

## **What Is PXE?**

Pseudoxanthoma elasticum, (PXE), is an inherited disorder that causes some tissue in the body to become mineralized, that is, calcium and other minerals are deposited in the tissue. This can result in changes in the skin, eyes, cardiovascular system and gastrointestinal system. PXE was recognized over a hundred years ago. A number of significant advances have been made in the past few decades.

## **PXE and the Gastrointestinal System**

Very rarely, PXE may cause acute upper gastrointestinal bleeding. This is sometimes not recognized immediately and can be life-threatening. It may involve vomiting of blood or passing black, tarry stools. There is not much known about the actual cause of this bleeding except that the bleeding can occur from multiple points in the stomach and/or intestines. In a few cases it is mistaken for bleeding ulcers. A person with PXE experiencing any gastrointestinal problem should be sure to tell their physician that they have PXE. A person with PXE should not take non-steroidal anti-inflammatory medications, such as aspirin, ibuprofen, and naproxen, because they increase the risk of gastrointestinal bleeding by causing superficial erosions in the stomach.

## **Gastrointestinal Bleeding**

Gastrointestinal (GI) bleeding can have many causes from esophagitis to gastritis (inflammation in the stomach) to peptic ulcers to polyps, inflammatory bowel disease, tumors, and hemorrhoids. Those with PXE can have the same diseases as the general population, so any of these could develop in individuals with PXE and have nothing to do with PXE.

Gastrointestinal bleeding can be silent, producing unnoticeable blood loss that gradually leads to iron deficiency and anemia. It can also present with obvious bleeding. Bleeding from the lower GI tract (colon and rectum) presents as bright red blood in bowel movements. Bleeding from the upper GI tract (stomach, duodenum, and small intestine) can present as "melena" (black tarry bowel movements) because of the effect of gastric acid and intestinal juices on the blood. Sudden upper-GI bleeding can also be associated with vomiting blood.

Upper GI bleeding, sometimes massive, has long been recognized as a symptom of PXE. It is not common, but when it occurs, it is very dramatic. The exact source can be hard to pinpoint, but it is usually from multiple small bleeding points or erosions in the stomach, but can also be from a single site. If it cannot be controlled medically, surgery is sometimes necessary to stop the bleeding. Aspirin and NSAIDs can increase the risk of bleeding, so these should be avoided in PXE unless the benefits (such as stroke prevention in those who have had symptoms or previous stroke) outweigh the risks. If you have questions about specific symptoms, see your doctor for diagnosis and a treatment plan.

The overall incidence of GI bleeding is unknown and it is probably not high. It is assumed that when an individual with PXE has minor erosions, such as from aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs) or from acid peptic disease bleed, the abnormal arterial vessels in PXE do not constrict normally to shunt blood away from the ulcerations. That is all conjecture. There is no published evidence that individuals with PXE have abnormal gastrointestinal linings or develop ulcerations more readily than the non-PXE population, but it hasn't been studied in any rigorous way.

### **Intestinal Angina**

Intestinal angina is a known and described complication of PXE. This is a rare condition that, depending on the location and extent of arterial narrowing, may be treated with balloon angioplasty or surgery. Usually an angiogram is used to diagnose this condition and plan appropriate treatment, which is usually coordinated among gastroenterologist, surgeon, and interventional radiologist.

### **Colonoscopy**

As far as PXE International is aware, there are no special risks of colonoscopy that are related to PXE - that is, the procedure should not be any riskier than in a person without PXE. There might be specific signs of PXE noted on colonoscopy, but these are not dangerous. You are encouraged to have this procedure if you are over 50, if you have risk factors for colon cancer, or if you have any medical issues, such as bleeding or anemia, that would warrant a colonoscopy. One recommendation: as with dental procedures, individuals who have mitral valve prolapse (floppy mitral valve) should consult a cardiologist or primary physician to learn whether they should take preventive antibiotics before the procedure. Let the gastroenterologist know if you have mitral valve prolapse. Though long ago mitral valve prolapse was thought to be a problem associated with PXE, this has since been debunked. Mitral valve prolapse is very common in the general population.

## **PXE and NSAIDs**

As mentioned above, certain medications such as aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs, such as Advil, Aleve and Naprosyn) and a whole host of others, such as piroxicam (Feldene) and Relafen, can damage gastric tissues and lead to GI bleeding, either occult (not clinically visible as blood) or acute (with immediate symptoms, and requiring immediate treatment).

Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) that is associated with an increased risk of gastrointestinal bleeding, both because it can cause gastric stomach inflammation, and because it can inhibit the activity of platelets, which help to form blood clots when you are injured. This increases the risk of gastrointestinal bleeding in PXE. The risk is not high, but such hemorrhages can be severe. If an alternative therapy can be considered, that might be preferable.

Celebrex, is a COX-2 inhibitor, which means it has no platelet effects and appears less likely to cause GI bleeding than standard COX-1 inhibitor drugs, although it is not completely free of such risk. If a person with PXE needs a NSAID (nonsteroidal anti-inflammatory drug), Celebrex is probably the best choice, although it is not risk-free. Vioxx, a similar drug, has been withdrawn from the market because of an increased risk of cardiac complications such as heart attack. Therefore the potential cardiovascular risks of COX-2 inhibitors in PXE, a disease which is already associated with an increased risk of cardiovascular disease, must be taken into account by those prescribing these medications.

Disalcid (salsalate) is a non-steroidal anti-inflammatory drug (NSAID) that does not have an aspirin-like effect on platelets and is somewhat less irritating to the stomach than aspirin, so it is safer than aspirin for someone with PXE. However, as with Celebrex, the risk of GI bleeding is lower but not zero. Nothing is perfectly safe.

There are treatments for rheumatoid arthritis, such as Enbrel and Remicade, that are injected or infused and do not cause GI bleeding, but they are very expensive and must be given under the supervision of an experienced rheumatologist. If you suspect arthritis, an internist or a rheumatologist (specialist in arthritis) should evaluate you so that a specific diagnosis as to the type of arthritis you have can be made, and the safest therapy for you can be prescribed.

PXE International would not suggest narcotic medication as an alternative to a NSAID (nonsteroidal anti-inflammatory drug) as it is habit-forming. You should discuss this issue with your doctor, who should be aware of the risk of gastric bleeding in PXE and choose the drug with the lowest risk-benefit ratio.