Why shouldn't general pathologists analyze skin biopsies?

I read with interest the article in the March issue by Dr. Gary Fox ("10 derm mistakes you don't want to make"), who makes some excellent points about evaluation and diagnosis of skin disorders.[1] However, I was greatly concerned about his comments regarding "Mistake #4—Assuming that pathology is a perfect science." In his Quick Tip on page 165, he makes the recommendation that all skin biopsies be sent to a dermatopathologist.

With the stroke of a pen, he dismisses the skills, abilities, knowledge, training, and experience of the estimated 20,000 board-certified general pathologists in the United States.

The ability to interpret and diagnose skin specimens is an integral part of the training of the general pathologist, and is a component of their evaluation for certification by the American Board of Pathology. Many general pathologists have been providing successful dermatopathology services to their physician colleagues for years. Undoubtedly, occasional cases will require additional expertise, but part of the training and responsibility of a general pathologist is to recognize and refer such cases appropriately.

Dr. Fox's argument is a double-edged sword, especially regarding family practitioners. One could argue from his viewpoint that if all skin biopsy interpretations and differential diagnoses are themselves so esoteric as to warrant direct referral to a dermatopathologist, would it not also be to the patient's advantage to be seen initially directly by a dermatologist with more training and experience in cutaneous disease than by a family practitioner? Of course not!

Furthermore, pathologists have subspecialty certification fellowships available not only in dermatopathology, but also in areas such as cytopathology, hematology, immunopathology, and molecular genetic pathology—to name a few. Should family physicians insist that abnormal Pap smears be read only by subspecialty boarded cytopathologists, or peripheral blood smears reviewed only by subspecialty boarded hematopathologists? Of course not!

What must remain the focus in the diagnosis of cutaneous lesions is the correct diagnosis and optimal care of the patient. These objectives require good clinical history, adequate biopsy, and perceptive pathologic interpretation. Challenging or clinically unusual cases require communication about the issues and concerns, which may indeed require specialist referral. But do not be misled into believing that your worries are over by following Dr. Fox's recommendation to "Send all 'skin' to a dermatopathologist."

I would urge family practitioners to discuss these issues with their local general pathologists. Good communication will go a lot further than will Dr. Fox's specious recommendation.

David A. Wiese, MD, PhD
Flint Clinical Pathologists, PC, Flint, MI
Dr.davew@comcast.net

Reference

1. Fox GN. 10 derm mistakes you don't want to make. *J Fam Pract.* 2008;57:162-169.

Dr. Fox responds

I welcome Dr. Wiese's opinion and offer my own in continuation of the conversation.

For a number of reasons, I would not

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compare family physicians' assessment of skin lesions with that of pathologists. For a lesion with dubious clinical character, it should not matter who recognizes it as such. Once such a lesion is recognized, only one choice remains: Cut it out.

The issue is: Then what? Histopathology is considered the "gold standard." Because the pathologist's word will usually be taken as "gospel," and may determine subsequent surgery and even life and death, one wants to assure the most accurate answer.

For "simple, routine" things, there is no issue.

However, when it comes to clinically questionable melanocytic lesions, a clinical conundrum I face multiple times daily, a quote from an editorial by H. Peter Soyer et al says it all: "The boundary between benignity and malignancy is not as sharp as our mental categories would like it to be. … Pathologists … have been regarded to be more scientific than many of their colleagues. A mystic perversion of this assumption prevails among those clinicians who believe that the pathologist, given only a piece of the patient's tissue, has all the other ingredients necessary to produce a statement of absolute truth at the end of his report. More dangerous to mankind is a pathologist with the same concept."[1]

In my article, I cited references—bolstered by experience—that even expert dermatopathologists exhibit substantial interobserver variation. Because of the imprecision, "severely dysplastic nevi" (severe architectural disorder, severe melanocytic atypia, or both) are usually treated similarly to melanoma in situ (full thickness excision with minimum 5-mm margins). I like the comfort of conveying to my patients that in such cases, an expert dermatopathologist (often 2) has interpreted their slides. In fact, to help improve diagnostic accuracy in histopathology of melanocytic lesions, it has even been suggested that dermatopathologists use ex vivo polarized dermoscopy.[2]

There are 2 paths to dermatopathology, one of which is dermatologists who subspecialize. When I have lesions of particular interest, I send my dermatopathologists dermoscopic photographs, because these are meaningful to them. The thought would not cross my mind to send clinical/dermoscopic photographs to general pathologists.

Furthermore, dermatologists may have sufficient knowledge of the pathology to review slides themselves and make judgments. Family physicians are not likely to have the background to review slides themselves and are going to be fully reliant on the pathologist and the report. My suggestion is to get the best expert advice when there can be substantial, clinically important disagreement among the best of the best.

Clinically, the issue often is not benign/malignant, but "What is it?" A dermatopathologist is better equipped to assist in an expanded "skin" differential diagnosis, in my experience.

I try to avoid skin biopsies when not necessary. When they are necessary, it is because I need assistance. I consider my dermatopathologists full-fledged consultants in my skin practice. For the same price, in the same time frame, I can have the expertise of a dermatopathologist for my skin biopsies. Why should I not avail myself of that? If I were to daily deal with kidney, liver, thyroid, brain, bone, lung, adrenal, pancreas, gut, etc, I would become friendly with my knowledgeable and well-trained general pathologist.

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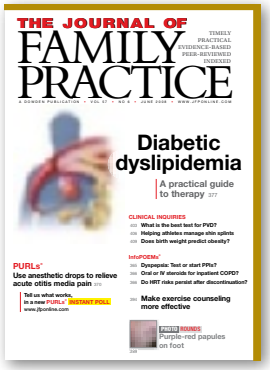
For the same price, I can have the expertise of a dermatopathologist. Why should I not avail myself of that?

Gary N. Fox, MD, Defiance Clinic, Defiance, OH
foxgary@yahoo.com

References

1. Soyer HP, Massone C, Ferrara G, Argenziano G. Limitations of histopathologic analysis in the recognition of melanoma: a plea for a combined diagnostic approach of histopathologic and dermoscopic evaluation. *Arch Dermatol*. 2005;141:209-211.
2. Scope A, Busam KJ, Malvehy J, et al. Ex vivo dermoscopy of melanocytic tumors: time for dermatopathologists to learn dermoscopy. *Arch Dermatol.* 2007;143:1548-1552.



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The ADA and ACC recommend LDL <70 mg/dL as a goal for diabetic patients with 1 additional risk factor

DIABETIC DYSLIPIDEMIA COVER STORY

Statin/ezetimibe mention misses the mark

I have one problem with your otherwise excellent article, "Diabetic dyslipidemia: A practical guide to therapy,"[1] in the June issue. In a remark concerning Vytorin, the authors state: "This combination has been questioned recently, as the addition of ezetimibe provided no improvement in surrogate markers." I believe this sentence, which references a *JAMA* commentary by Philip Greenland and Donald Lloyd-Jones,[2] is inaccurate and misleading.

I am not here to praise or bury Caesar, but I agree with Drs. Greenland's and Lloyd-Jones' interpretation of the ENHANCE trial and the lessons to be learned by the media, research scientists, and pharmaceutical firms. ENHANCE found statistically significant benefits in several cardiovascular surrogate markers (low-density lipoprotein, total cholesterol, and C-reactive protein) from the combination of agents in Vytorin (ezetimibe and simvastatin); it simply failed to find a statistical difference in carotid intimal thickness. The mistake repeated by the authors was to equate the failure to determine a difference with proof that no difference exists.

Oliver T. Willard, MD, ABFM
Piedmont Health Group
Greenwood, SC
owillard@phgrp.com

References

1. Tovar JM, Bazaldua OV. Diabetic dyslipidemia: a practical guide to therapy. *J Fam Pract.* 2008;57:377-388.
2. Greenland P, Lloyd-Jones D. Critical lessons from the ENHANCE trial. *JAMA*. 2008;299:953-955.

What about consensus statements?

The authors of the June cover story on diabetic dyslipidemia do a nice job of describing the lipid studies, but draw some conclusions that several national organizations and authorities in the field do not support.

I do not agree that data suggesting low-density lipoprotein (LDL) <70 mg/dL is controversial. A recent consensus statement by the American Diabetes Association and the American College of Cardiology[1] reviews the existing literature and recommends LDL <70 mg/dL as a goal for diabetic patients with 1 additional risk factor.

Nor do I agree that patients whose aspartate aminotransferase/alanine aminotransferase (AST/ALT) is 3 times the upper limit of normal (ULN) are not eligible for lipid-lowering therapy. If all patients with diabetes had liver biopsies, most would be found to have fatty livers—but not all would manifest this condition with elevated liver enzymes. Many such patients receive lipid-lowering therapy, with no adverse effect. After an extensive literature review, the National Lipid Association (NLA) Statin Safety Task Force determined that statins are safe when enzymes are >3 times ULN. The task force has published extensive guidelines[2] that review the subject and offer helpful recommendations. Among them is the suggestion that routine monitoring of liver enzymes not be done. The issue is also addressed on the NLA web site (http://www.lipid.org).

Granted, consensus statements are a different level of evidence than the studies the authors cite. In fairness, however,

consensus statements and the articles that support them should be included in a review so readers have all the information they need to make clinical decisions.

Edward Shahady, MD
Diplomate, American Board of Family Medicine
Diplomate, American Board of Clinical Lipidology
Diabetes Master Clinician Program
Florida Academy Family Physicians Foundation
Fernandina Beach, FL
eshahady@att.net

References

1. Brunzell JD, Davidson MH, Furberg CD, et al. Lipoprotein management in patients with cardiometabolic risk: consensus statement from the American Diabetes Association and the American College of Cardiology Foundation. *Diabetes Care.* 2008;31:811-822.
2. McKenney JM, Davidson MH, Jacobson TA, Guyton JR. Final conclusions and recommendations of the National Lipid Association Statin Safety Assessment Task Force. *Am J Cardiol.* 2006; 97(suppl 8A):89C-94C.

Some statins are safe with these drugs

In "Statins and elevated liver tests: What's the fuss?"[1] in the July issue, you emphasize—in a Fast Track—that cyclosporins and macrolide antibiotics are relatively contradicted in statin use. My concern is that physicians with patients taking a cyclosporin or a macrolide antibiotic will completely avoid statin use, even in patients at high risk for coronary artery disease. That's not necessary, however. There are significant differences in the pharmacokinetics of various statins, and some of them can be used safely with these drugs.

Allow me to clarify:

• Macrolide antibiotics are metabolized through the cytochrome P450-3A4 pathway only. Therefore, only statins with significant 3A4 pathway involvement (atorvastatin, lovastatin, and simvastatin) are contraindicated in patients taking macrolides.

• Although all statins interact with cyclosporin, this interaction is a matter of degree: The 3 statins cited above interfere with cyclosporin through the cytochrome P450-3A4 pathway; rosuvastatin and pravastatin interfere via the hepatic organic ion transporter system and the P-glycoprotein efflux pump. The safest statin for posttransplant patients and others on long-term cyclosporin therapy is fluvastatin.[2]

• Pravastatin has no significant cytochrome P450 drug interactions. It is therefore the preferred statin for patients with HIV, who often require lifelong multiple drug combinations, many of which have cytochrome P450-3A4 drug interactions.

It is important for physicians to be aware of such differences and to realize that there are statins that patients can take when they are taking macrolides, cyclosporins, or azole antifungals and have high cardiovascular risks.

Frank J. Johnson, Jr, MD, FAAFP
Diplomate, American Board of Clinical Lipidology
Bluefield Family Medicine, Bluefield, VA

References

1. Onusko, E. Statins and elevated liver tests: what's the fuss? *J Fam Pract.* 2008;57:449-452.
2. Fellstrom B, Abedini S, Holdaas H, et al. No detrimental effect on renal function during long-term use of fluvastatin in renal transplant recipients in the Assessment of Lescol in Renal Transplant (ALERT) trial. *Clin Transplant.* 2006;20:732-739.

Risk of interrupting warfarin is not "little"

I take issue with the conclusion of the POEM entitled "Can you safely interrupt warfarin for an elective procedure?" in your May issue.[1]

The Fast Track excerpt says "Most patients who stop taking warfarin for 5 or fewer days are at little risk of a thromboembolic event." But the article says the prevalence of events was 0.54%. There are 3 problems with characterizing that number as "little risk":

1. This percentage probably represents the low side of the actual risk, based on previous reports that the risk of thromboembolic events when withholding warfarin is about 1%.[2]

2. One event is not insignificant.

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There are statin options for patients who are taking macrolides, cyclosporins, or azole antifungals and have high CV risks.

I have several hundred patients in my practice taking warfarin. If only 100 of them have a skin biopsy, cataract surgery, or dental procedure in a given year, then the practice of withholding warfarin for these procedures causes 1 thromboembolism a year. Hardly insignificant to the affected person!

3. You failed to ask what the other side of the risk equation is. What would be the consequence of continuing warfarin during such procedures? My reading of the literature suggests the burden would be less onerous than 1 thromboembolism every year in my practice.

As a result, we do not routinely withhold warfarin for dental procedures, skin procedures, or cataract surgery.

Douglas R. Morrissey, MD, Cornerstone Family Health Associates, Lititz, PA
doug777morrissey@hotmail.com

References

1. Can you safely interrupt warfarin for an elective procedure? *J Fam Pract*. 2008;57:304.
2. Wahl MJ. Myths of dental surgery in patients receiving anticoagulant therapy. *J Am Dent Assoc*. 2000;131:77-81.