The Journal of Southern California Clinicians

IN THIS ISSUE:

Editorial
Preface for 3rd Edition 4
On Practicing Medicine 5

Original Article
Diagnosis of Celiac Disease: An Update for Primary Care Physicians 7
Hyperthyroidism in the General Population and Hypothyroidism in Older People: A Clinical Assessment 12
Recent Advances in Nephrology 15
Neurosurgery and Neuronavigation at Pomona Valley Hospital Medical Center 20
Osteopathic Medicine & the Geriatric Patient 25

Case Reports
Hypercoagulability State 31
Non-Invasive Imaging Strategies in Vascular Disease 36
Natural Killer (NK) T-Cell Lymphoma Presenting as Skin Lesions of Undetermined Etiology 39

Orthopedic Review
Current Concepts in Treating Rotator Cuff Tears 48

Special Reports
Use of Ultrasound in the Emergency Department 51

Miscellaneous
Our Mission and Purpose 1
Guidelines for Authors 2
Addresses of Article Authors 3
Vitruvian Man 4
Who Should be the Father of Human Anatomy 11
A Letter to all Southern California Clinicians 53
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 specialties 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.

As a self-supported publication, we welcome and depend upon your generous contributions for support. Contact Dr. Yin Lai at (909) 985-0699 to make a contribution.

Southern California Clinicians is published biannually by the medical staff of Pomona Valley Hospital Medical Center at 1798 N. Garey Ave., Pomona, California, 91767. Telephone (909) 985-0699. Fax (909) 985-2399. Copyright 2006 by Southern California Clinicians. No part of this publication may be reproduced, stored in a retrieval system or transmitted by any means without the prior written permission of Southern California Clinicians.

The opinions expressed in articles are the authors’ and do not represent the publication or the Editorial Board. The publisher assumes no liability for any material published herein.

We welcome letters to the editor.
Guidelines for Authors

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 disk, CD or E-mail to:

Yin H. Lai, M.D.
S.C.C.
1060 E. Foothill Blvd., Suite 203
Upland, CA 91786
e-mail address: yinhlai@gmail.com
Fax: (909) 985-2399  Tel: (909) 985-0699

Special acknowledgement goes to Rich Yochum, President/CEO of Pomona Valley Hospital Medical Center. He continues to be the main supporter of Southern California Clinicians, both financially and spiritually. Thank you Rich!

Our Supporters

Alpha Care Medical Group
A&B Collaborative, Inc.
Aesthetic Plastic Surgery Institute
California Emergency Physician Medical Group
Casa Colina Centers for Rehabilitation
China Gate Restaurant
Doctor's Hospital Medical Center of Montclair
Durameds, Inc.
Femcare OB-GYN Associates
Greater Pomona Independent Physicians Medical Group
Interlink Health Care, Inc.

Individual Physicians Supporters

Vandana Agarwal, M.D.
M. Feruz Alam, M.D.
Sam Arazoglhi, M.D.
Bijan Badhian, D.O.
Steven Barag, M.D.
Mark H. Barak, M.D.
Linda D. Bosselman, M.D.
Mary Bui, D.O.
Ligoria A. Calaycay Jr., M.D.
Elbert Chang, M.D.
Daniel Channell, M.D., Inc.
Frank Chang, M.D.
Harvey Cohen, M.D.
Stephanie Cooper, M.D.
Alian Candrai, D.O.
Simmi Dhulavi, M.D.
Rasdyn Dinsey, M.D.
Lawr Duney, M.D.
Herbert L. Duverie, M.D.
Behnam Ebrahimi, M.D.
Bharati Ghosh, M.D.
Gene S. Hong, M.D.
Richard C. Homs, Jr, M.D.
Joseph Hourany, M.D.
Frank J. Hsu, M.D.
Che-Yang Huang, M.D.

LDR Neurosurgery Group of Southern California
New Hope Cancer and Research Institute
Nephrology Associates of Inland & Pomona
Pomona Valley Hospital Medical Center In Pomona
San Antonio Community Hospital in Upland
Stanley Kim Cancer Clinic
Sleep and Diagnostic Center at Montclair
Western University of Health Sciences in Pomona
Western University Medical Center in Pomona
Wilshire Oncology Medical Group

Our Supporters

Vandana Agarwal, M.D.
M. Feruz Alam, M.D.
Sam Arazoglhi, M.D.
Bijan Badhian, D.O.
Steven Barag, M.D.
Mark H. Barak, M.D.
Linda D. Bosselman, M.D.
Mary Bui, D.O.
Ligoria A. Calaycay Jr., M.D.
Elbert Chang, M.D.
Daniel Channell, M.D., Inc.
Frank Chang, M.D.
Harvey Cohen, M.D.
Stephanie Cooper, M.D.
Alian Candrai, D.O.
Simmi Dhulavi, M.D.
Rasdyn Dinsey, M.D.
Lawr Duney, M.D.
Herbert L. Duverie, M.D.
Behnam Ebrahimi, M.D.
Bharati Ghosh, M.D.
Gene S. Hong, M.D.
Richard C. Homs, Jr, M.D.
Joseph Hourany, M.D.
Frank J. Hsu, M.D.
Che-Yang Huang, M.D.
John Kim, M.D.
Stanley Kim, M.D.
Amarin Kongphalai, M.D.
Lawrance Lai, M.D.
Scott C. Lederhaus, M.D.
Hedy Lou, M.D.
Paul Lou, M.D.
Sadig Mandilawi II, M.D.
Hla M. Maung, M.D.
M. Rahmi Mowjood, D.O.
Ken Nakamato, M.D.
Brian O’Neill, D.P.M.
Genenoso S. Nery, M.D.
M. Jay Porcelli, D.O.
Jose L. Rodriguez, M.D.
Burr Roermer, D.O.
Rohinder K. Sandhu, M.D.
Jason H. Shen, M.D.
Lance Siegel, M.D.
Max Soliguen, M.D., Inc.
Vanessa Marie Louise Taylor, D.P.M.
Erlinda T. Uy-Concepcion, M.D.
Jin Wang, M.D.
<table>
<thead>
<tr>
<th>Name</th>
<th>Address</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steve Becker, D.O.</td>
<td>309 E. 2nd Avenue, Pomona, CA 91766</td>
</tr>
<tr>
<td></td>
<td>Tel. (909) 981-8943 Fax (909) 981-8943</td>
</tr>
<tr>
<td>Patrick J. Bryan, M.D.</td>
<td>13251 Ventura Blvd., #1, Studio City, CA 010604</td>
</tr>
<tr>
<td></td>
<td>Tel. (909) 450-0369 Fax (909) 450-0366</td>
</tr>
<tr>
<td>Harvey D. Cohen, M.D.</td>
<td>309 E. 2nd Avenue, Pomona, CA 91766</td>
</tr>
<tr>
<td></td>
<td>Tel. (909) 985-2709 Fax (909) 985-3688</td>
</tr>
<tr>
<td>Jose L. Rodriguez, M.D.</td>
<td>1350 W. Covina Blvd., San Dimas, CA 91773</td>
</tr>
<tr>
<td></td>
<td>Tel. (909) 599-0600 Fax (909) 598-0678</td>
</tr>
<tr>
<td>Jin Wang, M.D.</td>
<td>1330 W. Covina Blvd., #205, San Dimas, CA 91773</td>
</tr>
<tr>
<td></td>
<td>Tel. (909) 599-8421 Fax (909) 592-7999 Email: <a href="mailto:rzipsr@msn.com">rzipsr@msn.com</a></td>
</tr>
<tr>
<td>Parris Ware, R.N.</td>
<td>1350 W. Covina Blvd., San Dimas, CA 91773</td>
</tr>
<tr>
<td></td>
<td>Tel. (909) 599-8421 Fax (909) 592-7999 Email: <a href="mailto:rzipsr@msn.com">rzipsr@msn.com</a></td>
</tr>
<tr>
<td>Robert D. Zipser, M.D., FACP, FACG, FACE</td>
<td>1330 W. Covina Blvd., #205, San Dimas, CA 91773</td>
</tr>
<tr>
<td></td>
<td>Tel. (909) 599-8421 Fax (909) 592-7999 Email: <a href="mailto:rzipsr@msn.com">rzipsr@msn.com</a></td>
</tr>
<tr>
<td>Steve Becker, D.O.</td>
<td>1330 W. Covina Blvd., #205, San Dimas, CA 91773</td>
</tr>
<tr>
<td></td>
<td>Tel. (909) 599-8421 Fax (909) 592-7999 Email: <a href="mailto:rzipsr@msn.com">rzipsr@msn.com</a></td>
</tr>
</tbody>
</table>
It's our goal to produce a high-quality medical journal for our medical community. The purpose isn't just to share information, we want readers to join us. Readers might be inspired to write their own articles for publication once they've read the work of their colleagues. This phenomenon is just like a Krebs cycle. All we need is a catalyst. We hope our journal will serve as the catalyst you need.

In this edition, you'll find articles from Dr. Robert Zipser, who gives us the most updated tests for diagnosis of celiac disease, clear, complete and concise. What is “Stereotactic Neurosurgery”? Dr. Rodriguez introduces the concept of neuronavigation to us in a historical approach. Quite amazingly, the technique of trephination was attempted as early as 5000 years ago. The LDR Neurosurgery group, including Drs. Disney, Lederhaus and Rodriguez, is the pioneer that brought the neuronavigational program to Pomona Valley Hospital Medical Center. “The Recent Advances in Nephrology,” by Dr. Jin Wang enlightens our vision in the new world of Nephrology. In “What is Hypercoagulability?”, Dr. Stanley Kim has an unsurpassed answer to satisfy our curiosity. How do we apply osteopathic concept to treat geriatric patients? Dr. Raymond Hruby depicts a thorough coverage on this subject. Also in this issue, we have a concise review of new concepts in treating Rotator Cuff Tears by Dr. Asghar Husain. And our endocrinologist, Dr. Harvey Cohen, has an updated review on diagnoses of thyroid dysfunctions.

We've created a website for our magazine, so that more physicians will have access to our publication. Our website is www.pvhmc.org/publication/.

As usual, we welcome any comments and opinions from readers. When you write to us, please include your name and address. Please direct any communications to Yin H. Lai, M.D. at the address shown on page two.

from Editor

Vitruvian Man

Created by Leonardo da Vinci

"If a man lies on his back with hands and feet spread out, his navel should be the center of the circle; if he spreads his arms straight out, the length from finger tip to finger tip is equal to his height."

from Editor
When I graduated from medical school in 1968, I swore that I would devote my life to saving lives, treating and curing illnesses with all of my knowledge.

But I’ve learned a few things in 38 years. First, I shouldn’t treat my own family. Second, I can’t treat poor patients who have no money to fill out their prescriptions, go to the hospital, or pay for the tests that they need.

Third, I shouldn’t treat patients who are suspicious of me. I had a few patients who had permanent disabilities due to injuries from Vietnam War. They thought I was Viet Cong before my nurse explained that I am from Taiwan.

Finally, I can’t treat patients who belong to IPAs that I have no contract with.

I got so frustrated with just these problems. And, that was just the tip of the iceberg: The insurance companies hire nurses to approve any requests patients needed. At first I thought I’d need debating skills to force those nurses to approve my requests. Then I figured it out: I’d just ask the patients to use legalese to threaten their insurance companies. Believe it or not, it always works, and saves me a lot of time.

It seems lately that the more time I spend in the medical practice, the less income I will earn. And I’ve been told that the same thing is happening to all of my colleagues. The problem is related to the financial deficits on both the state and federal levels. And CMS (the Center for Medicare and Medicaid Services) has been the main player in the whole scene, and behind the stage, the whole play has been presented by policy writers, including the state, congressmen, and senators. And these, again, depend on whether the president is Democratic or Republican.

Now, it’s obvious. Our medical practice is not that simple any more. As a physician, I can’t just learn only Medicine. I have to learn business administration. I have to learn how to make my voice heard by the community, by the county, by the state, and, by congressman, senators and Mr. President. In order to achieve this, many physicians have joined county medical associations, CMA, AMA, and many other organizations. Then they run for delegates and chairpersons in order to speak for physicians. And, instead of taking care of their patients personally, they have to hire physician assistants and/or nursing practitioners so that they can go to meetings in local communities and fly to state capitals and to D.C. to make their voices heard by government officials at all levels. Some even go to law schools to obtain a J.D. to get broader influences. Eventually some physicians are running super-sized medical practices; some become politicians and even try to run for congressional offices or even, in the case of our most famous case, Howard Dean, U.S. President!

There is a saying in Taiwan: “A good Physician treats People; a good Prime Minister treats a country.”
A great American educator, Dr. Mark Hopkins, in his lecture on “The Law of Love and Love as a Law” said, “The quality of an action can never be the ground of an obligation to do that action. Think of a man’s doing good to another, not from good will, but for the sake of the rightness of his own act. Certainly, if we regard right as the quality of an action, no man can be under an obligation to do an act morally right for which there is not a reason besides its being right, and on the ground of which it is right.” My fellow colleagues, in the twenty-first century, no matter what your specialty is, all of us are practicing Community Medicine. But Hopkins’ message is clear: As doctors, we can’t go wrong by treating the human body. By making our patients healthy, we allow them to be part of—and go on to build—a healthier community.

—Yin H. Lai

Editor
Introduction

Celiac disease is an inherited intolerance to ingestion of wheat and related cereals ("gluten intolerance") causing an immune-mediated damage to the lining of the small intestine. Many of us were taught in medical school that celiac disease was a rare disorder of Northern Europeans, presenting in early childhood with severe diarrhea, malnutrition and growth retardation. However, it is now well-established that celiac disease is not rare; instead it affects more that 1 in 200 Americans. It is also not primarily a childhood disease. Over 80% of patients first develop symptoms in adulthood, with a mean age of 40 to 60 years. Indeed, in one large survey, 15% were elderly with onset of symptoms after age 64, up to age 90. The disease is not limited to Northern European ancestry as it is equally common in the Middle East, India and South America with the greatest prevalence in the sub-Sahara populations of North Africa. Furthermore, the classic presentations of diarrhea and weight loss are also no longer typical, and many patients have predominantly non-intestinal symptoms (see below).

Over the last 2 decades the diagnosis of celiac disease has been revolutionized by the widely available screening blood tests, including antigliadin antibodies, anti-endomysial antibodies (EMA) and anti-tissue transglutaminase antibodies (TTG). However, these simple blood tests are widely under-utilized. A recent consensus conference on celiac disease held by the National Institutes of Health concluded that celiac disease is markedly underdiagnosed in the United States. Further education of health care professionals was recommended to increase recognition and treatment of this disorder.

We recently surveyed 2440 patients with celiac disease and confirmed that primary care physicians made the diagnosis in only 11% of celiac patients. Diagnosis typically required evaluation by 2 or 3 specialists often after long delays. Over 20% of patients had celiac symptoms for more than 10 years before diagnosis. We then surveyed all family physicians in San Bernardino County (70% response rate) to determine their awareness of celiac disease. The physicians were in practice for an average of 20 years, but only 35% had diagnosed even one patient with celiac disease, and only a minority were aware of common adult presentations, associated disorders and the use of blood tests for diagnosis.

The purpose of this review is to provide guidelines to help recognize the presentations of adult celiac disease, the patient groups at increased risk, the associated conditions, and, especially, the non-invasive tests to diagnosis this disorder.

Associated Disorders

In our survey of primary care physicians, most were unaware of those patient groups at higher risk for...
celiac disease. These high risk patients are listed in Table 1. Most important to primary physicians is the association with diabetes mellitus, type 1. Approximately 4% of insulin-dependent diabetics have celiac disease. Treatment with a gluten-free diet reduces episodes of hypoglycemia in those celiac patients with brittle diabetes, although any long term benefit on progression of diabetic complications is not established.

**Common Presentations**

Table 2 lists the common presentations of celiac disease as identified in our survey of over 1000 patients. Note that many of the symptoms, including irregular bowel habits, fatigue, depression and anxiety, and muscle aches are common to other disorders. It is not surprising that many patients were initially diagnosed with irritable bowel syndrome, fibromyalgia or chronic fatigue syndrome before the correct diagnosis was made.

**Less common Associations of celiac disease**

There are several uncommon disorders associated with celiac disease. The intestinal disorders include collagenous and lymphocytic colitis, primary biliary cirrhosis, unexplained elevations of liver enzymes, and added risk of hepatic failure in patients with other causes of liver disease. Most intriguing are the non-intestinal associations with celiac disease. Full explanations for these associations are usually speculative, attributed to lack of micronutrients due to malabsorption, shared genetic linkage, or possibly celiac antibodies cross-reacting with other tissue. Some of these many associated conditions are listed in Table 3.

**Diagnosis**

Although celiac disease, as determined by serology and biopsy, is a common disorder, screening of the general American population is not recommended. It appears that the vast majority of patients with celiac disease have a latent or silent form of the disease, without symptoms. Certainly, celiac disease will progress in some patients with development of anemia, osteoporosis or other symptoms of celiac disease. However, until there is more data on disease progression and on economic issues, there is no mandate to identify all asymptomatic celiac patients and place them on rigid gluten-free diets. Instead, screening is recommended for very high risk individuals and those with symptoms consistent with celiac disease. In these patients, dietary treatment may markedly improve quality of life.

There are several diagnostic tests available for celiac disease. Among the screening blood tests, the anti-gliadin antibody assays have very poor specificity (i.e. many false positives), and this test is no longer a standard for diagnosis. Measurement of anti-endomysial antibodies (EMA) has excellent sensitivity and specificity, generally in excess of 95%, and it is still a very useful test for diagnosis. However, EMA is an immunofluorescent assay requiring subjective grading, with variability among commercial laboratories. The EMA positive predictive value is close to 100%, but the negative predictive value is considerably less. The specific antigen bound by the endomysial antibodies has recently been identified as tissue transglutaminase. Assays of antibodies to human recombinant tissue transglutaminase (TTG) are widely available commercially and utilize the reproducible enzyme-linked immunosorbent assay (ELISA) techniques. TTG assays also have close to 100% positive predictive value, with a good negative predictive value probably better than 90%. It is also less expensive than the EMA assay. Thus, the TTG assay has become the preferred single screening test.
gluten free intervals. The HLA typing is also useful for exclusion in patients with equivocal small bowel biopsies. Small bowel biopsy is considered the gold standard of diagnosis. Biopsy is still required to confirm the diagnosis. EMA and TTG assays measure IgA antibodies, and these assays fail to detect the 1-2% of celiac patients who have IgA deficiency. The antibody tests may have undetectably low titers in patients with only mild or patchy small bowel disease. Thus, patients at high risk with symptoms suggestive of celiac disease deserve small bowel biopsy, even if serology tests are negative (Figure 1). Alas, there is also some variability in the biopsy gold standard. Advanced celiac disease has total villous atrophy on duodenal biopsies, but milder cases may have only patchy areas of atrophy (“subtotal villous atrophy”). Even milder cases may have more subtle villous blunting. However, in all patients with active celiac disease there is increased infiltration of lymphocytes into the epithelium, the single cell layer that lines the villi. Thus, if the biopsy interpretation is equivocal, review of the biopsy specimen for increased intraepithelial lymphocytes is often helpful (normal non-celiac small bowel has approximately 1 intraepithelial lymphocytes per 6-10 enterocytes). As with all pathology specimens, it is essential to provide adequate tissue for analysis. Since mild celiac disease may have only patchy areas of villous atrophy, the standard recommendation is to obtain at least 5 biopsies at the time of endoscopy.

Celiac disease is also increasingly diagnosed as an incidental finding during upper intestinal endoscopy done for other indications. The duodenal appearance suggesting celiac disease and warranting biopsy includes a mosaic appearance or nodularity of the duodenal mucosa, “scalloping” of duodenal folds, and diminished number of folds; although none of these signs are specific. Duodenal villi are easily visualized by immersing the tip of the endoscope into water that had been infused via the biopsy channel. The water magnifies the appearance of villi; lack of visualized villi warrants biopsy. Capsule endoscopy provides similar close up and magnified view of villi, and this procedure has the added benefit of identifying the extent of villous atrophy in the small bowel.

**Conclusions**

Celiac disease is a common disorder in adults, but it is still uncommonly diagnosed. As noninvasive serology tests are widely available, celiac disease can be diagnosed readily by primary care physicians. We encourage greater awareness of the presentations and risk factors for this disorder. Celiac disease diagnosis and treatment should no longer be the realm solely of pediatricians and gastroenterologists.

### Table 1. Disorders with high risk for celiac disease

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Prevalence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus type 1</td>
<td>3-8%</td>
</tr>
<tr>
<td>First degree celiac relative</td>
<td>4-15%</td>
</tr>
<tr>
<td>Sjogren's syndrome</td>
<td>2-3%</td>
</tr>
<tr>
<td>Down syndrome</td>
<td>4-14%</td>
</tr>
<tr>
<td>Turner syndrome</td>
<td>4-8%</td>
</tr>
<tr>
<td>IgA deficiency</td>
<td>2-7%</td>
</tr>
<tr>
<td>Dermatitis herpetiformis</td>
<td>100%</td>
</tr>
</tbody>
</table>

* Approximate prevalence of celiac disease (2,5,12)

### Table 2. Common presentations of adult celiac disease

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Prevalence (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowel habits</td>
<td></td>
</tr>
<tr>
<td>Frequent diarrhea</td>
<td>52</td>
</tr>
<tr>
<td>Varying diarrhea &amp; constipation</td>
<td>24</td>
</tr>
<tr>
<td>Constipation</td>
<td>8</td>
</tr>
<tr>
<td>Change in weight</td>
<td></td>
</tr>
<tr>
<td>Loss</td>
<td>55</td>
</tr>
<tr>
<td>Gain</td>
<td>21</td>
</tr>
<tr>
<td>Stable</td>
<td>24</td>
</tr>
<tr>
<td>Abdominal symptoms</td>
<td></td>
</tr>
<tr>
<td>Gas or bloating</td>
<td>73</td>
</tr>
<tr>
<td>Frequent pain</td>
<td>56</td>
</tr>
<tr>
<td>Infrequent pain</td>
<td>23</td>
</tr>
<tr>
<td>Nausea, cramping, vomiting</td>
<td>46</td>
</tr>
<tr>
<td>General</td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>63</td>
</tr>
<tr>
<td>Fatigue</td>
<td>82</td>
</tr>
<tr>
<td>Depression/irritability/anger</td>
<td>46</td>
</tr>
<tr>
<td>Muscle, joint, bone pain</td>
<td>42</td>
</tr>
<tr>
<td>Confusion/memory loss</td>
<td>37</td>
</tr>
<tr>
<td>Hair loss</td>
<td>29</td>
</tr>
</tbody>
</table>

* Prevalence of presenting complaints (Modified from reference 3)
Table 3. Non-intestinal disorders related to Celiac Disease*

Neurological disorders
- Peripheral neuropathy
- Epilepsy
- Migraine headaches
- Ataxia

Hematologic-Oncologic disorders
- Hyposplenism
- Folate deficiency
- Iron deficiency
- Intestinal lymphoma
- Small bowel adenocarcinoma

Gynecological disorders
- Infertility
- Delayed menarche
- Premature menopause

Dermatological disorders
- Aphthous stomatitis
- Alopecia areata
- Dermatitis herpetiformis

Metabolic Disorders
- Diabetes mellitus type 1
- Osteopenia and osteoporosis
- Autoimmune thyroiditis
- Addison’s disease
- Growth failure

Other disorders
- Idiopathic dilated cardiomyopathy
- Dental enamel defects
- IgA deficiency

*Partial list (1-3,5,7,12)

Figure 1. Diagnostic protocol proposed by the author (RZ) based on assay of antibodies to tissue transglutaminase (TTG) (modified from references 5,7).

*High suspicion of celiac disease may include unexplained iron deficiency or mixed anemia, premature osteoporosis, unexplained infertility, and unexplained chronic diarrhea.

REFERENCES


Who Should Be The Father of Human Anatomy?

------- YOUR CHOICE -------

(1) Mondino De’ Luzzi (1270-1326)
An Italian physician and anatomist, wrote “Anathomia Mundini” in 1316. That was the first textbook of anatomy in Europe, entirely based on the dissections of human cadavers. He was a professor of Anatomy and Surgery at the University of Bologna. The book went through 39 editions until 1543.

(2) Leonardo da Vinci (1452-1519)
The famous artist who created the “Vitruvian man”. He dissected more than thirty cadavers and depicted more than one thousand drawings on human body but never got published. He applied anatomy into his paintings showing power of muscles, including expression of facial muscles in happy smiling, agony, and ecstasy.

(3) Jacopo Berengario da Cardi (1470-1550)
He was a very accurate anatomist, a professor at Pavia and Bologna. He wrote “Commentaria super anatomia Mundini” in 1521. He also practiced in Rome and Ferrara.

(4) Andreas Vesalius (1514-1563)
Vesalius studied at Louvain and Paris and taught at Padua, where he became the chair of Medicine and Anatomy. He published “Tabulae Anatomicae Sex” in 1538 when he was only twenty-four years old. Then, in 1543, he finished “De humani corporis fabrica”, printed at Basle, Switzerland. This revolutionary work resulted the end of Galenism.

(5) Gabriele Fallopio (1523-1562)
Studied at Ferrara, taught at Pisa, later became a professor of Anatomy at Padua. He was the first anatomist describing clitoris and Fallopian tubes. He wrote “Observationes anatomicae”, first published in 1561 in Venice. He made corrections on Vesalius work. Unfortunately he died at age of only thirty-nine.

from Editor
Hyperthyroidism in the General Population and Hypothyroidism in Older People: A Clinical Assessment

Harvey D. Cohen, M.D.

The term hyperthyroidism encompasses a heterogeneous group of disorders. Thyrotoxicosis is defined as the situation in which increased levels of thyroid hormone in the serum lead to biochemical and/or clinical signs of excess thyroid hormone at the tissue level. The most common causes of the hyperthyroid syndrome is Graves’ disease, followed by toxic multinodular goiter and solitary hyperfunctioning nodule. Toxic multinodular goiter, i.e., Plummer’s disease, covers about 50% of hyperthyroidism in people older than 60 years of age. Autoimmune, postpartum, subacute thyroiditis, as well as tumors that secrete thyrotropin, and drug-induced thyroid dysfunction are also important causes. The diagnosis of hyperthyroidism is generally straightforward; with raised serum thyroid hormone and suppressed serum thyrotropin in almost all cases.

Hyperthyroidism has many causes (see table 1). The symptoms of hyperthyroidism is because of an excess of thyroid hormone in the cell as well as enhanced beta adrenergic activity. The patient should be interviewed and queried about nervousness or anxiety, fatigue, palpitations, weight loss (occasionally weight gain), heat intolerance, tremor, muscle weakness, increased frequency of bowel movement, sweating, change in appetite (increase or decrease), and thyroid enlargement. Patients should also be asked about photophobia, eye irritation, diplopia, or change in visual acuity. Women might have irregular menses and decreased fertility. Men can have reduced libido and sometimes, painful gynecomastia. Other indications of hyperthyroidism include osteoporosis, hypercalcemia, congestive heart failure, premature atrial contractions, and atrial fibrillation. In older patients, weight loss might be accompanied by anorexia rather than increased caloric intake. Deterioration of a patient’s glycemic control of diabetes may suggest hyperthyroidism.

A thorough physical examination is imperative. The weight, height, pulse rate and rhythm should be assessed. The clinician should review medications as well as herbs and over the counter medications. Any recent history of iodine contrast for radiological imaging in the recent past? Is there a history of thyroid treatment? Recent pregnancy? Anterior neck pain? Any family history of goiter or thyroid illness? Any weight gain? Any emotional stress in the last year or so? The hand shake can be revealing. Is the skin fine, warm and moist? Is the patient restless with hyperkinetic behavior (can’t sit still)? Is there emotional lability?
Inspect the eyes, the skin, and the neck. Is there lid retraction? Exophthalmos? Is there patchy vitiligo? Is the hair fine, soft, and straight? Sparseness of the hair is common, but alopecia is rare.4

Evaluate by inspection, palpation and auscultation for a goiter (diffuse, nodular, painful). Is there a bruit over the thyroid? Is there proximal muscle weakness? Is tachycardia or atrial fibrillation present? Pretibial myxedema is very rare.

Apathetic hyperthyroidism occurs more frequently in older people. It is characterized by lethargy, disinterest, and an inability to respond to stress instead of the usual hyperkinetic activity.

**Laboratory Testing**

After the diagnosis of hyperthyroidism is secured, other tests may be performed according to the clinical situation. One might request thyroid autoantibodies, T3 and a radioactive iodine uptake (RAIU) and scan, especially if the diagnosis of Graves' disease is not secure.1

Painless thyroiditis, post partum thyroiditis, and subacute thyroiditis will have decreased rather than an increased RAIU.1 The three common causes of hyperthyroidism in the older patient (in descending order of frequency) is toxic multinodular goiter, Graves' disease, and thyroiditis.3

The radioactive iodine uptake and scan are important to establish these diagnoses. In Graves' disease or toxic multinodular goiter, there is an increased uptake with a diffuse or heterogeneous scan respectively. In toxic adenoma a hot spot will be seen. In thyroiditis low or no uptake will be seen. RAIU may be useful in the differentiation of Type I and Type II amiodarone induced thyrotoxicosis. Specific therapy should generally be withheld until a definite diagnosis is ascertained or if judged clinically prudent.

Overt hyperthyroidism is diagnosed in patients with subnormal TSH level and an elevated Free T4 and/or T3. Subclinical hyperthyroidism is diagnosed in patients with a low TSH and a normal Free T4 and T3.5

A suppressed TSH when associated with a low or low normal Free T4 concentration may indicate central hypothyroidism, euthyroid sick syndrome, starvation, corticosteroid administration, or depression.5

When the Free T4 is elevated in a clinically hyperthyroid patient, and the TSH is not suppressed, the clinician should be alerted to the possibility of hyperthyroidism resulting from TSH producing pituitary adenoma or thyroid resistance.

**Hypothyroidism in Older People**

Many non-specific symptoms such as tiredness, fatigue, dry skin, impairment in concentration, and weakness are frequently reported by aging patients.5 An elevated TSH when associated with a low Free T4 is characteristic of primary hypothyroidism. Subclinical hypothyroidism is characterized by an elevated TSH with a normal Free T4 (may not manifest the above symptomatology)

Hoarseness, deafness, mental confusion, dementia, ataxia, depression, and hair loss have also been reported in older persons.1 Because of the insidious nature of hypothyroidism in the elderly, when untreated, may progress into profound myxedema coma, and even death.6 Hypothyroidism in older women is usually because of an autoimmune disorder, an intrinsic disease of the thyroid gland. A high prevalence of thyroid autoimmune disease, i.e., Hashimoto's disease, is seen in the older female population.3

An increased frequency of thyroid autoantibodies was observed in the Wicham survey which demonstrated that an increase in autoantibodies increases the chances of a patient developing hypothyroidism.7

Because of the high prevalence of hypothyroidism in women past 60 years of age, it is recommended that such individuals be screened with a TSH measurement.1 In addition, patients with other autoimmune disease, unexplained depression, hypercholesterol as well as cognitive dysfunction should be screened with a TSH measurement as well. Therefore, when an elderly patient has cold intolerance, constipation, dryness
of the skin, forgetfulness, and hair loss, the clinician must have a high index of suspicion for hypothyroidism.

The pathophysiology of hyper/hypothyroidism and treatment modalities were not addressed in this article. The reader is referred to the references and standard texts for more information.

Table I

Causes of Hyperthyroidism

<table>
<thead>
<tr>
<th>Circulating thyroid stimulators</th>
<th>Thyroidal Autonomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graves' disease</td>
<td>Toxic multinodular goiter</td>
</tr>
<tr>
<td>Neonatal Graves' disease</td>
<td>Toxic solitary adenoma</td>
</tr>
<tr>
<td>Thyrotropin secreting tumor</td>
<td>Congenital hyperthyroidism</td>
</tr>
<tr>
<td>Hyperemesis gravidarum</td>
<td>Iodine-induced hyperthyroidism (Jod-Basedow)</td>
</tr>
<tr>
<td>Choriocarcinoma</td>
<td>Destruction of thyroid follicles (thyroiditis)</td>
</tr>
<tr>
<td>Abnormal thyrotropin receptor</td>
<td>Subacute thyroiditis</td>
</tr>
<tr>
<td></td>
<td>Painless or postpartum thyroiditis</td>
</tr>
<tr>
<td></td>
<td>Amiodarone-induced thyroiditis</td>
</tr>
<tr>
<td></td>
<td>Acute (infectious) thyroiditis</td>
</tr>
<tr>
<td></td>
<td>Exogenous thyroid hormone</td>
</tr>
<tr>
<td></td>
<td>Iatrogenic</td>
</tr>
<tr>
<td></td>
<td>Facitious</td>
</tr>
<tr>
<td></td>
<td>Hamburger thyrotoxicosis</td>
</tr>
<tr>
<td></td>
<td>Ectopic Thyroid tissue</td>
</tr>
<tr>
<td></td>
<td>Struma ovarii</td>
</tr>
<tr>
<td></td>
<td>Metastatic follicular thyroid cancer</td>
</tr>
<tr>
<td></td>
<td>Pituitary resistance to thyroid hormone</td>
</tr>
</tbody>
</table>

REFERENCES


Permission from David Cooper, Lancet 2003
Recent Advances in Nephrology

Jin Wang, MD, FACP
Diplomate, American Board of Internal Medicine and Nephrology

Over the past decade, many advances have taken place in the field of nephrology and resulted in our enhanced ability not only as nephrologists but as non-renal physicians to more effectively diagnose and treat various types of renal diseases. In this review, I intend to cover some aspects of nephrology which in my view best reflect some of the important renal advances in recent years and therefore may benefit all of us as clinicians with a goal to deliver optimal care to kidney patients.

Chronic Kidney Disease—A Silent Epidemic
Chronic kidney disease (CKD) is emerging as a worldwide public health problem. The rising incidence and prevalence of CKD are associated with poor outcomes and high cost. Approximately 50 million people worldwide suffer from progressive CKD, and more than 1 million are being treated with chronic dialysis. In the United States, 20 million people are estimated to have CKD, and over 300,000 people are currently receiving chronic dialysis (Stage 5 CKD, defined as glomerular filtration rate < 15 ml/min), with the annual cost exceeding $20 billion for dialysis care, a figure that may well double in the next ten years as the incidence of ESRD (end stage renal disease) is predicted to double during this period of time. By 2030, the ESRD population in the United States is expected to reach 2 million. Currently, the ESRD patients represent less than 1% of the total Medicare population but consume more than 6% of the Medicare budget. Out of 20 million people with CKD, about 400,000 have Stage 4 CKD with glomerular filtration rate (GFR) between 15-30 ml/min, roughly 7.5 million have Stage 3 CKD with GFR between 30-60 ml/min, and over 10 million patients suffer from Stage 1 (GFR >90ml/min) and Stage 2 CKD (GFR between 60-90 ml/min).

CKD is not just a threat to kidney function, but more importantly, it is a major determinant for the development of progressive severe atherosclerosis, ischemic vascular and cardiovascular death. Even earlier stages of CKD are known to be associated with increased incidences of cardiovascular disease and overall mortality. Unfortunately, CKD is under-diagnosed and under-treated in the United States, resulting in lost opportunities for prevention. In order to avoid the devastating health and economic effects of CKD, the action is clearly needed to develop and implement the management strategies. Currently recommended strategies are to 1) identify reversible causes of kidney disease, 2) optimize control of glucose, blood pressure and lipids, 3) prescribe angiotensin converting-enzyme inhibitor and/or angiotensin receptor blocker even in the setting of normal blood pressure, 4) monitor and treat co-morbid conditions such as anemia, metabolic acidosis, secondary hyperparathyroidism and cardiovascular disease, and 5) refer patients to a nephrologist in the early stage of kidney disease in order to reduce the rate of progression of CKD and better prepare those patients with progressive renal disease for renal replacement therapy.

ACE Inhibitor versus ARB for Renal Protection
CKD is characterized by a gradual loss of renal function and an increased cardiovascular risk. Many landmark studies over the past decade have shown that renin-angiotensin system blockade by angiotensin-converting enzyme inhibition or angiotensin receptor blockade has distinct...
Continuous Renal Replacement Therapy (CRRT)

Over the past decade or so, CRRT has become an essential part of critical care with the intent to treat acute renal failure in hemodynamically unstable patients, preserve existing renal function, manage acid base and electrolyte imbalance, and deliver precise volume control in a slow and continuous fashion. In comparison, intermittent hemodialysis has its limitations and in general is not suitable for hemodynamically unstable patients.

The most common forms of CRRT are CVVH (continuous venovenous hemofiltration), CVVHD (continuous venovenous hemodialysis) and CVVHDF (continuous venovenous hemodiafiltration). They vary in their operational characteristics. Solute removal is achieved either by convection, diffusion, adsorption, or a combination of these methods. Volume removal can be precisely regulated continuously according to patients' clinical needs. If used correctly and timely, CRRT could be a very useful addition to the overall management of critically ill patients in the ICU setting.

CRRT may have an effect as an adjunct therapy in sepsis because it has been shown to eliminate the pro-inflammatory cytokines commonly associated with sepsis and SIRS (systemic inflammatory response syndrome). High volume hemofiltration with 6 liters of ultrafiltrate produced every hour has been used to remove middle- and large-molecular-weight cytokines in sepsis.

Despite the recent advances in CRRT, acute renal failure continues to be an ominous complication in critically ill patients and its mortality remains very high. New research and clinical developments to guide the application of CRRT in ICU patients will be much awaited and well received by the renal community.

Cystatin C versus Creatinine

Cystatin C is an endogenous marker of renal function and has been shown to be a better indicator of changes in glomerular filtration rate (GFR) than serum creatinine. Human cystatin C is a basic low molecular mass protein freely filtered through the glomerulus and almost completely reabsorbed and catabolized by proximal tubular cells. In contrast, approximately 10% of creatinine is secreted into the proximal tubules, thus overestimating GFR. Cimetidine and sulfa drugs are two known agents that inhibit the secretion of renoprotective and cardiovascular protective effects. Both types of drugs inhibit the effects of angiotensin II, the former by inhibiting the angiotensin II conversion and the latter by blocking the type 1 receptor of angiotensin. In addition to the antihypertensive effect, angiotensin inhibition exerts specific effects in the vasculature and the kidney. These effects include decreased intraglomerular pressure, improved glomerular-barrier size selectivity and reduction of proteinuria.

All renoprotection trials have invariably shown that the strongest predictor of long-term renoprotective efficacy is the anti-proteinuric effect. It is becoming increasingly clear that ACE inhibitors and ARBs have a dose-dependent relationship for proteinuria, and that this relationship is different among individual patients. In general, patients with a poor response to ACE inhibitor also respond poorly to ARB.

Recent studies have also found an additional anti-proteinuric effect when the combination of halved doses of ACE inhibitor and ARB was used to reduce the blood pressure to a level similar to that achieved by full dose of monotherapy, and this extends previous findings showing the additional anti-proteinuric benefit of combination therapy. Other studies have also shown that long-term renoprotection with dual renin-angiotensin system blockade is better than one with monotherapy. However, no formal comparison studies are available so far to conclude that either ACE inhibitor or ARB is superior to the other.

For renoprotection, the first step is full titration of the ACE inhibitor or ARB aimed at optimal reduction of proteinuria. To achieve maximal cardiovascular and renal protection, in terms of blood pressure control, dyslipidemia, and proteinuria, will usually require a multidrug regimen, based on dual renin-angiotensin system blockade and combined therapy with diuretics and lipid-lowering agents.
creatinine from proximal tubules, hence raising serum creatinine by about 10 percent, with no real effect on GFR. Furthermore, studies have also shown that serum cystatin C measurement offers a simpler and more sensitive screening test than serum creatinine for early changes in GFR.

Serum cystatin is also more effective at predicting cardiovascular morbidity and mortality in elderly people than creatinine or estimated GFR\textsuperscript{10}. Shlipak et al studied 4,637 elderly people from four areas of the US. Baseline values of serum cystatin C and creatinine were analyzed against cardiovascular outcomes measured seven years later. They were able to show that even a small increase in baseline serum cystatin C was associated with a higher risk of death or major cardiovascular events including stroke, MI or heart failure, and that this marker was a stronger predictor for these outcomes than serum creatinine.

Just like creatinine, cystatin C has its shortcomings as a measure of kidney function. There are few data on the production rate of cystatin C and its molecule is subject to substantial extrarenal clearance. Finally, measurement of cystatin C is not yet standardized for clinical practice at this time.

**Herbal Nephrotoxicity**

A recent survey of alternative medicine revealed that 42% of Americans use alternative therapies, with 12% of these therapies being use of herbal supplements\textsuperscript{11}. These supplements are not regulated by the FDA. No proof of safety is required, and there is little standardization of labeling.

Herbal nephropathy was first described in Belgium from 1990-1992 when over 100 people who ingested a Chinese weight loss remedy containing aristolochic acid developed acute renal failure. Seventy of them required either dialysis or renal transplants, and thirty subsequently developed urothelial carcinoma\textsuperscript{12}. Hundreds of additional cases have been reported in other parts of the world since these earlier reports. The FDA has imposed strict guidelines to prevent any herbal products containing aristolochic acid from entering the U.S. market.

Other herbal remedies such as licorice root, senna, cascara, and rhubarb may cause potassium imbalance or increase the risk of oxalate renal calculi. There have been reports of acute renal failure in individuals ingesting wild mushrooms containing the nephrotoxin orellanine and in people taking the popular Peruvian herb cat’s claw\textsuperscript{13}.

CKD exposes patients to additional risks from herbal supplements. Most patients with CKD already take multiple medications. Adding herbal supplements raises the risk of drug interactions. The inability of the failed kidneys to remove toxins and lack of knowledge about how dialyzable many herbal supplements are often create a potential for overdose.

Transplant patients must be made aware of the potential risks from Echinacea and St John’s wort as these medicinal plants may alter level of cyclosporine possibly resulting in transplant rejection\textsuperscript{14}.

**The Dark Side of Recombinant Human Erythropoietin**

With recent development of recombinant human erythropoietin (EPO), both Epogen and Procrit (and more recently Aranesp) have become widely used to treat anemia not only for renal patients due to erythropoietin deficiency but also for oncology patients with bone marrow suppression. Increasing hemoglobin concentration improves cardiovascular function, cognitive function, quality of life, and sense of well-being, and is associated with reduced hospitalizations and mortality\textsuperscript{15}.

However, the potential side effects of EPO have been increasingly recognized in recent years. 3-11% of patients may develop headache, body aches, fever, lethargy and anxiety.

There have been concerns that correction of anemia would result in lower dialysis clearance, hyperkalemia, volume overload and vascular access thrombosis.
The most common side effect of EPO treatment is worsening hypertension in about 25-30% of treated patients. Direct effects are possible as EPO receptors are present on endothelial cells, and other mechanisms including reversal of hypoxic vasodilatation, increased cardiac contractility and output, or endothelin effects have all been proposed.

Pure red cell aplasia (PRCA) is an uncommon but potentially serious adverse consequence of EPO administration. Since 1999, there has been a substantial increase in the number of cases of antibody-mediated PRCA in CKD patients receiving EPO. The explanation for the development of anti-EPO antibodies in some patients remains unknown. Administration by the subcutaneous route is likely to be more immunogenic and exposure through the skin may facilitate the development of anti-EPO antibodies.

The EPO resistance is defined as a failure to achieve target hemoglobin with increasing EPO dose. The common causes of EPO resistance include iron deficiency, chronic inflammation, secondary hyperparathyroidism, occult GI bleeding, vitamin deficiencies (folate, B12), multiple myeloma, aluminum toxicity, and severe malnutrition.

Uric Acid and the Kidney
In clinical conditions of uric acid excess, uric acid may precipitate in the renal tubules and cause acute uric acid nephropathy. It has most commonly been associated with neoplastic diseases. The diagnosis can be made in a clinical setting suggesting tumor cell lysis by a serum uric acid typically greater than 15 mg/dl and a uric-to creatinine ratio above 1 in a random urine sample. In contrast, chronic uric acid nephropathy is much rare clinically. A 20-year clinical study concluded that hyperuricemia and gout alone were not associated with deterioration in renal function. Rather, the decline in renal function was better explained by associated co-morbidities such as diabetes or hypertension.

The co-existence of chronic hyperuricemia and renal insufficiency should raise concern over lead exposure. Lead accumulation in the proximal tubule leads to tubular cell atrophy and interstitial fibrosis and a reduction in urate secretion. Early cases describing chronic uric acid nephropathy may have actually been lead nephropathy.

An association between hyperuricemia and increased coronary heart disease (CHD) has been recognized for many years. However, whether there is an independent association between these two entities remains debatable. Patients with hyperuricemia often have many co-morbidities including diabetes, hypertension and renal disease. It is well known that there is increased incidence of CHD in CKD patients. Therefore, it would be a good clinical practice to strive to correct hyperuricemia so that it may potentially reduce the risk of CHD in CKD patients.

Adult Stem Cells in the Repair of Acute Tubular Necrosis
The ability of the kidney to regenerate functional tubules following acute injury is an important determinant of patient morbidity and mortality in the hospital setting. When the injury is less severe, renal tubules can regenerate and regain normal or near-normal functions within days; however, in more severe cases, the repair process can be prolonged or even fail completely, resulting in a requirement for dialysis and a marked increase in patient mortality. Recent studies have indicated that adult stem cells, either in the kidney itself or derived from the bone marrow, could participate in this repair process and might therefore be utilized clinically to treat acute renal failure. Bone marrow probably harbors a population of poorly understood cells that, when infused in large numbers, has a protective effect in animal models of acute renal failure. It is also possible that the kidney contains a population of endogenous tubule progenitor cells that participates in tubule regeneration. Further studies are being carried out with the long-term goal of developing strategies that will minimize the severity of tubular injury and increase the capacity for tubular repair in patients with acute renal failure.

Wearable or Implantable Artificial Kidney
Researchers have recently developed a human
nephron filter (HNF) that would eventually make possible a continuously functioning wearable or implantable artificial kidney, according to a publication in the September 2005 issue of Hemodialysis International.

The HNF is the first application in developing a renal replacement therapy to potentially eliminate the need for dialysis or kidney transplantation in patients with end-stage renal disease. The HNF uses a unique membrane system created through applied nanotechnology. This technology would be used to mimic the function of natural kidneys, operate continuously, and be based on individual patient needs. Researchers hope that the device will substantially improve patient outcome and quality of life. Animal studies using this technology are scheduled to begin soon, with clinical trials to follow.

Future Nephrology Directions
As both CKD and ESRD population continues to grow, more focus will be devoted to optimizing management strategies, reducing cardiovascular mortalities, improving the quality of life, modifying many co-morbidity conditions and, in doing all above, controlling the continually increasing Medicare budget for renal care. New therapies and technologies will continue to benefit all renal patients and especially those undergoing CRRT or various forms of chronic dialysis treatments. It remains a challenge to improve the mortality of acute renal failure in the ICU setting in spite of CRRT. Nephrology practices will need to integrate and develop strategies to adapt to the new direction being taken by the Centers for Medicare & Medicaid Services towards value-based reimbursement (pay for performance) while maintaining high quality patient care.

REFERENCES
Neurosurgery and Neuronavigation at Pomona Valley Hospital Medical Center

Jose L. Rodriguez, M.D. FACS,
LDR Neurosurgery
Pomona, California

Stereotactic Neurosurgery has been refined to an armless and frameless neuronavigational system in recent years. In the past 50 years we have seen a significant advancement in this field from its humble birth to today’s CT, MRI and computer application. Stereotactic (from the Greek stereo, three dimensions; tactic, to probe) is a term to describe procedures done in a precise and defined three-dimensional space.

Historically, burr holes, or trephination, was performed in China approximately 5000 years ago. A well known legend in China describes a doctor, Hua Tuo, to have attempted a craniotomy on King Cao Cao (AD 222 to 280) for headaches caused by a brain tumor.1,2

Incan artifacts (AD 1000 to 1600) have demonstrated early use of trephination techniques and craniotomy with gold plate. (Fig. 2)

Surgeon John Collins Warren was the first to use ether anesthesia in surgery, on October 16, 1846. With the advent of general anesthesia, the scope and duration of surgeries were dramatically broadened.

Neuronavigational concepts began early in neurosurgery with the development of the Horsely-Clark stereotactic apparatus. Sir Victor Horsely (Fig. 3) is considered by many as England’s father of neurosurgery. Robert Clarke and Victor Horsely kept early animal investigation strictly in the laboratory at Queen Square’s Hospital, London England. This knowledge was the roots for the development of today’s concepts but never was used on humans despite attempts by Dr. Clarke to persuade neurosurgeons to use it. This unit was patented and kept on the shelf for years. Later different versions were developed for human use.6,10
Harvey Cushing, MD (1869-1939) is considered as the father of neurosurgery in the U.S. Consider the difficulty of the 2000 brain tumor surgeries he performed in his lifetime, during the infancy of neurosurgery where even simple illumination was sparse compared to today’s microscopes ability to magnify and illuminate deep crevices of the brain.

Rapid interest in finding ways to probe into the brain resulted in the interest in the treatment for Parkinson's and other disorders. The CT scan quickly replaced the ventriculogram in the 70's and distinctly made improvements in stereotactic surgery. The now outdated ventriculogram was used to delineate the anterior and posterior commissure, aqueduct, and the fourth ventricle, which allowed for accurate placement of an electrode to areas of the thalamus or midbrian.

Today’s complex computerized applications that are applied to neuronavigation are based on the origins of Cartesian principles developed in the 17th century by French philosopher “Rene Descartes; mathematical principle of locating a point in three dimensional space. Neuronavigation has been developed by many giants in the field of neurosurgery. Dr. Philip Gildenberg describes his mentors, Drs. Ernst A. Spiegel and Henry T. Wycis, as the parents of stereotactic surgery. They were the first to apply Cartesian knowledge to humans brains. Many neurosurgeons have contributed and it certainly would not have been possible without the work of Patrick Kelly at the Mayo Clinic. Functional and stereotactic neurosurgery was advanced at the University of Toronto, Ontario Canada by Dr. Ronald R. Tasker. There are too many individuals to list in this short article to give it any justice. Clear and thorough details of this history have been precisely elaborated by Dr. Patrick Kelly.

POMONA: The beginnings of the neuronavigational program at PVHMC

Stereotactic neurosurgery in private practice can be rewarding by applying these same principles in clinical practice. This idea was initially introduce to Pomona Valley Hospital Medical Centers (PVHMC) by LDR Neurosurgery in the late 80's by Scott Lederhaus, M.D. The initial phase and introduction of this technology was kept simple. He introduced the use of a simple and cost effective device, the Polaris neuronavigational unit. This was an effective tool which adhered to principles of Ockham's razor. Keeping it simple allowed the Polaris system to perform early brain biopsies safely. Under local anesthesia a bedside application of a small skull ring attached to the patient's skull was done in minutes, followed by transporting the patient to the radiology department to obtain a CT scan. The surgeon proceeds in acquisition of computerized coordinates follow by actual applying coordinates to a phantom stereotactic frame. Final steps in the operating room application of similar coordinates to the patient's skull mounted device and finally using an arc-arm instrumentation to obtain the brain biopsy. Difficult stereotactic brain biopsy of
certain brain lesions can best be appreciated when tackling the Pineal region which is surrounded by a moat of vascularity. This was first accomplished at PVHMC by Dr. Lederhaus using the Polaris system. Biopsy of lesions within the Pineal region has been successfully reported in 103 cases as a relatively safe procedure in experienced hands. Although Polaris had an advantage of a simple system, it did not allow for the use of the intraoperative computerized technology for more advance cases.

Dr. Lederhaus’ training in this field was guided by Ron Young, MD at the University of California, Irvine (UCI) with the use of the Leksell stereotactic instrumentation and frame (Elekta).

Dr. Lederhaus’ training in this field was guided by Ron Young, MD at the University of California, Irvine (UCI) with the use of the Leksell stereotactic instrumentation and frame (Elekta).

**Neuronavigation at PVHMC Today:**

**BrainLab VectorVision**

The field was progressing rapidly and we needed a more advance system that could be used by other specialties at PVHMC including spine, ENT, Radiotherapy and even functional neurosurgery. The program at PVHMC has been developed by LDR Neurosurgery to its current phase with the BrainLab VectorVision neuronavigation system. It has been defined as “an intraoperative, image-guided, frameless, localization system.” Its current components are; computer workstation situated in the operating room used for registration of images and physical spaces, an intraoperative camera localization device, and a computer image display that allows for passive reflections of infrared flashes. Instantaneous computer reformation provides surgeons with real-time responses regarding the locations of surgical instruments in relationship to the brain and lesion. It’s versatile software capacity allows for a computer formatted visual overlay-view of the lesion, within the right eyepiece of the operating microscope, allowing the surgeon to work without looking up onto the monitor. Advanced “Z touch” technology will permit laser facial recording and delete the use of fiducial skin markers for registration. A special pointer tool, equipped with two highly reflective markers, is used for registration of the patient. To achieve real-time imaging of patient head movement during surgery, a star-shaped tool is fastened to the Mayfield headrest as a rigid reference point. To guarantee exact navigation, this so-called “Mayfield adapter” must remain in the same position, with respect to the head of the patient, throughout the operation.

**CASE REPORT**

**PVHMC’s first pediatric case**

A young child was transferred to PVHMC with seizures and a brain lesion that was considered a possible hemorrhage or brain tumor. MRI and CT scans are done and surgery is rendered without complications. Final diagnosis is cavernous malformation.

**CASE REPORT**

**PVHMC’s first pediatric case**

A young child was transferred to PVHMC with seizures and a brain lesion that was considered a possible hemorrhage or brain tumor. MRI and CT scans are done and surgery is rendered without complications. Final diagnosis is cavernous malformation.
Surgical Procedure: The computer images with tumor overlay is rotated to mimic the head position (Fig. 10). The patient is position in the operating room with Mayfield head device applied. The skin is marked with location of tumor and allowing surgeon to minimize surgical entry with extreme accuracy without relying on traditional head landmarks (Fig. 11).

Surgical planning and tumor reconstruction is done at the work station with the use of images formed from a triplanar format and obtained in 2mm slice CT scan, or MRI. The scans can then be seen in three-dimensional reconstruction, and viewed in different planes or angles allowing for improved surgical planning (Fig 12 & 13).

BrainLab surgical planning allows for improved surgical positioning and use of smaller linear incisions and smaller craniotomy opening. This has decreased the risk to patients undergoing elective craniotomy (Fig. 14).

The surgeon will proceed with microsurgical techniques to remove the lesion. The magnified surgical view of this patient’s lesion is seen after it was excised without injury to surrounding structures of the brain (Fig. 15).

This patient did very well and did not have any neurological deficits as seen in his first post op visit (Fig. 15). The final post-operative MRI of the brain with contrast reveals complete resolution of the lesion with a final diagnosis consistent with familial cavernous hemangioma (Fig. 16).

Neuronavigation with BrainLab VectorVision has the ability to get assist surgeons to operate safely in deep seated brain tumors or lesions in eloquent brain structures with improve safety and accuracy. It has been devised as a tool to assist the doctor in navigating through the brain when traditional surface landmarks were not sufficient to perform complex brain surgery.
REFERENCES


http://www.neurosurgery.org/cybermuseum/stereotachall/stereoarticle.html

Question: Who Is He?

Hint: His name became the unit to measure the amount of radiation.

Answer on Page 47.
Introduction
Geriatric patients require special considerations for certain aspects of their medical care. Changes in anatomy and physiology that occur with aging, the psychosocial aspects of aging, and the potential for age-related diseases dictate that geriatric patients cannot simply be considered older adults. Medical care of geriatric patients is a multidisciplinary and holistic endeavor, with the ultimate goal of assisting the geriatric patient to maintain optimum health and function. Osteopathic medicine, with its distinctive philosophy and principles, can provide physicians with some useful approaches to achieving this goal.

Osteopathic medicine is defined as follows: “A complete system of medical care with a philosophy that combines the needs of the patient with the current practice of medicine, surgery, and obstetrics, that emphasizes the relationship between structure and function and that has an appreciation of the body’s ability to heal itself.”

The philosophy of osteopathic medicine may be briefly stated as follows: “The osteopathic concept emphasizes four general principles from which are derived an etiological concept, a philosophy and a therapeutic technique that are distinctive, but not the only features of osteopathic diagnosis and treatment:

1. The body is a unit.
2. The body possesses self-regulatory mechanisms.
3. Structure and function are reciprocally interrelated.
4. Rational therapy is based upon an understanding of body unity, self-regulatory mechanisms, and the inter-relationship of structure and function.”

Who is the Geriatric Person?
There is no strong consensus or definition of the "geriatric person". In other words, when it comes to old age, no one really knows who exactly fits in this category. Heilig3 has stated the following:

At the onset it becomes necessary to decide who the geriatric patient is. I suspect that the recent medical school graduate would consider anybody over 50 years of age in this category; the man (sic) who has been in practice for 20 years would raise the definition of geriatric patient to those of retirement age; and then as we ourselves approach the retirement age we begin to classify patients in their eighties or nineties as geriatric! This is human. I think we have to establish that we are referring to the patient who is beyond a certain point in

---

his metabolic life, where certain changes in tissue, metabolism, circulation, etc. are bound to be occurring. The female menopause or male climacteric will have occurred to some degree, but this is not a total point of change, though it may be dramatic. Perhaps the evidences of aging significant in this classification are to be seen in the musculoskeletal system; the amount of structural change gives early and objective evidence. There is no one age and no one patient who would fit in the category of being aged on a chronological basis alone.

The above quote makes the point that factors other than chronology must be considered when defining the aging process.

Most developed world countries have accepted the chronological age of 65 years as a definition of “elderly” or older person, but like many westernized concepts, this does not adapt well to the situation in less developed countries. Although there are commonly used definitions of old age, there is no general agreement on the age at which a person becomes old. The common use of a calendar age to mark the threshold of old age assumes equivalence with biological age, yet at the same time, it is generally accepted that these two are not necessarily synonymous. As far back as 1875, Britain’s Friendly Societies Act defined old age as, “any age after 50,” yet pension schemes mostly used age 60 or 65 years for eligibility.¹

**Body Unity**

Taking the holistic view of the geriatric patient means, among other considerations that the physician must be aware of certain changes in the musculoskeletal system that occur with aging. For example, older patients may not perceive or react to pain as sharply as younger patients do. One should also be aware of the osseous changes (e.g., demineralization, joint stiffening) that may occur with aging, and also with changes in soft tissues associated with aging. These soft tissue changes include tightening of fascial sheaths, muscle atrophy (sarcopenia), and an increase in abdominal fat stores. These changes all combine to produce a change in the body composition of the elderly person.

Changes in the bone density of vertebrae and intervertebral discs may contribute to changes in spinal curvatures that in turn result in postural changes associated with aging. Other common problems seen with aging include degenerative arthritis (osteoarthritis), rheumatoid arthritis, osteoporosis, and an increased risk of falling, which may result in fractures.

In addition older patients may also experience a slowing down in the production and circulation of neurotransmitters, and a slowing of axoplasmic flow. Such physiologic changes may contribute to clinical problems such as sleep disturbances or depression. Other associated signs and symptoms may include changes in balance and coordination, decreased mental acuity, and mood changes.

All of these changes may alter the elderly patient’s response to treatment approaches such as pharmaceutical agents, rehabilitative measures or osteopathic manipulation. The elderly patient’s ability to exercise or perform activities of daily living may also be affected. Awareness of these situations will assist the physician in determining appropriate pharmaceutical regimens, rehabilitation procedures, exercise programs and other activity levels for the patient.

**Self-Regulation**

In order to help the geriatric patient optimize his or her functional abilities, health promotion and disease prevention must be included in the patient’s overall care plan. Some important topics to consider are:

- Nutrition and weight control
- Posture and exercise
- Healthy lifestyle
- Reduction of emotional stress
- Prevention of illness and injury

---

Keeping the musculoskeletal system healthy can contribute to the patient’s overall level of health and quality of life. Certain behaviors and certain aspects of lifestyle can affect the health of the musculoskeletal system. Educating patients in these areas is an important part of their overall health care.

A regular exercise program also helps to maintain the health of the neuromusculoskeletal system. Regular exercise helps to maintain the strength and mass of bones and muscles, and helps to keep the joints stable. A good exercise program should include cardiovascular and strength-building maneuvers, and a stretching program to help maintain flexibility and good posture.

Patients should also maintain a healthy lifestyle. They should be encouraged to avoid such things as smoking and alcohol abuse. It is also probably safe to say that everyone experiences varying degrees of stress. The physician, however, can help the patient to find substantive methods to cope with stress even under the most trying of circumstances. It is also important for the physician to assist the patient in seeking out adequate support systems, including family, friends and community support services.

The health of the neuromusculoskeletal system can also be maintained by having patients take measures to avoid accidents or injuries, both at work and at home. For example, patients should be encouraged to maintain their automobiles properly and to make sure they utilize auto safety devices such as seat belts. Home and work safety can also be encouraged by educating patients about such topics as fire safety, gun safety, prevention of falls, prevention of power tool injuries, and avoidance of exposure to chemicals or toxins in the environment.

The interrelationship of structure and function
An osteopathic structural examination can be a distinctive part of the history and physical examination of the patient. This part of the patient evaluation combines palpation of musculoskeletal tissues and certain anatomical landmarks with motion testing in order to assess the musculoskeletal system for evidence of somatic dysfunction. Somatic dysfunction is defined as impaired or altered function of related components of the somatic (body framework) system: skeletal, arthrodial, and myofascial structures, and related vascular, lymphatic and neural elements.

Somatic dysfunction is present with virtually every condition that may affect the patient. It is present whenever there is trauma to, or disease of, the musculoskeletal system. Through complex neurological interconnections, disease or dysfunction of internal organs or systems also often results in somatic dysfunction being present in segmentally related areas of the musculoskeletal system. Thus the finding of somatic dysfunction gives the examiner important information that may help in determining precisely what is affecting the patient, and may also aid in determining more precise diagnostic and treatment options. In addition, treatment of somatic dysfunction related to the patient’s illness might offer a faster recovery of health and a better ability to maintain this recovery. Relief of somatic dysfunction is accomplished by the application of osteopathic manipulative treatment (OMT). Specific goals for the use of OMT in the geriatric patient are discussed later in this article.

The criteria for identifying somatic dysfunction are: Tissue texture abnormalities, Asymmetry of position of bony (or other) anatomical landmarks, Restriction of motion (quantity and/or quality), and Tenderness. These criteria are easily remembered by using the mnemonic TART. These criteria are further defined as follows:

* **Tissue texture abnormalities** (TTAs) are palpable changes in tissues from skin to periarticular structures that represent any combination of the following signs: vasodilation, edema, flaccidity, hypertonicity, contracture, fibrosis; and the following symptoms: itching, pain, tenderness, parasthesias. Types of TTAs include: bogginess, thickening, stringiness, ropiness, firmness (hardening), increased or decreased temperature, and increased or decreased moisture.
1. Return of the patient to a degree of independence in daily activity.
2. Prevention of secondary disabilities; restoration of functional ability; prevention of succumbing to multisystem diseases.
3. Postural drainage.
4. Respiratory assistance.
5. Stretching of tight fascial sheaths.
7. Aiding of digestion and elimination.
8. Relief of pain.
9. Restoration and maintenance of autonomic balance.
10. Increase the patient’s feeling of well-being.
11. Maintenance care and palliation.

The success or outcome of treatment should be measured by the patient’s ability to successfully resume daily activities. In the case of maintenance and palliation, the patient’s overall level of comfort and peace of mind may be measurable outcomes for determining the success of manipulative treatment.

**Indications and contraindications for OMT in the elderly**

In general, OMT is not contraindicated in the geriatric population. Indications for the use of OMT are by and large the same as that of any other adult age group. The development in recent years of indirect techniques, and direct techniques other than high velocity low amplitude (HVLA), has eliminated some cautions and contraindications. Most precautions and contraindications may be thought of as relative, and absolute contraindications (with few exceptions) are usually associated with the use of HVLA techniques. According to Heilig:

**Goals of Osteopathic Manipulative Treatment**

Like any other clinical situation, the goals of manipulative treatment in the geriatric patient vary with the specific problem at hand. Experts in osteopathic manipulative medicine have enunciated some of the goals of manipulative treatment for the elderly as follows:

5 Heilig, op. cit., pp. 90-91.
7 Dodson D. Manipulative therapy for the geriatric patient. Osteopathic Annals, 7:3; March, 1979;114-119.
8 Hofener VC. Osteopathic Manipulative Treatment in Gerontology. Osteopathic Annals, 10:12; December, 1982; 546-549.
9 Reich M. Less velocity used in OMT for elderly. The DO, February, 1994;93-94.
10 Heilig, op. cit., pp. 91-92.
The use of the term ‘absolute contraindication’ should be reserved for an area of involvement, or it should be a matter of the physician’s judgment in view of the overall condition of the patient rather than in view of the title given to a dominant pathology. We must remember that if the patient has more than one pathology, he (sic) has more than one source of aggravation."

Frequently contraindications are defined in terms of ‘thrust’ techniques or vigorous articulatory techniques; and we forget the possible hazards of myofascial or ‘soft tissue’ techniques in some of the vascular diseases such as thrombophlebitis, phlebitis, arteritis, arteriosclerosis and atherosclerosis. With the aging patient, who (sic) we know may have some of these vascular changes, we should use considerable caution as to the amount of myofascial manipulation. There should be particular caution in certain areas: for example, the cervical techniques which might involve excessive mobilization around the carotid sinus in the arteriosclerotic patient or manipulations affecting the abdominal content where there are advanced changes in the mid-aorta.

Considerations in the applications of OMT Techniques

Most OMT techniques can be used in the elderly population. Again, as Heilig\textsuperscript{11} has stated:

Every form of technique, from superficial lymphatic drainage through myofascial techniques of stretching and muscular relaxation, ranges of motion, articulatory and springing type of techniques, and even modified thrust techniques, can be utilized in the aging patient. Certain conditions would mitigate against forceful or extreme forms of manipulation, and these would include such conditions as the arthritides, osteoporosis of the disseminated type, multiple myeloma, Paget’s disease of bone, and of course primary bone tumors or metastatic lesions of bone. I think a word should be said even concerning these, because these are the conditions which we are liable to encounter in the aging patient, who may have been under osteopathic care for a number of years prior to the onset of his (sic) bone or joint condition.

It may be necessary to avoid or modify the use of HVLA techniques in the geriatric patient, depending on the clinical situation. In addition, the patient may require modifications in treatment position because of concomitant clinical conditions, such as arthritic joints, muscle contractures, or other similar situations. Because of some of the musculoskeletal changes associated with aging, and because of some of the precautions noted above, the practitioner may find it more efficacious to utilize such OMT modalities as counterstrain, muscle energy, soft tissue, myofascial release, and articulatory and joint play techniques.

Some clinical conditions in the elderly that may be amenable to the use of Osteopathic Manipulative Treatment

Hypertension

Hypertension has been shown to respond favorably to OMT. Northup\textsuperscript{12, 13} has recommended the use of appropriate OMT techniques to segmentally related spinal areas such as the cervical spine, the T1-T4 region, and the upper rib cage.

Arthritis

Many osteopathic physicians have reported a decrease in joint pain, decreased use of anti-inflammatory medications, and increased functional ability in patients with rheumatoid and osteoarthritis. These patients may respond well to soft tissue, myofascial and articulatory techniques.

\textsuperscript{11} Heilig, op. cit., p. 90.
\textsuperscript{12} Northup, TL. Manipulative management of hypertension. JAOA, Vol. 60, August 1961.
in particular. HVLA may be used with caution and often with modification, and is avoided in the case of acutely inflamed joints.

**Congestive Heart Failure**
These patients may respond to the use of techniques that would improve respiration and circulation of fluids. Maintaining good biomechanical motion at the cervicothoracic, thoracolumbar and lumbosacral areas will help to maintain good motion at the thoracic inlet, and the abdominal and pelvic diaphragm areas. These diaphragms may also be treated directly. Other techniques are available which may assist the movement of fluids throughout the body.

**Constipation**
OMT to help alleviate this problem should be directed at treating segmentally related areas such as the thoracolumbar and lumbosacral regions. Myofascial release to the abdomen, the mesenteries, and abdominal and pelvic diaphragms may also be helpful.

**Respiratory Diseases**
Any techniques that would improve respiratory mechanics and ventilation would be helpful with these problems. Treatment might be needed at the cervical area to attempt to influence phrenic nerve function, to the thoracic spine and rib cage to improve rib cage mechanics, and to the thoracoabdominal diaphragm. Knoll\textsuperscript{14, 15} has shown that OMT to elderly patients with pneumonia can shorten length of hospital stay and decrease the time needed for antibiotic usage.

**Parkinson’s Disease**
Some experts in OMM have described improvements in Parkinsonian patients with the use of OMT. Reports of decreased tremors and improved functionality have been noted. Research in this area is just beginning. Wells\textsuperscript{16} showed improvement in gait performance in Parkinsonian patients.

**Summary**
The philosophy and principles of osteopathic medicine can provide physicians with some distinctively useful approaches to health issues that are specific to the elderly population. In particular, OMT can be very useful for geriatric patients. Most of the commonly used OMT modalities may be used in the elderly population. The use of some techniques may require alterations in treatment position to accommodate the patient’s clinical situation. Some direct techniques, such as HVLA, may require modification for their use in the geriatric patient, and some clinical conditions may preclude the use of HVLA technique.

\textsuperscript{14} Knoll DR. Adjunctive osteopathic manipulative treatment in the elderly hospitalized with pneumonia: a pilot study. JAOA, Vol. 99 No. 3 March 1999;143-152.


The predisposition to form clots may arise from genetic factors, acquired changes in clotting homeostasis, or, more commonly, an interaction between genetic and acquired factors. About 35% of spontaneously occurring Deep Vein Thrombosis (DVT) of extremities can be attributed to genetic factors. Since the 1990’s, there has been an explosion of literature relating to both genetic and acquired aspects of thrombophilia, broadening understanding of causes of DVT and many other important clinical phenomena. (Table 1 and Table 2).

Table 1.

**Disorders associated with genetic hypercoagulability conditions**

1. Deep and Superficial Vein Thrombosis
2. Pulmonary Embolism
3. Chronic Venous Ulceration
4. Ischemia of Intestine
5. Warfarin-induced Skin Necrosis
6. Cerebral Vein Thrombosis
7. Myocardial Infarction
8. Portal and Hepatic Vein Thrombosis
9. Neonatal Purpura Fulminans
10. Retinal Vein Thrombosis
11. Miscarriage and Stillbirth

Table 2.

**Known predisposing factors associated with hypercoagulability state**


2. Hematological Disorders: Myeloproliferative diseases such as Polycythemia Vera, Essential Thrombocythemia, and others.

3. Hormonal drugs: Oral Contraceptives, Estrogen and/or Progesterone for hormone replacement therapy, Tamoxifen, Megace, or Aromatase Inhibitors such as Arimidex.


5. Autoimmune Disorders: Lupus Anticoagulant, Antiphospholipid Syndrome, Thrombotic Thrombocytopenic Purpura (TTP), Heparin-induced thrombocytopenia

6. Nephrotic Syndrome
Case Studies

Case 1
A 30-year-old male nurse was admitted to the San Antonio Community Hospital with a painful swelling of the right leg. About one week prior he noticed some redness and swelling in the right lower leg, and he had been taking Keflex as it appeared to be mild cellulites. Because the pain and swelling got worse, he was brought to the Emergency Room. The ultrasound and Doppler study showed that he had deep vein thrombosis of the right leg involving the iliac, femoral and popliteal vein. He was started on Lovenox injection followed by oral warfarin, with improvement of the symptoms and signs.

Hematology evaluation was requested for further investigation because there was no obvious predisposing factor triggering the thrombosis in this young man. Although he did not have significant respiratory symptoms, the spiral CT scan of the chest was done as the deep vein thrombosis was rather extensive. It showed a pulmonary embolus in the right segmental pulmonary artery, and subsequently the inferior vena cava filter was placed. He has no significant family history except his uncle having a history of myocardial infarction.

Laboratory tests with CBC, Comprehensive Metabolic Panel, Prothrombin Time and Partial Thromboplastin Time were all normal. A series of hypercoagulability test was done, and it revealed that he is a heterozygote for the Factor V Leiden mutation. The Prothrombin G20210A mutation was negative.

Case 2
A 50-year-old white woman who recently developed DVT was found to have a low level of Protein S.

Three weeks ago, she was hospitalized in the Chino Valley Medical Center with acute DVT of the right leg. This was the second episode of DVT. Her family doctor ordered the levels of Protein C, Protein S and Antithrombin before initiating the anticoagulation therapy. The Protein S level came back low at 54%, and the rest of the tests were normal. By the time she was seen for the hematology consultation, she was taking oral Warfarin, and the leg swelling was much improved.

In order to confirm the Protein S deficiency, the Warfarin was stopped, and she was instructed to self inject the Low-Molecular Weight Heparin (LMWH) for 2 weeks before the blood drawing for the Protein S level. This is because the Warfarin can lower the blood level of the Protein S, thus causing a falsely low result. The repeated test turned out to be normal; Protein S Activity 103% and Protein Antigen 94%.

However, the test for the Factor V Leiden mutation came back positive. In addition, the Homocysteine level was high at 13.2 Unit, with the normal values ranging from 2-9 Units.

She was prescribed to take Vitamin B complex in addition to the Warfarin therapy.

Case 3
A 59-year-old white woman was referred for evaluation of hypercoagulability condition. She has a history of multiple thrombophlebitis involving both lower extremities resulting in chronic venous insufficiency. She also has a long history of chronic abdominal pain after meals, suggestive of abdominal angina.

The family history includes that both parents had Cerebrovascular Infarction.

The laboratory tests revealed negative ANA, negative Factor V Leiden, and negative Prothrombin Mutation G20210A. The Homocysteine level was abnormally high at 17.5 Unit. She was started on subcutaneous Vitamin B12 injections and oral Vitamin B complex.

A follow-up test after one-month of the Vitamin B therapy showed improvement of Homocysteine level at 10.4 Unit. The abdominal pain improved substantially.

Discussion

Factor V Leiden Mutation
In 1994, a defect in the factor V gene resulting in activated Protein C resistance was described. Normally functioning Factor V is essential to the
anticoagulation property of activated Protein C. In Factor V Leiden, a single genetic defect involving replacement of G by A causes the amino-acid replacement of Arg5063 by Gln.

This Factor V Leiden gene has autosomal dominant inheritance. It is the most common genetic thrombophilia presenting in 3-12% of Caucasians and is rare in other ethnic group5. The relative risk of venous thrombosis in patients heterozygous for factor V Leiden is increased by four- to eight-fold, and the risk of idiopathic venous thrombolism increases with age. Homozygous carriers of factor V Leiden have 50 to 100 times higher risk in development of thrombosis.

In addition to the venous thromboembolism, coronary artery thrombosis has been notably associated with the factor V Leiden mutation in young men and women6,7.

Pregnancy and estrogen-containing hormonal therapy substantially raise the risk of thrombosis in women with factor V Leiden. Similarly, Tamoxifen or Raloxifene also increases the risk of thromboembolism8.

For asymptomatic carriers of factor V Leiden, vigorous prophylaxis during high risk periods such as surgery, avoidance of hormonal products and prolonged immobility should be provided.

In case of life threatening thrombosis such as pulmonary embolism, recurrent thrombosis, or atypical thrombosis, therapeutic heparin or low-molecular-weight heparin, followed by lifelong oral warfarin therapy is recommended2.

Prothrombin G20210A Mutation
The Prothrombin G20210A mutation involves a single amino acid change in the 3’ untranslated region of the gene encoding prothrombin. It was first reported in 1996. This change causes elevated levels of prothrombin and thrombin. The prevalence of the prothrombin gene mutation is about 2-3% in Caucasians, making it the second most common genetic thrombotic risk factor after factor V Leiden. Similar to factor V Leiden, the prothrombin gene mutation is uncommon in non-Caucasian population, and has autosomal dominant inheritance2. It is associated with an elevated risk of DVT. The heterozygotes having this mutation have about a two to four fold risk of increase over baseline.

Protein C and Protein S Deficiency
Typically, hereditary deficiency of protein C results from an autosomal dominant trait in which affect ed individuals have approximately 50% of normal level of functional plasma protein C. Protein C is synthesized in the liver, and is activated by limited proteolysis by thrombin. Activated Protein C (APC) is a potent anticoagulant enzyme which inactivates factor Va and factor VIIIa, and its deficiency is linked to thrombosis with odd ratio 6.5-89. Protein C deficiency occurs in 0.2-0.4% of normal individuals.

Because acute thrombosis can alter the level of protein C1, testing of protein C deficiency, even if the test after the thrombosis event is positive, should be repeated. In this case, initial protein C level before starting the warfarin therapy was abnormally low; but repeated protein C level came back normal.

The levels of both Proteins C and S will be lowered by the warfarin therapy. Therefore the test should be done while the patient is off warfarin for at least two weeks.

Treatment of protein C (and protein S) deficient individuals with warfarin can result in a rare condition called warfarin-induced skin necrosis. This disorder is thought to arise as a result of the transient decrease in protein C and protein S levels caused by warfarin binding in the bloodstream, which worsens a preexisting hypercoagulable state10.

Protein S is a co-factor for APC, and decreased levels of free protein S contribute to hypercoagulability. Its deficiency is similar to protein C deficiency clinically, biochemically, and genetically2.

Antithrombin Deficiency
Antithrombin (also known as antithrombin III) is a plasma protease inhibitor that neutralizes thrombin, factors IXa, Xa, and Xla. Its rate of inhibition of thrombin is catalyzed by heparin. Antithrombin deficiency with its prevalence of 0.2% of popula-
tion results in an increase in the level of thrombin activity and increase conversion of fibrinogen to fibrin, and tendency toward thrombosis.

Resistance to the anticoagulant effects of heparin has been observed in some patients with antithrombin deficiency. However, heparin resistance is quite common in general patients with thrombosis. Both acute thrombosis and several days of heparin therapy can decrease antithrombin level, which may lead to an erroneous diagnosis of hereditary antithrombin deficiency. Therefore, it is necessary to repeat the test when the patient is not on heparin therapy after the auto thromboisis event is over. Acquired conditions leading to lowered levels of antithrombin are common and include liver disease, DIC, nephrotic syndrome, chemotherapy and preeclampsia.

Hyperhomocysteinemia
Hyperhomocysteinemia is commonly associated with both venous and arterial thromboembolism, with the odd ratio for venous thrombosis at 2.5-3. The association of hyperhomocysteinemia and venous thrombosis is stronger among women with odd ratio 7, and it also increases with age. It also increases risk of atherosclerosis and myocardial infarction.

Hyperhomocysteinemia can be caused by either genetic defect or acquired vitamin B deficiencies. The most common genetic cause involves a methyltetrahydrofolate reductase (MTHFR) gene polymorphism, C677T, that occurs in 5-15% of white population, and results in mild hyperhomocysteinemia. Suboptimal levels of folate, Vitamin B6 or Vitamin B12 can also contribute to acquired mild to moderate hyperhomocysteinemia by providing inadequate cofactor levels to support the enzymes regulating homocysteine metabolism. Conversely, administration of folate with vitamins B6 and B12 can reduce homocysteine levels.

Testing recommendations for thrombophilia
Clinicians most commonly order testing genetic thrombophilia when presented with an individual with idiopathic DVT or with a family history of thrombotic events (Table 3, Table 4). The result of testing in these patients may be helpful in determining duration of anticoagulation therapy, in counseling family members, and in guiding thrombosis prophylaxis.

Table 3.

<table>
<thead>
<tr>
<th>Indications of Genetic Thrombophilia Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Any patient with DVT less than 50 years old</td>
</tr>
<tr>
<td>2. Idiopathic DVT any age</td>
</tr>
<tr>
<td>3. Strong family history of thrombosis</td>
</tr>
<tr>
<td>4. Venous thrombosis in usual site</td>
</tr>
<tr>
<td>5. Recurrent venous thrombosis</td>
</tr>
<tr>
<td>6. Life-threatening thrombotic event</td>
</tr>
<tr>
<td>7. Relatives of patients with genetic thrombophilia</td>
</tr>
<tr>
<td>8. Recurrent adverse pregnancy outcome and still birth</td>
</tr>
</tbody>
</table>

Table 4.

<table>
<thead>
<tr>
<th>Tests to consider:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. CBC, Prothrombin Time (PT) and Partial Prothrombin Time (PTT)</td>
</tr>
<tr>
<td>2. Factor V Leiden</td>
</tr>
<tr>
<td>3. Prothrombin G20210A</td>
</tr>
<tr>
<td>4. Protein C, Protein S and Antithrombin</td>
</tr>
<tr>
<td>5. Lupus Anticoagulant</td>
</tr>
<tr>
<td>6. Antiphospholipid Antibody</td>
</tr>
<tr>
<td>7. Homocysteine level</td>
</tr>
</tbody>
</table>

Primary care physicians should consider several issues when choosing test to perform in suitable individuals. First, testing for the genetic thrombophilia is costly. Second, the use of “panels” of tests is not the best appropriate approach. Testing should be individualized to the clinical situation. Many of these tests are affected by the presence of the acute thrombosis itself and anticoagulation therapy as described earlier. Only genetic testing for the Factor V Leiden and Prothrombin G20210A mutation can be reliably interpreted in the setting of a recent thrombotic event or oral anticoagulant therapy.
REFERENCES


Who is this Lady?

Answer on Page 47
Non-Invasive Imaging Strategies in Vascular Disease

In recent decades an increasing number of vascular problems are being solved with non-invasive imaging rather than catheter angiography. Diagnostic catheter arteriography is seldom done nowadays as the initial study to evaluate peripheral vascular disease, carotid arteriosclerosis or pulmonary embolism. In the venous system, contrast venography is seldom done to diagnose deep vein thrombosis or venous incompetence.

There are several non-invasive modalities to choose from and the most appropriate one varies from one clinical problem to another. The commonly used modalities are ultrasonography with color and spectral Doppler, contrast enhanced CT arteriography (CTA) and MR angiography without or with gadolinium enhancement (MRA).

Abdominal Aorta
The abdominal aorta is usually evaluated with ultrasonography, which is less expensive than CT or MRI. Sometimes the abdominal aorta is obscured by bowel gas, in which case CT is necessary. It is best done with intravenous contrast, which will distinguish the lumen from surrounding thrombus and plaque. In evaluating aortic aneurysms, the most important measurement is the outer diameter of the aneurysm, and this can be measured without intravenous contrast. When an aneurysm of the proximal abdominal aorta is discovered on ultrasonography, CT is also indicated to precisely measure the distance of the aneurysm from the origin of the renal arteries as this has a major impact on surgical treatment. Occlusion of the abdominal aorta can be diagnosed by color duplex ultrasonography or with contrast enhanced CT or MRI.

Thoracic Aorta
The thoracic aorta cannot be imaged by ultrasonography, so CT or MRI must be used. Aneurysm of the thoracic aorta are best evaluated with contrast enhancement, but, as with the abdominal aorta, the outer diameter of aneurysm can be measured without contrast.

For aortic dissection, contrast enhancement with either CT or MRI is an absolute necessity to identify intimal flaps. When an aortic dissection is suspected, it is important that the entire aorta and iliac arteries are imaged to determine both the proximal and distal extent of the dissection. Scanning must also be done to the base of the neck, as dissections can extend into brachiocephalic vessels.

Trans esophageal echocardiography is also very accurate in diagnosing dissection of the aortic root, but cannot evaluate distal extension of the dissection.

Carotid Arteries
Ultrasonography with color and spectral Doppler is the mainstay of carotid imaging. It is very reliable and accurate and is usually the only test necessary.
Some vascular surgeons will do a carotid endarterectomy on the basis of ultrasonography alone, but most like to have an arteriogram-like study of the entire carotid to exclude additional stenotic lesions either more proximally at the origins of the brachiocephalic vessels or more distally in the carotid siphons or in the intracranial circulation. Such an anatomic display can be provided by MR angiography without or with contrast, or by contrast enhanced CT arteriography. If carotid angioplasty or stenting is contemplated, catheter angiography is, of course, necessary.

**Intra-cranial Circulation**

MRA without or with gadolinium enhancement can detect stenosis or occlusions of the intracranial circulation.

Intracranial aneurysms as small as 2 mm can be detected with a sensitivity of 97% per patient, although the sensitivity per aneurysm is lower. CTA has greater spatial resolution than MRA and was found in a study by Villablanca et al. to show aneurysms as small as 1.7 mm. Arteriovenous malformations are very well seen or MRA.

**Renal Arteries**

Ultrasonography is limited in evaluation of renal arteries for renal artery stenosis. The Doppler waveform in the intrarenal arteries can be evaluated for evidence of renal artery stenosis, but the main renal arteries are frequently obscured by overlying bowel gas. Contrast enhanced CT or MR arteriography are both better than ultrasonography in evaluating renal artery stenosis.

Multidetector (16 or 64 detectors) CT scanners have better resolution than MRA, but MRA is the procedure of choice when there is renal insufficiency, since it does not use iodinated contrast material.

**Peripheral Arteries**

Ultrasonography with color and spectral Doppler (color duplex) is the initial procedure of choice for the peripheral arteries. It can identify plaques, show stenoses and occlusions, and evaluate adequacy of peripheral run-off. CTA with a 64 detector scanner provides high resolution images of the peripheral arterial system. Contrast enhanced MRA has the disadvantage of relatively slow image acquisition which makes timing of the contrast bolus difficult in the more peripheral vessels (below the knee).

**Coronary Arteries**

Multidetector CT scanners are making CTA of the coronary arteries feasible with high spatial and temporal resolution. The coronary arteries can be imaged with ECG gating during a single short breath-hold. Because it is a cross-sectional technique it can directly image plaque, both calcified and non-calcified. MRA of the coronary arteries is more difficult as it does not have the temporal resolution of CTA.

**Venous System**

Evaluation of the peripheral venous systems is now almost exclusively the domain of ultrasonography. This is true in searching for deep vein thrombosis and also in evaluating venous insufficiency. Dialysis access grafts and arteriovenous shunts are also best evaluated by colour duplex ultrasonography. If stenosis or occlusion of the access graft is found, catheter angiography with de-clotting of the graft and angioplasty/stenting of stenotic lesions is then done.

Deep vein thrombosis of pelvic veins is not well seen by ultrasonography, and contrast enhanced CT with delayed scanning is the best modality when this diagnosis is suspected.

**Pulmonary Embolism**

Contrast enhanced CT has supplanting all other tests in the evaluation of possible pulmonary embolism. It is far more accurate and specific than radionuclide ventilation/perfusion scans and has also been found to be more accurate than pulmonary arteriography, which used to be considered the gold standard.

Some centers do delayed scanning of the lower
extremities and pelvis routinely after scanning of the chest for pulmonary embolism, as this provides “one stop shopping” for both DVT and pulmonary embolism. However, since most pulmonary embolism studies are negative, doing this routinely would entail considerable additional radiation exposure and cost, and it would be best reserved for those instances when pulmonary embolism is found.

Conclusion
Non-invasive imaging of the vascular system has improved dramatically in the past few years, and invasive catheter angiography is now largely reserved for those patients in whom an interventional procedure is contemplated.

REFERENCES
A 32-year-old Hispanic male, a poor historian, presented to an orthopedic clinic in Los Angeles with the incidental complaint of a skin lesion which he had noticed over the last two months appearing above his left knee. There was excoriating and erythema but no effusion, drainage, or any sign of infection. The lesion appeared like an allergic dermatitis or ‘psoriatic-like’ to the orthopedic physician. Topical corticosteroid cream was prescribed for treatment.

One month later, the patient returned for follow-up. There was no improvement of the skin lesion with the topical corticosteroid cream. According to the attending orthopedic physician the lesion resembled ‘pemphigus’ now and consultation with a dermatologist was recommended. However, the patient missed his dermatology appointment.

Two months later, the patient presented to a Medical Center in Bakersfield, California, with the same complaint. The lesion had increased in size from the initial papule of about 1 cm, five months prior, to about 7 cm by 6 cm. It had irregular borders with drainage. Upon further questioning, the patient stated that he was a gardener in Kern County and approximately 11 months prior, while working, he slipped and twisted his left ankle and injured his left knee. He was taken off work and was seen at an industrial clinic, where an X-ray of his knee did not show any fracture or dislocation. The pain persisted and he was seen three weeks after the time of injury at a hospital in Bakersfield, where a repeat X-ray did not show any abnormal findings. The patient was provided with physical therapy and pain medication without much relief.

A magnetic resonance imaging (MRI) of the knee finally showed some positive findings and the patient underwent video arthroscopic surgery of the left knee.

Four months after the operation, the patient still complained of pain in the left knee and left ankle, described as a constantly aching pain without any radiation. The pain was worse with prolonged standing, climbing, squatting, kneeling, or walking greater than 15 minutes. He also had weakness of the left lower extremity. The patient began noticing discoloration in various spots around the knee. He believed that “one of the spots opened up” and had been growing into the presenting ulceration. He had been on antibiotics without any relief of symptoms. The patient denied any fever, chills, nausea, vomiting, fatigue, night sweats, or weight loss.

The only significant medical history included a dog bite twenty years ago at the left knee and thigh area, and an industrial injury five years earlier to the right shoulder. He also mentioned having tuberculosis (TB) prophylaxis while in jail about nine years ago. There were no other operations besides the knee surgery. His family history was noncontributory. His social history revealed that the patient used to drink two-three beers daily, used cocaine about five years ago but denied intravenous drug abuse, denied tobacco or alcohol abuse, was monogamous for a year but had multiple sexual partners in the past with a history of genital warts.
but no other sexually transmitted diseases. His last human immunodeficiency virus (HIV) test was in Mexico about one year earlier, which was negative. He had completed the fifth grade.

The initial laboratory findings at Bakersfield included a leukocyte count of $3.14 \times 10^3$/mm$^3$, hemoglobin and hematocrit of 13.7 g/dL and 40.1%, platelets of 222,000/mm$^3$ with a normal leukocyte differential. The basic metabolic panel results were all within normal limits. The erythrocyte sedimentation rate was 28 mm/hr. Acid-fast bacilli (AFB) culture and smear were negative. Coccidiomycosis serology was negative. The HIV test was negative. The wet mount of the wound drainage did not show any fungi or yeast. Gram stain showed moderate numbers of neutrophils (PMNs) and many Gram positive cocci. Culture of the wound showed *Staphylococcus* coagulase positive sensitive to clindamycin and vancomycin; there were no yeast or fungi. The patient was treated with antibiotics post debridement and a biopsy of the leg lesion was obtained.

Two months after leaving a Bakersfield medical center, the patient was seen in a family practice clinic in Los Angeles with increased discomfort of the open, infected leg wound which made weight bearing difficult. At that point, the family physician admitted the patient to the current hospital in Long Beach for intravenous antibiotics with further work-up and management.

At the current hospital admission, wound cultures grew *Klebsiella pneumoniae*, *group D Enterococcus*, *Proteus mirabilis*, and *Bacteroides vulgatus*, but were negative for fungus or AFB. Blood cultures were also negative. The X-Ray and MRI of the left knee did not show any significant findings. Considering the patient was unresponsive to antibiotic treatment, he was worked up for more uncommon infections and diseases which may cause an immunocompromised state. The HIV, VDRL, histoplasma, blastomycoses, sporothrix, and leishmaniasis serology were all negative. The patient was also negative for ANA, HLA B-27, and tuberculosis.

The patient’s physical examination was unremarkable except for a 7 cm by 6 cm, irregular bordered, ulcerated wound with serosanguineous drainage, without pus, with some granulation tissue, and tenderness on palpation above the left knee. There were multiple hyperpigmented (purplish), erythematous, thickened, annular lesions approximately 0.5 cm – 1.5 cm in diameter, some with crusting at different stages of healing, on all four extremities, chest, back, and dorsum of the penis (Fig. 1). There was a surgery scar over the left knee noted.

![Figure 1A-C](image-url)

*Figure 1A-C: The discolored, occasionally ulcerated, purplish skin plaques and papules on the patient’s leg, chest, and abdomen.*
The initial serum liver functions showed an aspartate aminotransferase (AST) of 99 U/mL, an alanine aminotransferase (ALT) of 50 U/mL, alkaline phosphatase of 194 IU/L, and albumin of 2.1 g/dL. The AST and ALT became elevated as high as 218 and 268. The albumin dropped further to a value of 1.2. A gastroenterologist was consulted and attributed the elevated liver functions to the probable related systemic infectious or infiltrative process, drug toxicity (the patient had fluconazole initially), total parenteral nutrition (TPN), and possibly hepatitis. However, hepatitis serology was negative.

The patient had a repeat wound debridement and biopsy, after which he had prolonged bleeding. The partial thromboplastin time (PTT) was 37 seconds, the prothrombin time (PT) was 15.9 seconds, and the international normalized ratio (INR) was 1.9. The initial complete blood count showed a leukocyte count of $2.8 \times 10^3$/mm$^3$, hemoglobin and hematocrit of 9.4 g/dL and 28.3%. During the hospital course, the patient became pancytopenic with a leukocyte count of $0.2 \times 10^3$/mm$^3$ with a hemoglobin and hematocrit of 6.7 g/dL and 22.2%, and platelet count of 22,000/mm$^3$. He had a total of 12 units of packed red blood cells transfused during the hospital course. The patient also had spiking temperatures, diaphoresis, and developed a mild, nonproductive cough. A chest X-ray did not show any acute disease and blood cultures remained negative. The patient was put on reverse isolation and a hematologist was consulted.

Skin biopsies of the lesions were then performed. The latter showed an atypical lymphoid infiltrate with a perivascular, periadnexal, and subcutaneous distribution (Fig. 2). There was evidence of angioinvasive properties suggestive of a malignant lymphoproliferative process.

Fig. 2A-D: Histomorphologic features of the lesion: A and B, an ulcerated lesion exhibiting a malignant lymphoproliferative process with angiocentric properties infiltrating the dermis and subcutaneous adipose tissue (100 X); C, A high-power magnification (400 X) of the homogeneous population of malignant lymphocytes; D, A large atypical malignant lymphocyte surrounded by a polymorphous, predominantly reactive, mononuclear cells (400 X).
Immunohistochemical studies revealed negative staining for CD20 and CD30. The atypical lymphocytes were positive for CD3 and CD56, consistent with malignant lymphoma, natural killer (NK)/T-cell lymphocytic origin. Additional studies revealed Epstein-Barr virus (EBV) positivity, with no expression of CD4 or CD8, which again, is supportive of the diagnosis of NK/T-cell lymphoma. A summary of the results of his immunohistochemical studies follows:

The peripheral smear contained a few atypical cells suggestive of the neoplastic lymphocytes (Fig. 3). A bone marrow biopsy was subsequently performed and the results showed a hypercellular marrow exhibiting an atypical lymphoid infiltrate with marrow fibrosis and absence of stainable iron consistent with NK/T-cell lymphoma.

A computed tomography (CT) scan of the abdomen and pelvis was negative for any mass or metastatic disease process.

The patient also developed other complications during the hospital course including candidiasis of the bladder, bronchitis (sputum culture negative), conjunctivitis, and left orchitis.

The final diagnosis was NK/T-cell lymphoma, stage IVB. The patient was started on chemotherapy which included fludarabine, cyclophosphamide, doxorubicin, and prednisone. He also had weekly injections of erythropoietin for anemia and daily filgrastim as needed for leukopenia. Chemotherapy was repeated every 3-4 weeks as tolerated for a planned total of 6 cycles. The patient tolerated the initial round of chemotherapy and was then transferred to a tertiary care center to be followed there for the rest of his treatment of NK/T-cell lymphoma.

DISCUSSION

Malignant lymphoproliferative diseases involving the skin are primarily cutaneous T-cell lymphomas and less commonly cutaneous B-cell lymphomas. Recently, a third line of non-Hodgkins lymphoma was discovered, the natural killer (NK)/T-cell lymphoma, which can involve the skin in a primary or secondary fashion. These lymphomas are further subdivided into nasal NK/T-cell lymphomas and non-nasal NK/T-cell lymphomas.1

Natural killer (NK) cells are a third lymphocyte lineage, in addition to B- and T-cells, that mediate cytotoxicity without prior sensitization.1, 3 NK cells were once called null cells since they lack most of the usual T- and B-cell surface antigens. They comprise 10-15% of normal circulatory lymphocytes in the blood. They are capable of killing a wide variety of target cells, including tumor cells and cells infected with bacteria and viruses.2 Morphologically, NK cells are hand-mirror-shaped lymphocytes (Fig. 4) with abundant, pale cytoplasms with azurophilic granules on Giemsa staining by touch smear.2, 3 NK tumor cells can vary in size, ranging from small to medium sized to large and pleomorphic.2

Immunophenotypically, an NK-cell marker, CD56

<table>
<thead>
<tr>
<th>PARAFFIN SECTION IMMUNOHISTOCHEMICAL STUDIES:</th>
<th>Antibody</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leg Lesion:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD20</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>CD3</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>CD56</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>CD30</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>CD4</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>CD8</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Bone Marrow:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD20</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>CD3</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>CD56</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>CD30</td>
<td>Negative</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PARAFFIN SECTION IN SITU HYBRIDIZATION STUDIES:</th>
<th>Antibody</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBER</td>
<td>Positive</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 3: a circulating atypical lymphocyte exhibiting morphologic features reminiscent of a “hand-mirror.”
antibody, recognizes N-CAM (neuronal adhesion molecule).\textsuperscript{3,4} CD56 is found in a small population of normal T-cells as well. In contrast to B and T lymphoid cells, NK-cells do not possess a rearranged T-cell receptor (TCR) locus; they have a germline configuration.\textsuperscript{1,3} They express receptors for major histocompatibility complex (MHC) class I but not class II antigens and do not require expression of the MHC molecules on the target cells to mediate cytolysis.\textsuperscript{1-3} Recent studies suggest that NK-cells and T-cells may originate from a common precursor cell.\textsuperscript{3} In the fetal thymus, there is a bipotential T/NK progenitor capable of differentiation into either T cells or CD56+ NK cells. In adults, the bone marrow is the main site of NK-cell development. The primitive NK-cell precursor can be both CD34- and CD34+; further development leads to the loss of the CD34 molecule, CD7 surface expression, CD3 cytoplasmic expression of the epsilon chain, and CD3 surface expression. The mature NK-cell phenotype is CD2+/-, CD4-, CD5-, CD7+, CD3epsilon+, CD16+/-, and CD56+.\textsuperscript{2} Due to the uncertainty regarding the cell of origin in NK/T-cell lymphomas in the past, these lymphomas were often diagnosed as one of the following: lethal midline granuloma, midline malignant reticulosis, lymphoma of large granular lymphocytes, CD56+ T-cell lymphoma, CD56+ angiocentric lymphoma, and CD56+ hematolymphoid malignancy.\textsuperscript{1}

**INVASIVENESS:** NK-cell lymphomas often show angiocentricity, angiodestruction, and zonal necrosis.\textsuperscript{1-3} Tumor cells concentrate around and within blood vessels, with infiltration and destruction of the blood vessel wall within the dermis and subcutis. Cytologically, there is commonly an admixture of reactive inflammatory cells including small lymphocytes, histiocytes, polymorphs, eosinophils and plasma cells.\textsuperscript{2} The number of neoplastic lymphocytes may be small, mimicking a reactive infiltrate, especially when there is minimal cytologic atypia. Hemophagocytosis can be observed in involved tissues, including the liver and bone marrow, and may account for the pancytopenia; it may be seen rarely, in the peripheral blood as well.\textsuperscript{6}

**PATHOGENESIS:** The molecular mechanisms leading to the malignant transformation of NK-cells remains unclear. One consistent association is the pathogenetic infection of the tumor cells by Epstein-Barr virus (EBV), which has been shown to present as a single episomal form localized to the neoplastic cell. This is consistent with infection of a single precursor cell that subsequently gives rise to the entire tumor clone, suggesting the important role of EBV in tumor pathogenesis. EBV is a member of the herpes virus family, and primary infection usually causes a mild, self-limiting illness or infectious mononucleosis. Normal immune surveillance by HLA-restricted cytotoxic T-cells prevents continuous proliferation of EBV-infected cells.\textsuperscript{3} EBV-infected cells may show three patterns of latency. Type I latency express only EBV nuclear antigen 1 (EBNA1). Type II latency express EBNA1 and latent membrane protein (LMP) 1 and 2. Type III latency express the full spectrum of EBV latent genes, including EBNA 1 to 6, and LMP 1, 2A and 2B. The downregulation of the immunogenic EBNA2-EBNA6 proteins means that the neoplastic cells may escape from surveillance by cytotoxic T-cells. LMPs are expressed and they are potentially immunogenic.\textsuperscript{2} Interestingly, there have been rare cases of NK cell post-transplantation lymphoproliferation disorder with strong association with EBV as a late

![Image](https://via.placeholder.com/150)

Fig. 4: A circulating lymphocyte exhibiting “hand-mirror” morphology in a patient with acute infectious mononucleosis.
complication of solid organ transplant (renal and cardiac transplant).7-9 There have also been at least 58 cases reported, mainly in Japan, of people who have acquired hypersensitivity to mosquito bites with associated chronic EBV infection and subsequent NK-cell leukemia/lymphoma.10

**Epidemiology:** EBV infection is much more prevalent in Asians.11 As of 1997, there have been greater than 150 cases of NK lymphoma/leukemias reported in the Chinese and the Japanese, compared to greater than 30 cases reported in the Western patients, and a small number in the South American patients.2 NK-cell lymphoma is more common in men and peaks during the fifth decade. It is also uncommonly found in children.12

**Subclassifications:** Most of the NK-cell lymphomas are of the nasal NK/T-cell lymphoma type that commonly presents as midfacial destructive disease. Initial signs and symptoms may resemble chronic-recurrent sinusitis. There may be obliteration of the nasal passages and maxillary sinuses, with involvement of adjacent alveolar bone, hard palate, orbits, and nasopharynx.1, 13 On an immunophenotypic and genotypic basis, many of the lethal midline granulomas and nasal lymphomas have been shown to be of NK-cell origin with an immunohistochemical profile of CD2+, CD3 (Leu4)-, CD3 (epsilon)+, CD56+ and T-cell receptor (TCR) in the germline configuration.3 This group of lymphomas is also consistently associated with EBV positivity demonstrated via in situ hybridization (ISH) techniques using EBV-encoded small nuclear RNA (EBER) probes.14

The non-nasal NK/T-cell lymphoma cases affect extranodal sites including the upper aerodigestive tract, skin, liver, spleen, gastrointestinal tract, testis, and muscle. N-CAM shows homophilic binding properties. Thus, it has been postulated that these sites may strongly express CD56, favoring homing of NK-cell lymphoma cells. The non-nasal group is further subdivided into primary cutaneous and 4 types of secondary cutaneous lymphomas: nasal-type, aggressive, blastoid, and other specific lymphoma types (i.e., T-cell lymphomas, such as lymphoblastic lymphoma, and true histiocytic lymphomas that can stain positively with CD56).1

The nasal-type NK/T-cell lymphoma is the most common subtype among the secondary cutaneous non-nasal NK/T-cell lymphomas. It is morphologically, immunophenotypically, and genotypically identical to nasal NK/T-cell lymphoma. However, the most common site of involvement is the skin, followed by the soft tissues.1

There is a particularly rare and aggressive type of NK-cell lymphoma with widespread organ infiltration and a leukemic phase. This type of lymphoma is characterized by fever, pancytopenia, circulating malignant cells resembling large granular lymphocytes, infiltration of the liver, spleen, lymph nodes, bone marrow and rarely skin.1 Typically, these cases are CD2+, CD3-, CD56+, EBV+, and TCR gene in the germline configuration. The clinical course is fulminant multi-organ infiltration with an extremely poor prognosis (death often within 6 weeks). There have been about 3 reported cases of aggressive NK-cell leukemia/lymphoma.1, 2

Blastic NK-cell lymphoma, also termed CD4+CD56+ hematodermic neoplasm (CD4/CD56 HD) is the least common type of the non-nasal lymphoma encompassing distinct genetic, morphologic, etiologic, and diagnostic criteria.34 It frequently involves the skin like nasal-type NK/T-cell lymphoma; but it may be distinguished by its lymphoblastoid-like morphologic characteristics, the frequently CD2-immunophenotype, and the lack of EBV association.5, 16-18

The other specific lymphoma types with CD56 expression category have variable clinical presentation with either nodal or extranodal disease. Extranodal predilection sites include the spleen, bone marrow, and skin. Unlike the other secondary cutaneous non-nasal CD56+ lymphomas, these lymphomas are positive for both NK cells and additional T-cell markers (i.e. CD3), and TCR genes are typically rearranged.1
Primary cutaneous CD56+ lymphoma is very rare, with only 6 reported cases as of 2002. It is defined as a lack of extracutaneous disease for at least 6 months from the time of diagnosis. Cutaneous eruptions may present as a few to multiple erythematous, reddish-blue macules, papules, hyperpigmented plaques, or hard nodules.1, 3

Cases involving the liver and spleen can mimic the hepatosplenic-gamma/delta T-cell lymphoma; however, in contrast to the NK-cell lymphomas, these T-cell lymphomas do express Leu4 and TCR-delta, have rearranged TCR gene and are not EBV related. In disseminated NK-lymphoma/leukemia, there is frequently an associated severe impairment of liver function, leading to jaundice and coagulopathy. Serum Fas ligand levels tends to be elevated. The Fas/Fas ligand system is known to cause liver damage through induction of apoptosis. Production of Fas ligand by the lymphoma is postulated to be partly the cause of liver damage in NK lymphoma.2 Yet, in a study of 23 cases of NK lymphoma, findings suggest frequent Fas gene mutation can result in resistance to apoptosis and increased tumor immunology.19

DIAGNOSTIC PITFALLS: Although most cases of nasal lymphoma are NK lymphomas, true T-cell lymphomas with rearranged TCR can present as nasal lymphoma and may express CD56 as well. Most of these cases have CD3 (Leu4)+. It is generally agreed that CD3 (epsilon)- is not helpful in predicting lineage but Leu4 negativity is useful in delineating the NK cell lineage in a CD56+ lymphoma.2

TREATMENT AND PROGNOSIS: Treatment of NK cell lymphoma/leukemia has been unsatisfactory so far. Localized disease may be treated with irradiation. High dose, aggressive radiotherapy in combination with chemotherapy may be effective in achieving local tumor control. Chemotherapy medications include cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) typically given for about 7 cycles. Thereafter, maintenance treatment may be with cyclophosphamide, vincristine, and prednisone (COP) for about 1 year.3 NK-cell lymphoma involving skin and other organs tend to be refractory to chemotherapy. There is a high recurrence rate even with repeated courses of CHOP chemotherapy. High dose chemotherapy and autologous stem cell transplantation have resulted in improvement in survival in some cases, especially those that have been refractory to treatment or have had recurrence.12, 20-24, 32 There are no suitable clonal markers for tumor cell detection in NK lymphoma, making monitoring of minimal residual lymphoma difficult.25

Prognosis has been variable. The median survivals have been less than 15 months in many cases. Staging did not appear to have a major impact on survival. However, young age does have a more favorable prognostic value.2 In a retrospective study of 30 patients with CD56+ lymphomas initially presenting with cutaneous lesions, it was found that the presence of extracutaneous disease at presentation is the most important clinical variable and is associated with a poorer prognosis than those without skin involvement at presentation. However, the extent of initial skin involvement does not predict outcome. A more favorable outcome is seen in patients with coexpression of CD30.26 Another study of 108 patients with angiocentric nasal NK/T-cell lymphoma showed overall survival at 8 years to be about 82-90%, and disease-free survival was 80%.27

CONCLUSION: Information about NK lymphoma is still relatively scant, in part due to the fact that this third lymphoma lineage has only recently been recognized and there have been an insufficient amount of reported cases for observation and research. There is currently much confusion and lack of consensus regarding nomenclature and classification for NK-cell lymphoma.28 The origin, diagnosis, clinical spectrum, optimal therapy, long-term outcome, and prognostic factors remain unclear for this disease entity.29, 30 We do know that NK lymphoma can be rapidly aggressive with an
extremely poor prognosis. The initial presentation is often nonspecific, as is in our case report, and commonly lacks the initial constitutional symptoms associated with many cancers (fever, weight loss, night sweats, lymphadenopathy); this can be misleading in our search for the final diagnosis. Therefore, it is imperative that we keep NK-cell lymphoma in mind in our differential when faced with an unusual nasal/midfacial complaint or an atypical dermatological manifestation, especially if the patient is of Asian descent. Proper work-up for NK lymphoma requires immunophenotyping particularly for CD56 positivity (a marker of NK cell lymphoma), along with germline TCR genotype, and the presence of EBV infection. Future gains in the understanding of the nature of NK-cell malignancy will hopefully enable us to recognize this disease in a timely manner and come up with new treatment approaches or alternatives to improve the prognosis of this aggressive lymphoma.

REFERENCES


Answers:

page 24: Wilhelm Konrad Roentgen (1845-1923)

page 35: Madam Marie Curie in 1910

page 38: These are pictures from Positron Emission Tomography. The left picture shows an Alzheimer’s brain. The right picture shows a normal brain.
Current Concepts in Treating Rotator Cuff Tears

Asghar Husain, MD
University Orthopedics

Anatomy

The rotator cuff is a musculotendinous complex consisting of the subscapularis, supraspinatus, infraspinatus, and teres minor. These muscles originate from the scapula and insert together around the humeral head. The biceps tendon travels between the supraspinatus and subscapularis, and inserts onto the superior aspect of the glenoid. The labrum is a fibrocartilaginous structure which encircles the glenoid, and serves as an attachment site for the stabilizing glenohumeral ligaments. The rotator cuff centers the humeral head in the glenoid, in conjunction with the upper back and chest muscles, during active shoulder motion.

Incidence

Degeneration and tearing of the rotator cuff appears to be an inevitable consequence of aging, with the prevalence of rotator cuff tears increasing with patients’ age. These tears can be partial or complete. Patients with partial rotator cuff tears are often labeled as having “tendinitis” by their physicians. The pain experienced in these situations is partly due to the tension on the torn rotator cuff fibers as well as inflammation of the bursal tissues that lie around the partly torn rotator cuff fibers. With significant tears, daily activities can become more difficult. Pain is often worse at night, even causing waking from sleep. Approximately 30% of 60 year olds and 50% of 70 year olds will have radiographic evidence of cuff degeneration. Interestingly, many of these individuals are asymptomatic.

Patients presenting with a full-thickness rotator cuff tear have an increased risk of developing a tear on the opposite side within two years. Additionally, there appears to be a higher incidence with a family history, and also a higher incidence of rotator cuff tears in smokers.

Evaluation

Evaluating a patient with shoulder pain requires careful consideration of many factors, including age, occupational activities, health, recreational activities, including smoking, use of medications, and mechanism of injury if present. Symptoms may arise following an injury, most commonly a fall on an outstretched hand. Often, however, symptoms begin insidiously without an identifiable event. The most common symptoms identified in patients with rotator cuff tears include: pain in the anterior and superior shoulder radiating to the lateral arm, pain with lifting the arm away from the body, and pain worsening at night. Examination findings do not always demonstrate weakness. Often there is pain with resistive muscle testing and tenderness over the attachment of the rotator cuff at the greater tuberosity. Patients may also express increased pain in certain arm positions, most often when overhead, possibly indicating the presence of impingement of the rotator cuff between the humeral head and acromion.

In assessing patients felt to have rotator cuff disease, it is imperative to exclude the presence of other conditions such as cervical radiculopathy, costoclavicular compression, and cardiopulmonary conditions. Generally, history and physical exam
parameters are the most important factors in establishing an accurate diagnosis. Diagnostic tests such as radiography and MRI scanning are additionally helpful in confirming the presence of rotator cuff tears and can also identify pathology of the biceps tendon, and the condition of the glenohumeral and acromioclavicular joints. MRI in conjunction with an arthrogram can be useful for identifying partial rotator cuff tears and labral pathology, and is used more often in patients below 50 years of age5,6,8.

Treatment Concepts
Treatment is still not standardized due to the variable natural history of patients with rotator cuff tears. A thorough evaluation assists with decision making during treatment, and is important in determining the relative risk of each individual patient for nonsurgical and surgical treatment. While the natural history suggests tears may increase in size over time, this does not always correlate with symptoms. Some patients are at a higher risk than others for developing irreversible changes. While treatment of rotator cuff problems should be individualized for each patient based on their specific issues, it is helpful when choosing treatment options to consider three general groups and their expected outcomes.

Patients presenting with shoulder pain and an intact rotator cuff may have primary tendon degeneration or partial tearing of the cuff attachment. These patients are generally considered to be at low risk of having irreversible changes, and often have a high success rate with nonsurgical management programs, including activity modification, shoulder-specific rehabilitation programs, and occasional use of analgesic agents5.

A second group includes patients usually below 60 years of age, with small to medium sized complete tears, or large partial rotator cuff tears (>50% thickness). Patients with acute traumatic tears within the past three months are also in this category. These patients often have activity levels which involve frequent rotator cuff muscle activity, which can lead to progressively increasing tear size over time. With nonsurgical treatment, these patients are at a higher risk for irreversible changes, such as tear retraction and stiffening, muscle deterioration and atrophy, fatty infiltration, and loss of vascularity at the tear margin7. Outcomes may be better in this group with early surgery to repair the torn tendon. With lengthy delays, repair can become much more difficult.

Tears in the elderly (over 70 years of age) make up the third group. Usually these are patients with large chronic tears that have already developed irreversible changes to the tendon tissue. These patients can do relatively well with nonsurgical management, including rehabilitation, analgesic agents, and judicious use of anesthetic/corticosteroid injections in the subacromial and/or glenohumeral joint space. When surgery is considered, it is usually done in a minimally invasive fashion to gently debride inflamed tissues, if cuff repair is not possible. The goal is to decrease symptoms despite lack of rotator cuff attachment and healing.

Nonsurgical Treatment
Physical therapy programs work best when specific goals are set, and patients have an active role in the program. This requires an accurate diagnosis, and careful physician-directed protocols to minimize overloading of the rotator cuff. Emphasis is on gaining parascapular muscle control, shoulder flexibility, and learning how to use specific muscle groups to protect torn rotator cuff tissues, as well as avoidance of aggravating activities. Gradual transition is made to previous work or sports activities under physician supervision. Anti-inflammatories and non-narcotic analgesics may be considered as an adjunct. If utilized, narcotic agents generally should be reserved for those patients with acute injuries or flare-ups on a short-term basis. Steroid injections into the shoulder may be used to provide temporary relief of pain and inflammation. Caution should be used considering their adverse effect on tissue healing.

Surgical Treatment
Generally, surgery is considered when pain significantly hinders lifestyle, and other treatments have failed. Outcome is most predictable when considering patient factors mentioned earlier, such
as age and general health. Injury-specific assessment is made of the potential “pain generators” in the shoulder. These include the subacromial bursa, rotator cuff tendons, biceps tendon, labrum, acromioclavicular joint, ligaments, synovial and articular surfaces. If these structures are not considered during the course of patient evaluation, surgery is less likely to be successful. The advent of shoulder arthroscopy has allowed a thorough assessment of structures within the glenohumeral and subacromial space. Correlating structural integrity seen at arthroscopy with presurgical examination findings allows for decision making to be made most optimally. Further treatment can then be carried out arthroscopically or through open incisions. The author’s preference is an all-arthroscopic repair for primary rotator cuff repairs.

The advantage of arthroscopic techniques is the ability to visualize and treat intrarticular pathology, as well as improved visibility during rotator cuff repair without the need for dissection or detachment of the deltoid muscle. Initial postsurgical pain also tends to be less than open shoulder procedures.

Postoperatively, patients are initially immobilized and instructed to avoid active shoulder movement for at least a six-week period. Patient-specific rehabilitation protocols facilitate regaining function as pain diminishes and healing progresses.

When all pain generators are surgically addressed, the result of rotator cuff repair is generally good. Historically, initial results of arthroscopic shoulder procedures were less satisfactory than open procedures. However, with improvements in technique and understanding of anatomic and repair factors, clinical results have generally equaled those of open procedures. Recent studies critically analyzing rotator cuff healing after arthroscopic and open procedures have shown a 30% to 80% incidence of retear following repair. Interestingly, most patients, including those with retears, demonstrated satisfactory pain relief. However, persistent shoulder weakness was present to a greater degree in those without cuff healing than in those who healed.

A current focus of the author’s practice as well as several other centers is to improve healing after rotator cuff repair. This involves critically evaluating presurgical issues, intraoperative factors, including specialized techniques and use of biologic-enhancing agents such as growth factors, and stringent postsurgical rehabilitation to minimize rotator cuff tension and activity while healing.

In conclusion, many patients with shoulder pain due to rotator cuff pathology can be treated nonsurgically. When surgery is indicated, a thorough assessment and treatment of pain generators will usually lead to a reliable result.

REFERENCES

Use of Ultrasound in the Emergency Department

Kenneth Moore, M.D.

Introduction
Ultrasound has been successfully used by a variety of specialties in medicine as a tool to improve the diagnostic ability of the physician. Ultrasound has been called “the stethoscope of the 21st century.” The use of this technology has a definite role in the modern practice of medicine by physicians other than radiologists. For example:

• Ob/Gyn physicians have learned the specific ultrasound skills used in their specialty.
• Critical care physicians use ultrasound for CVP placement and other line placement.
• Urologists, cardiologists, trauma and vascular surgeons have also used ultrasound technology.
• The American Institute of Ultrasound in Medicine is an organization, accepted by the American College of Radiology, which gives credibility to a multitude of specialties in medicine who use ultrasound in their practice.
• The AMA has acknowledged that ultrasound has a place in patient evaluation by any physician trained to use the technology.

The Emergency Department physicians frequently order ultrasound exams on emergency patients. In many cases what we really need is a very focused exam to provide a limited amount of information immediately. Our patients would be better served if we could perform these limited exams in the ED and refer the patients to Radiology for formal, comprehensive ultrasound exams at a later time. The limited information obtained from these focused ultrasound exams would help to speed up the patient’s diagnosis and disposition in many instances.

Emergency Department ultrasound is designed to be focused, limited, goal directed and is used to answer a specific clinical question. Are gallstones present? Is there a living intrauterine pregnancy? It is not meant to be comprehensive nor does it replace formal sonography. Some of the diagnostic and procedural applications suited for emergency department ultrasound are the bedside determination of cardiac activity in cases of cardiac arrest, pericardial effusion, free fluid in the abdomen or thorax, aortic aneurysm, the establishment or exclusion of intrauterine pregnancy, identification of foreign bodies and ultrasound assisted vascular access.

Emergency Medicine residency training programs currently teach ultrasound techniques to their residents. Several of Pomona Valley Hospital’s more recently trained ED physician staff have had such training in their residency programs. The other ER physicians have enrolled in ultrasound courses designed to teach them to use this modern device.

Why use Ultrasound in the Emergency Department?
The ability to provide 24 hour, 7 day a week immediate limited ultrasound evaluations is a great improvement in the quality of care provided to the ED patients. Bedside ED ultrasound enables us to:

• enhance our ability to accurately diagnose conditions
• improve the turnaround time for scans
• reduce the need to send unstable patients away from the ED for ultrasound
• reduce the patient’s overall time in the ED
What is the Scope of Emergency Physician Ultrasound Privileges?
Emergency physicians perform limited focused ultrasound examinations on patients presenting with immediate and urgent indications and procedural indications. Emergency physicians will not perform routine comprehensive ultrasound examinations in the ED. These will be referred to the Radiology Department.

Examples of immediate indications include but are not limited to the diagnosis of:
- Pericardial effusion and cardiac tamponade
- Diagnosis of PEA (pulseless electrical activity) in cardiac arrest
- Aortic aneurysm
- Presence or absence of intrauterine pregnancy in an unstable patient
- Documentation of fetal life in trauma or other maternal instability
- Evaluation of intra-abdominal hemorrhage in trauma

Examples of urgent indications include but are not limited to the diagnosis of:
- Presence or absence of intrauterine pregnancy in a stable patient
- Evaluation of gallbladder disease
- Presence or absence of obstructive uropathy

Procedural indications include but are not limited to:
- Vascular access
- Suprapubic urinary bladder aspiration
- Foreign body localization and removal
- Pericardiocentesis
- Thoracentesis
- Paracentesis

What are the Emergency Physician Credentialing Requirements?
The Emergency Physicians seeking ED Ultrasound privileges are given such privileges after it is determined that they have completed an appropriate ultrasound course and then have shown competence in the performing and interpretation of the limited ultrasound exams. The ER ultrasound exams are not meant to be comprehensive. The ED physician privilege criteria should not be confused with the Radiology criteria required to perform complete ultrasound examinations.

What has been the experience so far?
Pomona Valley’s Emergency Department currently uses the Sonosite Titan model ultrasound machine. The machines are mobile and rugged. They can be moved to the bedside without any difficulty. The knobs and buttons are at a minimum making them easy to operate. The transducers are compact and easy to handle. The screen graphics and resolution are satisfactory for our use. The machines have the capability for color Doppler flow and for printing. Overall, these are excellent machines for the ED.

Our ED ultrasound machines get used daily. Gallstones, ruptured ectopic pregnancies, central line IV placements, confirmation of living intrauterine pregnancies, presence of pus in a questionable abscess, presence of pericardial effusions, presence of soft tissue wooden foreign bodies are just some of the uses we have found for this technology. And now, after some training, the nurses are beginning to use ultrasound to help with finding peripheral veins for IV sites!
MISCELLANEOUS

A letter to all Southern California Clinicians

FROM EDITOR IN CHIEF

Dear Colleague:

The Gala Edition of Southern California Clinicians, the historical, one and only locally published medical journal, has received many accolades and encouragements from the entire medical community. The journal has proved its significant and value, and our editorial board has been asked to continue with publishing the next edition.

Based on the success of our first edition, we anticipate a demand to print even more copies of the next issue. In order to achieve this, we will have to rely on contributions from our colleagues.

The Southern California Clinicians Journal was established in November 2003 in the Pomona Valley and Inland Empire area. The editorial board involves all local physicians practicing in PVHMC and SACH. All contributing authors are your friends and colleagues. The Journal provides a means for modern California clinicians to publish articles, sharing their clinical experiences and opinions with other physicians, and showing their academic achievements in medical practice. It also provides a means of keeping a permanent record of valuable case studies and case reports from all departments and specialties in the modern era.

We invite all clinicians in Southern California to contribute interesting articles and reviews, including new developments in clinical skills and techniques, or new procedures applied during the medical practice.

We welcome and depend upon your generous contributions for support. Please consider the following categories for your contribution to this unique publication:

- One whole page with your name (or group name). 7.5” x 10”, your practice scope, location, address is $500.00
- A half page with your name (or group name), 7.5” x 5”, your practice scope, location, address is $250.00
- One quarter page with your name (or group name), 3.75” x 5”, your practice scope, location, address is $125.00

Dear friends, this medical journal belongs to you. Please help to make history by supporting this publication.

Contributions can be made payable to Southern California Clinicians and sent to Yin H. Lai, M.D., 1060 E. Foothill Blvd., Suite 203, Upland, CA 91786 (phone # 909-985-0699).

Thank you for your consideration.

Yin H. Lai, M.D.
Editor-in-Chief
Pomona Valley Hospital Medical Center, 1798 N. Garey Ave., Pomona, CA 91767
Phone #909-985-0699 Fax 909-985-2399 Email: yinhlai@gmail.com
The Greater Pomona Independent Physicians Medical Group

- Dependable
- Equitable
- Quality Care
- Quality Management
- Equal
- Friendly

Serving Pomona and Inland Communities

President
Sadiq Mandilawi, M.D.

Call Committee:
Samir Anabi M.D., Jalal Badday M.D., Lloyd Costello M.D., Ron Dunchok M.D.,
Jay Porcelli D.O., Chandrahas Agarwal M.D., Craig Endo M.D.,
Scott Lederhaus M.D., William Hale M.D., Joseph Hourany M.D.,
Frank Hsu M.D., Rohinder Sandhu M.D.

Greater Pomona Independent Physicians
(GPIP)
1234 Foothill Blvd.
La Verne, CA 91750

Phone: (909) 596-4879 • Fax: (909) 596-6612
Sam Arasoghli, M.D. is a Board Certified Otolaryngologist and currently on staff at Pomona Valley Hospital Medical Center, San Antonio Community Hospital, and Chino Valley Hospital Medical Center.

He completed his medical training at University of California, Irvine. Dr. Arasoghli provides treatment to areas of ear, nose, throat and facial/head & neck patients. He treats both children and adults. His special interests include treatment of snoring and sleep apnea. His office accept a variety of insurance plans and has offices in Pomona and Upland.

For an appointment, or for more information, please contact (909) 623-1503.

The Emergency Physicians at Pomona Valley Hospital and CEP (California Emergency Physicians Medical Group) congratulate Dr. Yin Lai and the editorial team at Southern California Clinicians for excellence in the publication of the journal.

Pomona Valley Hospital ER is pleased to announce our latest innovation called the ‘Rapid Medical Evaluation’ system. This is a new system for evaluating patients rapidly in the ER. Our patient turnaround times have been shortened considerably. This has led to improved patient and staff satisfaction.

We look forward to your referral of patients to our facility and invite you to call or visit our department and ask about the Rapid Medical Evaluation system.

Ken Moore, M.D.
Medical Director
909-865-9650
**John J. Kim, M.D.**

Member of American College of Gastroenterology

Practice at San Antonio Community Hospital

**Office Address:**
591 N. 13th Avenue
Upland, CA 91786

Tel. (909) 981-8905
Fax. (909) 982-8051

---

**M. Jay Porcelli, D.O. FACOFP**

President of American College of Osteopathic Family Physicians

Board Certified in Sport Medicine, Geriatric Medicine, Addiction and Pain Management

336 Ervilla Street
Pomona, CA 91767

Tel. (909) 620-1955
Fax. (909) 623-0720

---

**China Gate Restaurant**

365 South Mountain Avenue
Upland, CA 91786

(909) 982-2449

(In Mountain Plaza at Mountain Avenue and 7th Street)

---

**REAL ESTATE / NOTES & MORTGAGES**

Residential / Commercial Real Estate (Investing, Buy / Sell)

Note Appraisal, Seller Held Mortgages (Convert to ready cash)

Architectural Services

Bernard Feig
bernard.abc@gmail.com

Benyapa Tan
benyapa.abc@gmail.com

A&B COLLABORATIVE, INC.
1125 E. Broadway #204.
Glendale, CA 91205

T (909) 900-2119  F (818) 500-9359
FEMCARE OB-GYN ASSOCIATES
for Pomona Valley, Chino Valley, and Inland Empire

We provide comprehensive women’s healthcare in 3 convenient locations:

Pomona Office:
160 Artesia Street, Suite 330
Pomona, CA 91767
Tel. (909) 622-5654

Ontario Office:
756 N. Euclid Avenue, Suite A
Ontario, CA 91762
Tel. (909) 395-0030

Chino Office:
2140 Grand Avenue, Suite 120
Chino Hills, CA 91709
Tel. (909) 622-5654

FRANK CHIANG, M.D. FACOG
SIMMI P. DHALIWAL, M.D. FACOG
STEPHANIE J. CROPPER, M.D.
Nephrology Associates of Upland & Pomona

600 N. 13th Avenue • Upland, CA 91786
909/981-5882 • 909/946-0833

Soon to be located at:
536 N. Foothill Blvd.
Upland, CA 91786

Erlinda Uy-Concepcion, M.D., F.A.C.P.
Feroz Alam, M.D., F.A.C.P.
Jin Wang, M.D., F.A.C.P.
Hla Maung, M.D., F.A.C.P.
Mary Bui, D.O.

All Board Certified Internists and Nephrologists. Provides care for kidney disease, high blood pressure, dialysis (hemodialysis and peritoneal) and kidney transplant care.
Greeting and Best Wishes From:
Ligorio A. Calaycay, Jr., M.D., FACS, FICS, FPCS
Diplomate, American Board of Plastic Surgery
Aesthetic Surgery • Maxillofacial Surgery
Hand Surgery • Head and Neck Surgery
Reconstructive Surgery

AESTHETIC PLASTIC SURGERY INSTITUTE

SPECIALIZE IN

Laser Skin Rejuvenation
Liposuction (tumescent technique)
Ultrasound Liposuction
Face Lift
Neck Lift
Forehead/Brow Lift
Nose Reshaping
Eyelid Contouring
Ear Surgery (Otoplasty)
Fat/Collagen Injection
Breast Enhancement
Breast Reconstruction
Breast Lift
Breast Reduction
Tummy Tuck
Chemical Peeling
Dermabrasion
Chin Augmentation
Scar revision
Body Contouring
To assist you in giving your patient a better night sleep

Sleep and Diagnostic Center offers a wide range of fully attended diagnostics. Polysomnography testing at our sleep lab in a comfortable home-like setting. The sleep & diagnostics center of Montclair has two staff sleep specialists and a Board Certified Sleep Physician to interpret the results and to suggest the best treatment plan for your patients. Sleep & Diagnostic Center of Montclair is dedicated in helping you and your patients by gaining control and treating sleep-related disorders.

If you have any questions (Referral forms, patient information etc.) Please call the above phone numbers.
STANLEY KIM
CANCER CLINIC

Serving
Pomona - Inland Empire Communities

Dr. Stanley Kim provides the expert hematology and oncology services with the office hematology laboratory and the private chemotherapy infusion center.

1148 San Bernardino Rd. • Suite 300 • Upland • CA 91786 • Tel. (909) 985-1939

Generoso S. Nery, M.D., F.A.A.F.P.
PRACTICE IN FAMILY MEDICINE

8263 Grove Avenue, Suite 202,
Rancho Cucamonga, CA 91730
(909) 931-1368

Steven H. Barag, D.O.
BOARD CERTIFIED FAMILY PRACTICE

AUREUS MEDICAL GROUP, INC.
7874 Haven Avenue, Suite 250
Rancho Cucamonga, CA 91730
(909) 941-0855

AUREUS MEDICAL GROUP, INC.
160 E. Artesia Avenue, Suite 255
Pomona, CA 91767
(909) 623-9683
Jason H. Shin, M. D.

Announcement

I am pleased to announce the opening of my second office in the Rancho Cucamonga area located at 7974 Haven Avenue, Suite 250, Rancho Cucamonga 91730. Offering expertise in all aspects of gastrointestinal and liver diseases, cancer screening, endoscopy, colonoscopy, interventional ERCP and now capsule endoscopy.

Pomona Office
160 E Artesia, Suite 310
Pomona, CA 91767
Phone 909.629.5961

Rancho Cucamonga Office
7974 Haven Ave, Suite 250
Rancho Cucamonga, CA 91730
Phone: 909.980.1353

Board Certified in Gastroenterology and Hepatology

NEW HOPE
Cancer and Research Institute

Hematology & Oncology

Vandana Agarwal, M.D., F.A.C.P.
Trained at Kenneth Norris Cancer Center

Herbert L. Duvivier, M.D.
Trained at City of Hope

350 Vinton Avenue, Suite 101 • Pomona, CA
2140 Grand Avenue • Chino Hills, CA
412 Carroll Ave., Suite 108 • Glendora, CA 91741
www.newhopecri.com
(909) 620-5502

Restoring health,
Restoring harmony,
Restoring hope.
Wilshire Oncology Medical Group
Premier Cancer Care Team

Treatment close to home
Beginning in 1957 with just one office located on Wilshire Blvd. in Los Angeles, Wilshire Oncology Medical Group, Inc. now offers services within a network of seven cancer centers in the San Gabriel Valley and Inland Empire. Wilshire Oncology Medical Group, Inc. (WOMGI) offers a premier cancer care team of exceptionally trained, dedicated and compassionate cancer specialists from the front desk to the physician leadership.

Clinical Research
Wilshire Oncology has a long history of commitment to clinical research. At a time when clinical trials were offered only in large teaching institutions, Wilshire Oncology was enrolling qualified patients in studies to receive promising new therapies, which have enabled today's patients to have safer, more effective treatments. Wilshire Oncology is proud to have participated in clinical trials that proved so successful 10 cancer drugs were approved by the FDA for patient use after this research. By agreeing to take part in a clinical trial, patients receive cutting edge therapies two to five years before they are made available to the general public. In addition, Wilshire Oncology's affiliation with UCLA/Community Oncology Research Network and Translational Oncology Research International (TORI) provides access to many important clinical trials on the leading edge of science.

Our Mission
To relieve the burden and suffering of cancer by:
- Providing a collaborative environment that offers compassionate, comprehensive cancer care to patients and families.
- Excelling in prevention, diagnosis, education, integrated treatments, and access to innovative therapies through clinical trials.
- Optimizing quality of life while respecting individual patients and their families.
- Delivering to patients our unique personal commitment to their care.

RANCHO CUCAMONGA
8283 Grove Avenue, Suite 207
909-949-2242 • FAX 909-920-9863

POMONA
The Robert & Beverly Lewis Family Cancer Care Center
1910 Royalty Drive
909-865-9960 • FAX 909-865-9696

WILSHIRE ONCOLOGY MEDICAL GROUP, INC.
Giving hope for tomorrow while living for today
www.womgi.com
Western University Medical Center

Alan Cundari, D.O., Medical Director
M. Rahmi Mowjood, D.O.
Burt Routman, D.O.
Miguel Medina, P.A.-C
Trang Sparks, PA-C

For nineteen years, Western University Medical Center has provided exceptional community healthcare service and takes pride in its role as an osteopathic educational source for Western University of Health Sciences’ students.

887 E. Second Street, Suite B
Pomona, CA 91766
909/865-2565

Monday – Friday 9:00 am – 6:00 pm
Walk-in or appointments available
When Dr. Rahmi Mowjood returned to his native Sri Lanka to assist victims of the deadly tsunami, he drew upon the medical skills and compassion for others that are hallmarks of the education he received at Western University of Health Sciences. The result was a life-changing experience for his patients, himself and the students he teaches as a faculty member in the university’s Family Medicine Department. This independent, nonprofit, fully accredited graduate institution of health sciences salutes its extraordinary faculty and gifted graduates like Dr. Mowjood who routinely impact lives locally and the world over. The unique blend of science and compassion has earned a national reputation for this university, based in Pomona, California. Visit WesternU at www.westernu.edu.
INTERLINK HEALTH CARE, INC.

HOME HEALTH
Skilled Nursing
IV Therapy
Wound and Ostomy Care
Personal Care
Physical Therapy
Occupational Therapy
Speech Therapy
Medical Social Worker

HOSPICE
Bereavement Counselor
Spiritual Counselor
Volunteers
Skilled Nursing
Physician
Medical Social Worker
Pharmacy and Medical Supplies

HOME HEALTH LINE:
(800) 665-5181 or (626) 938-0344
REFERRAL FAX:
(626) 938-1959

HOSPICE LINE:
(800) 684-6445 or (626) 332-7073
REFERRAL FAX:
(626) 332-7333

-On-Call Nurse is available 24 hours a day, 7 days a week-

943 N Grand Avenue, Covina, CA 91724

DURAMED
Homecare Services, Inc.
861 Meridian St., Duarte, CA 91010
Tel (626) 357-6109 • Fax (626) 357-6706

Joseph Rex S. Cabado
Director of Patient Care
Willie Sia Sy
Marketing Director
Aimee Belmonte
Marketing Director

SALES • SERVICE • RENTALS
WE ACCEPT MEDICARE, MEDICAL AND PRIVATE INSURANCE

AMBULATORY DEVICES
✓ Canes or Quad Canes
✓ Crutches
✓ Walkers
✓ Herni Walkers
✓ Wheelchair and Accessories
✓ Motorized Wheelchair

HOSPITAL SUPPLIES
✓ Hospital Bed
✓ Bed Rail
✓ Tricpice Bar
✓ Patient Lift
✓ Seat Lift

RESPIRATORY AIDS
✓ Nebulizer and Accessories
✓ Oxygen Concentrator
✓ Portable Oxygen
✓ Suction Pump
✓ CPAP

DECUBITUS CARE
✓ Alternate Pressure Pad
✓ Gel Pressure Bed Overlay
✓ Gel Pressure Pad Wheelchair
✓ Alternating Pressure Mattress
✓ Low Air Loss Mattress

INCONTINENCE SUPPLIES
✓ Diapers or Panty Liners or Undergarments
✓ Underpads or Blue Chux or Tuckables
✓ Cream
✓ Wash
✓ Gloves

BATHROOM AIDS
✓ Commode
✓ Raised Toilet Seat
✓ Grab Bar
✓ Bath Bench and Transfer Tub Bench
✓ Guardrails for Raised Toilet Seat

MISCELLANEOUS ITEMS
✓ Glucose Monitor, Strips & Lancets
✓ TENS Units
✓ Diabetic Shoes
✓ Enteral Feeding Supplies
✓ Orthoses & Breast Prostheses
✓ Mastectomy Bras
✓ Lymphedema Pump
✓ CPM (Continuous Passive Motion Device)

"The Easiest, Fastest and Least Expensive Way To Order
Home Medical Equipment."
LDR NEUROSURGERY GROUP
of Southern California

Scott C. Lederhaus, M.D.
Lew B. Disney, M.D., Ph.D.
Jose L. Rodriguez, M.D.

Office: 255 E. Bonita Avenue, Bldg. #9 • Pomona, CA 91767
Phone: (909) 450-0369 • Fax: (909) 450-0366
The Difference is Caring

Doctors’ Hospital Medical Center of Montclair is an academic acute care facility offering a wide range of healthcare services to the Inland Valley. Our team of qualified professionals is committed to providing outstanding care and service excellence.

Our Services:
- Family-Centered Birthing Program
- 24-hour Emergency Services
- Surgical Services
- Intensive and Cardiac Care Services
- Telemetry and Med/Surg Services
- Diagnostic Imaging Services
- Laboratory Services
- Cardiopulmonary Services
- Rehabilitation Services
- Volunteer/Auxiliary Services

5000 San Bernardino Street
Montclair, CA 91763
www.dhmc.com