

PXE Awareness

National Association for Pseudoxanthoma Elasticum (NAPE, Inc.)

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NAPE, a non-profit 501(c)(3) support group whose mission is to provide education and support for PXE-affected persons, publishes *PXE Awareness*. Articles in this newsletter are provided for information only and are not a substitute for professional medical advice. You should not use information in this newsletter to diagnose or treat medical or health conditions. Please consult your healthcare provider before beginning or changing any course of treatment.

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President's Message

Dear NAPE Colleagues,

Thanks to all who contacted Matthew Lange about participation in his vitamin K study. He plans a small "proof of concept" study. If positive results are found, a larger study will need more participants. Remember, the gene search took seven years. Plan to exercise patience. I am so very pleased that, once again, our NAPE family is pulling together to solve our problem. We are on the way, and we'll get there!



Last fall at Salt Lake City the Board decided to hold the national meeting every other year. Thus we will not meet this fall, but will do so next year. As plans are made, you will be informed.

We continue to hear from newly diagnosed patients, almost all finding us through our website. We are working to make it easier to navigate and to include a special section for those recently diagnosed.

If you take Tylenol, please be sure to read the acetaminophen article. And please, note the update of Dr. Ken Neldner's July 2002 basic article on PXE. It needs to reflect recent findings important to all who live with PXE. The original will remain on the website.

We have worked with the Postal Service to reflect new requirements for bulk mailing. We now must provide not only your standard zip code, but also the plus four digits. Let us know if we do not have your address correctly stated.

As ever, we are here to serve you, so stay in touch - and thanks again for supporting Matthew's research.

Fran Benham





Pseudoxanthoma Elasticum PXE Update

Kenneth H. Neldner, MD

(earlier version appeared in July 2002 *PXE Awareness*)

What is PXE?

Pseudoxanthoma elasticum (PXE) is an inherited disorder in which the elastic fibers normally present in the skin, retina of the eyes and the cardiovascular system become slowly calcified, producing characteristic changes in these three sites.

4 PXE was first described about 100 years ago. Initially it was believed to involve only the skin. The skin changes were thought to be cholesterol deposits called xanthomas that occur in the skin of individuals with high blood cholesterol levels. When it was learned that the skin changes were not xanthomas but were due to calcified elastic fibers, the skin changes were called pseudo (false) xanthomas. It took another 20 to 30 years of study to link the eye (retina) and the cardiovascular changes together with the skin lesions, as we now know.

PXE occurs in about one in every 50,000 to 75,000 people, although most physicians who have studied PXE feel that it is more common. No doubt there are individuals with PXE who are never diagnosed because few physicians are familiar with PXE.

How is PXE diagnosed?

The first manifestation of PXE, and the one that almost always makes the diagnosis possible, is the appearance of highly characteristic skin lesions. They resemble cobblestone plaques of skin and most commonly appear first on the sides of the neck at an average age of 13 years (range of 2 to 25+ years). Later they appear in the folds of the arms, axillae (under arms), groin and behind the knees. A small (3mm) skin biopsy and special stains for calcified elastic tissue will confirm the diagnosis.

Eye (retina) involvement usually follows the skin lesions by several years. By age 20 to 25 years, most individuals will have angioid streaks (thin cracks in the retina due to calcified elastic fibers). The streaks cause no trouble on their own and most patients are unaware that they have angioid streaks. They are easily diagnosed by a routine retina exam by an ophthalmoscope or a retinal



photo. The angioid streaks are important, however, because they are the sites of future retinal hemorrhages that become common past the age of 40 to 45 years. The hemorrhages most commonly involve the central part of the retina called the macula and result in loss of central sharp vision. The hemorrhages leave peripheral vision intact and do not cause total blindness.



Cardiovascular problems usually involve the peripheral arteries and rarely the central vasculature (heart and major vessels). Aching in the thighs and legs after vigorous walking is the most common early symptom. This is called intermittent claudication and is due to calcification of elastic fibers in the arteries going to the legs.

Bleeding from the stomach occurs in about 10 to 15% of people with PXE. It usually begins suddenly with little or no warning and may be severe enough to require hospitalization and blood transfusions. In the most severe cases, surgical intervention may be required to stop the bleeding.

It is important to emphasize that there is a great deal of individual variation from one person with PXE to the next. One may have more extensive skin lesions and mild eye or cardiovascular involvement, while the next will be the opposite. Essentially 100% of individuals with PXE will sooner or later have some involvement of all three sites (skin, eye and vessels). It is believed that total life expectancy is affected little, if any, by PXE.

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How is PXE inherited?

The abnormal gene for PXE is passed from generation to generation usually without the knowledge of the individuals who pass and receive it through autosomal recessive inheritance. In recessive inheritance, parents who do not have PXE themselves must be carriers of the PXE gene in order to produce a child affected with PXE. The children of two parents who are carriers of the gene have a 25% chance of developing PXE. Those children who do not develop PXE are likely to be carriers but will not pass PXE to their children unless they marry another carrier - in which case the cycle will begin again.

The children of a parent affected with PXE mated to a parent who does not carry the gene will all be carriers of the PXE gene, but none will get PXE. Only if a parent with PXE marries a carrier of PXE will the child have the possibility of developing PXE. It is more common to see PXE, or any inherited disorder, in families where there are cousin marriages because it is more likely that cousins will carry the same abnormal genes.





Does PXE affect pregnancy?

Complications during pregnancy and delivery are always possible but are essentially no different than in those who do not have PXE. There also are no specific adverse effects in the newborn infant. Studies have shown, however, that women who have had multiple pregnancies do have more adverse effects from their PXE later in life compared to those who have had fewer or no full-term pregnancies.

The genetics of PXE

A search for the gene causing PXE was started in 1993 with the help of many NAPE members who donated blood samples and family histories. The gene mapping was performed in a laboratory at Harvard University by Drs. K. Lindpaintner and B. Struk with Dr. K. Neldner providing the DNA. This group reported the chromosome (16p13.1) that carries the abnormal gene in 1997 and the gene itself (ABC-C6) in 2000. These were major steps in finding the cause of PXE, but finding the gene does not automatically answer the question. Steps to find what this abnormal gene does (or does not do) that allows elastic fiber calcification is being conducted in labs around the globe. Recent reports indicate interference in vitamin K assimilation may be a primary cause. NAPE is involved in a study of vitamin K supplementation in PXE affected individuals.

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The management of PXE

It is important to keep in mind that with virtually every hereditary disorder that affects humans, there are both genetic and environmental factors which influence the natural course of the condition. We obviously cannot change our parents or our genes, but we can change our life styles and reduce environmental risk factors, thereby improving our chances for fewer complications and a longer and healthier life. There are many things that can be done from childhood on that will reduce the long-term risk factors for anyone with PXE. Recommendations include the following:

- Eat a well-balanced diet rich in fruits, vegetables and grains, with less emphasis on red meats. Chicken, fish and dairy products, such as suggested in the often cited Mediterranean Diet, provide a good guide for an overall healthy life. Today doctors encourage consumption of the Daily Recommended Allowance of calcium according to age and gender. NAPE's quarterly newsletter, *PXE Awareness*, provides up-to-date articles on nutrition with food sources.





- Avoid sports at all ages with potential head trauma or that require very heavy lifting and straining, such as boxing, soccer, football, rugby and weight lifting. Sports with little or no potential head contact, such as track, swimming, volleyball, bicycling, etc., should be encouraged. Head trauma and very heavy lifting can precipitate retinal hemorrhages.
- Maintain a normal weight for your age.
- Develop a regular exercise program and stick to it.
- Never, never, never start smoking. If you do use tobacco in any form - stop immediately.
- Check your lipid profile annually, including cholesterol, triglycerides, HDL-C, LDL-C and homocysteine. If any are elevated try reducing them with diet. If that doesn't work, see your doctor for cholesterol-lowering medications.
- Use aspirin and any of the so-called non-steroidal anti-inflammatory drugs sparingly (Advil®, Motrin® and ibuprofe), especially if there has been any retinal or stomach bleeding. These medications thin the blood and make bleeding easier. Occasional use is acceptable. Tylenol® has no such effect on the blood and may be used. Be sure to follow dosing instructions for all medications. Tell your doctor what medications you use each year at your annual checkup.
- Any slight vomiting of blood or appearance of black tarry stool is a medical emergency. See your doctor immediately.
- Check your blood pressure from time to time. If elevated, try to control it with diet and exercise. If this isn't enough, see your doctor for antihypertension medications.
- Anyone with mitral valve prolapse (MVP) and a heart murmur over the mitral valve should take antibiotics before surgery or dental procedures.
- Get to know a good retina specialist, preferably someone with experience in treating PXE. Most retina specialists feel that vitamin/mineral supplements of vitamins A, C and E plus copper, zinc and selenium (for example, OcuVite®) are helpful in preventing retinal hemorrhages. Get an Amsler Grid from your retina specialist and use it

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regularly. Laser therapy is no longer considered of value in the treatment of fresh retina hemorrhages involving the macula. Retina hemorrhages in PXE currently are treated with much success with injections of Avastin or Lucentis into the eye. Repeated injections are usually required with the result that vision is saved for many PXE patients.

- Avoid vigorous rubbing of your eyes. When outside in the bright sun for prolonged periods, wear good ultraviolet-protective sunglasses.
- Trental® is a prescription medication that may be helpful for intermittent claudication (pain in legs after walking). It should be stopped if there are signs of bleeding anywhere.
- And, finally, develop a healthy mental attitude towards your PXE. Strike a balance between excessive concern on one hand and denial or disregard for preventive measures on the other hand. Learning to cope with PXE may take years for some individuals. Don't hesitate to ask for help. Join the National Association for PXE (NAPE). Check our website (www.napxe.org) and receive newsletters which contain up-to-date information on PXE. Ask questions by email, telephone or regular mail service.



For more information

For more information, contact the National Association for PXE (NAPE), located in St. Louis, MO. Those with PXE, family members and anyone else interested in PXE are encouraged to join NAPE. Contributions to NAPE are welcome as they support our newsletter, website and telephone counseling service.

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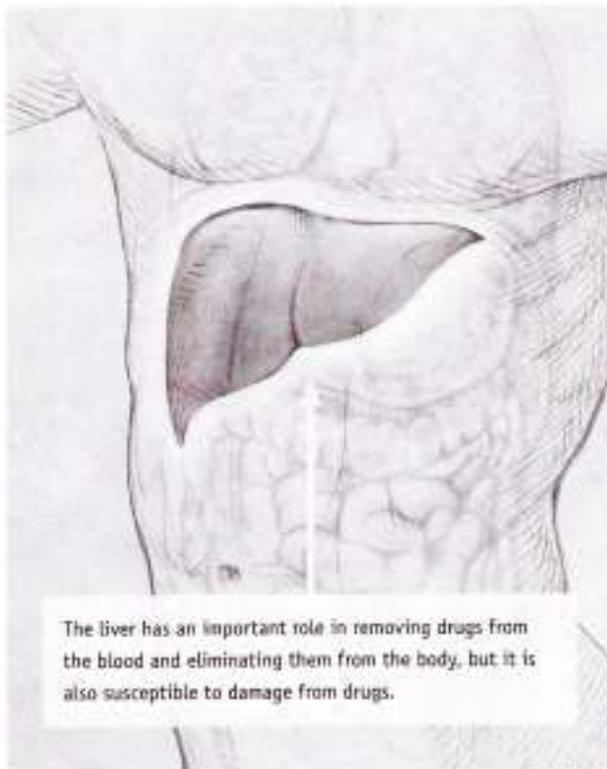


NAPE, Inc., is a 501(c)3 nonprofit organization. Contributions are tax deductible in the United States.

Acetaminophen: Read the Label

On June 29 and 30, 2009, FDA held an advisory committee meeting in Adelphi, Md., about how to address the problem of liver injury related to the use of acetaminophen in both over-the-counter (OTC) and prescription products. For more information about the meeting, visit the [Advisory Committee Web Page](http://www.fda.gov/AdvisoryCommittees/Calendar/ucm143083.htm) at (www.fda.gov/AdvisoryCommittees/Calendar/ucm143083.htm)

Acetaminophen is the generic name of a drug found in many common brand name OTC products such as Tylenol, as well as prescription products such as Vicodin and Percocet. Acetaminophen is an important drug, and its effectiveness in relieving pain and fever is widely known. This drug is generally considered safe when used according to the directions on its labeling. But taking more than the recommended amount can cause liver damage, ranging from abnormalities in liver function blood tests, to acute liver failure, and even death.



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Q: What is acetaminophen?

A: Acetaminophen (pronounced: a-seet-aminofen), is an active ingredient found in many OTC and prescription medicines to help relieve pain and reduce fever.

It is also found in combination with other active ingredients, called combination medicines, which treat conditions such as:

- symptoms of colds and flu
- allergy
- sleeplessness

Medicines containing acetaminophen are available in many forms, including drops, syrups, capsules, and pills.



Many people call OTC acetaminophen by a brand name, Tylenol. Others may know Percocet or Vicodin, which are prescription brand names that contain acetaminophen and other active ingredients to help relieve pain.

You might see acetaminophen abbreviated as “APAP” on prescription medicines.

In other countries, acetaminophen may have a different name. For example, acetaminophen is known as paracetamol in the United Kingdom.

Q. Are there risks from taking too much acetaminophen?

A: Yes, acetaminophen can cause serious liver damage if you take too much. It is very important to follow your doctor’s directions and the directions on the medicine label.

You may not notice the signs and symptoms of liver damage right away because they take time to appear. Or, you may mistake early symptoms of liver damage (for example, loss of appetite, nausea, and vomiting) for something else, like the flu. Liver damage can develop into liver failure or death over several days.

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Acetaminophen is generally safe when taken as directed. To lower your risk of liver damage make sure you do the following:

- Follow dosing directions and never take more than directed; even a small amount more than directed can cause liver damage.
- Don’t take acetaminophen for more days than directed.
- Don’t take more than one medicine that contains acetaminophen at a time. For example, your risk of liver damage goes up if you take a medicine that contains acetaminophen to treat a headache, and while that medicine is still working in your body, you take another medicine that contains acetaminophen to treat a cold.

Q: How can I tell which medicines contain acetaminophen?

A: Medicines have ingredients listed on their labels. On OTC medicines, check the “Drug Facts” label under the section called Active Ingredients. If your medicine contains acetaminophen, it will be listed in this section. On prescription medicine containers, the label will say “acetaminophen” or “APAP.”



Q: When should I talk to a doctor before taking acetaminophen?

A: Talk to your doctor before taking acetaminophen if you



- drink alcohol (three or more drinks every day)
- have liver disease

Under these conditions, taking acetaminophen puts you at greater risk of getting liver damage, even when taking acetaminophen at the recommended dose.

If you take the blood thinner warfarin, you should also talk to your doctor before taking acetaminophen because taking warfarin and acetaminophen together may raise your risk of bleeding.

Q: How can I safely take acetaminophen?

A: Follow this advice to take acetaminophen safely:

- Read all the information given to you by your doctor and follow directions.
- Read the information on the OTC “Drug Facts” label or on the prescription label and follow directions.
- Be sure you understand the following:
 - the dose, which is how much acetaminophen you can take at one time
 - how many hours you must wait before taking another dose of acetaminophen
 - how many doses of acetaminophen you can take safely each day
 - when to stop taking acetaminophen and ask a doctor for help
- Never take more than directed, even if your pain or fever isn’t any better. Taking more acetaminophen than directed can put you at risk for liver damage.
- Never take more than one medicine that contains acetaminophen. Check the active ingredients of all your medicines to make sure you are taking no more than one medicine containing acetaminophen at a time.

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Q: How can I safely give acetaminophen to my child?

A: You can safely give acetaminophen to infants, children, and teenagers if you

- Check the active ingredients in the other medicines that your child is taking (or that your child may take) to make sure they don’t contain the active ingredient acetaminophen. Your child should never be taking more than one medicine containing acetaminophen at a time.
- Read all the information given by your child’s doctor and follow directions.





- Read the information on the OTC “Drug Facts” label or on the prescription label and follow directions.
- Choose the right medicine based on your child’s weight and age. On OTC medicines, the Directions section of the “Drug Facts” label tells you:
 - if the medicine is right for your child
 - how much medicine to give
 - how many hours you must wait before giving another dose
 - when to stop giving acetaminophen and ask a doctor for help

If a dose for your child’s weight or age is not listed on the label, or you can’t tell how much to give, ask your pharmacist or doctor what to do.

- Use the measuring tool that comes with the medicine. It will give the exact dose. If you don’t have the right measuring tool, ask a pharmacist.
- Don’t use a spoon that’s meant to be used for cooking or eating. A spoon should not be used to measure medicine because it may give the wrong amount.
- Never give more than one medicine that contains acetaminophen. If you give more, it could harm your child.

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Prevent medicine accidents:

- Keep a record of the medicines you give your child. Write down the dose and time when you give the medicine. This will help everyone who cares for your child know how much medicine your child has had. This will help everyone avoid giving an extra dose by mistake.
- Keep medicine where it can’t be seen or reached by children and pets; a locked box, cabinet, or closet is best.

Q: What should I do if the pain or fever doesn’t get better after taking acetaminophen as directed?

A: Take the medicine only as directed. Don’t take more. If the medicine doesn’t help you feel better, talk to your doctor, nurse, or pharmacist.

Q: What should I do if I took too much acetaminophen? What should I do if I gave too much acetaminophen to my child?

A: Don’t wait! Call 9-1-1 or Poison Control at 1-800-222-1222 right away to find out what to do. The signs or symptoms of liver damage may not be noticeable for hours or even days after taking acetaminophen. By the time



you notice changes, the liver damage may be severe and could lead to death.



Q: *Where can I get more information on acetaminophen?*

A:

- Talk to a doctor, nurse, or pharmacist.
- Visit FDA's consumer Web pages:

[Don't Overdo It with Acetaminophen \(video\)](#)

www.accessdata.fda.gov/scripts/cdrh/cfdocs/psn/transcript.cfm?show-87#9

[Safe Use of Over-the-Counter Pain Relievers and Fever Reducers](#)

www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/SafeUseofOver-the-CounterPainRelieversandFeverReducers/default.htm

[A Guide to Safe Use of Pain Medicine](#)

www.fda.gov/ForConsumers/ConsumerUpdates/ucm095673.htm

- Contact the FDA at 1-888-INFO-FDA.
- Or, e-mail questions to FDA at druginfo@fda.hhs.gov

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This article appears on [FDA's Consumer Updates page](#) (www.fda.gov/ForConsumers/ConsumerUpdates/default.htm) which features the latest on all FDA-regulated products.





PXE Pals

If you would like a PXE friend with whom you can correspond, NAPE members listed would like to hear from you. Please notify the NAPE office if you have trouble contacting a PXE Pal.

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Donations - Membership

No membership fee is required, although donations are needed to pay operational expenses, including telephone, fax, email, website and newsletter services.

Donations can be made in Honor or Memory of a loved one, for the Research Fund and/or for the Low-Vision Fund. All donations are tax deductible in the USA.

Operations Honor Memory Low-Vision Research

Name of Loved One: _____

Address for Acknowledgement: _____

PLEASE COMPLETE THE SECTION BELOW IF YOU HAVE PXE, THINK YOU HAVE PXE,
OR ARE FILLING THIS OUT FOR SOMEONE ELSE

Name: _____ Phone: _____

Email: _____ Fax: _____

Address: _____

City: _____ State: _____ Zip: _____ Country: _____

Male Female Birthdate: _____ Age: _____

I am diagnosed with PXE Yes No Newsletter: Print CD

Are you legally blind? Yes No Email notification

Do others in your family have PXE? Yes No If so, who? (Mother, Father, Sibling, etc. & Name) _____

Please list any medical problem(s) you are experiencing: e.g., eye involvement, skin lesions, heart problems, gastric bleeding, etc., and comments/questions (use another page if required):

Are you willing to be contacted by another who wishes to talk with someone else who has PXE? Yes No

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Have You Changed Your Address?

Please help by letting us know. Please be sure to print your new zip code number, including the extra four digits (as required by the Postal Service for bulk mailing). Please help.

New Address

Name: _____

Street: _____

City, State, Zip _____

Old Address

Name, if different: _____

Street: _____

City, State, Zip _____

PLEASE PRINT NEATLY