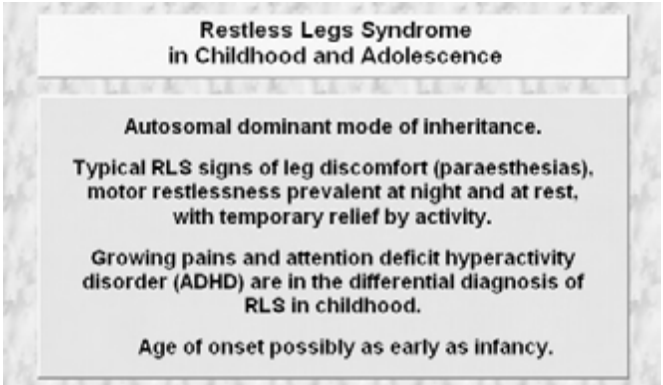

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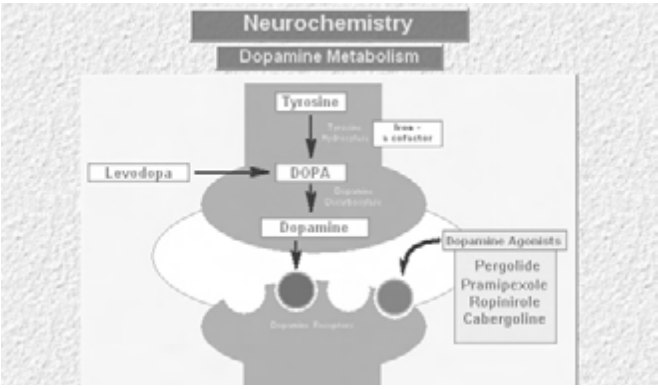

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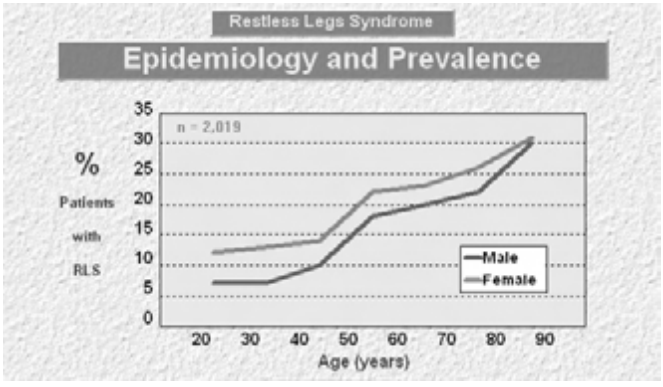

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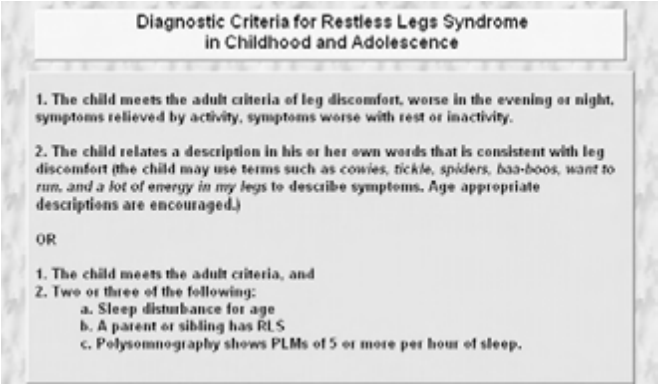
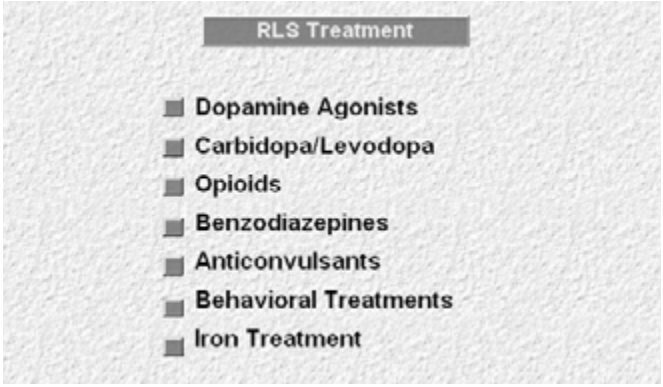


RLS+ Dx Criteria



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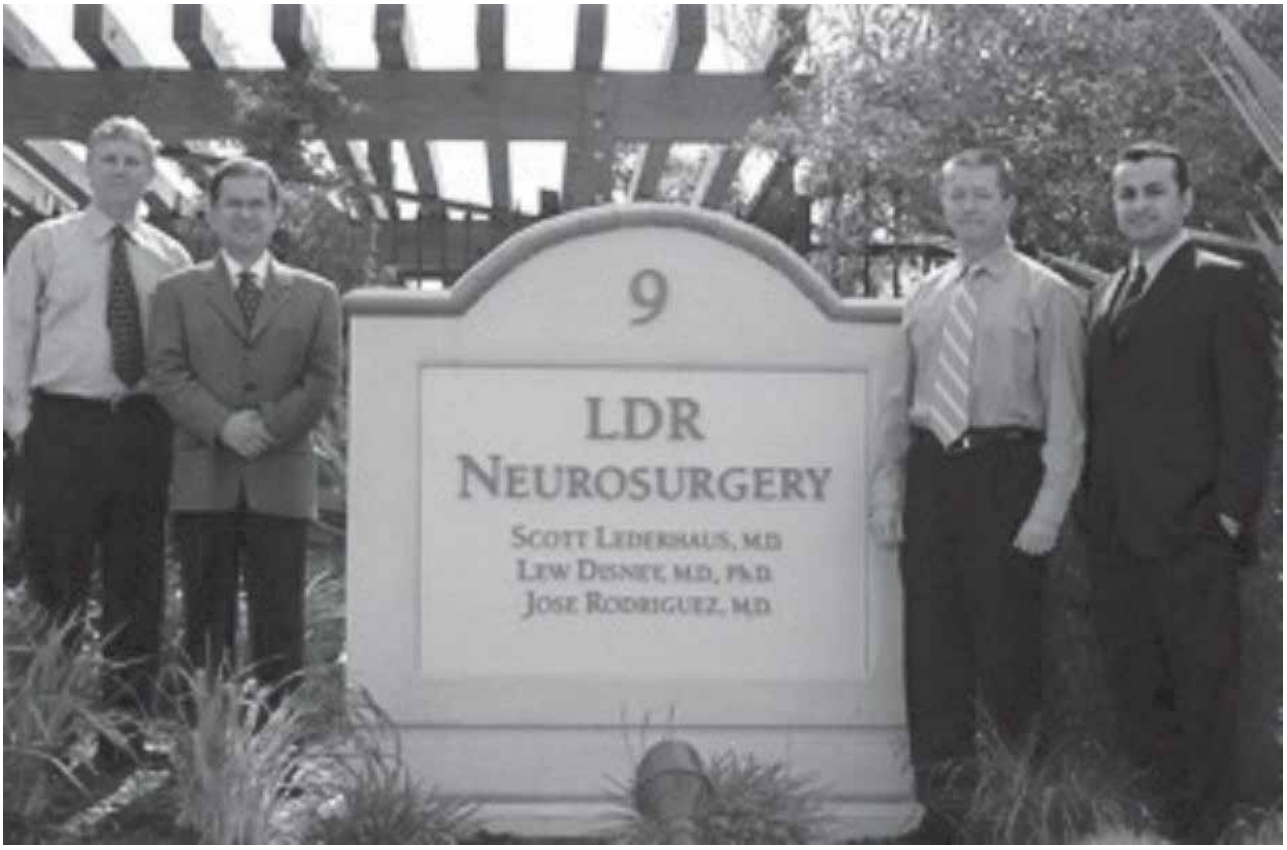

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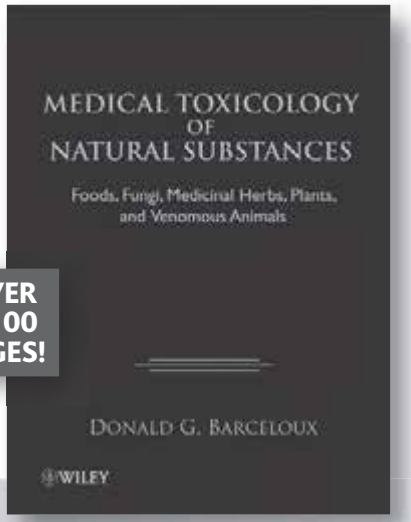

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