important. They include the use of ergonomic tools, antivibration padding and gloves to keep hands dry and warm, and reduction in the intensity of vibration to the hand through damping techniques, job rotations and scheduled rest periods.² Efforts are underway to establish evidence-based limits to vibration exposure. Smoking cessation is also recommended, given the

vasoconstrictive effects of cigarette smoking on the peripheral arteries.

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CLINICAL VISTAS

Alkaptonuria and photography: A patient's urine tells the story

This picture of a patient who had alkaptonuria (Fig. 1) was taken by my father, Dr. Ian Maxwell, in 1957 and was developed using the patient's own urine.

Alkaptonuria was the first described "inborn error of metabolism." This rare (< 1 per 250 000 births) hereditary recessive disorder is characterized by

a triad of excretion of homogentisic acid in the urine, ochronosis (dark pigmentation of the connective tissues) and early-onset arthritis. It results from the absence of an enzyme, homogentisic acid oxidase. Homogentisic acid is produced during the metabolism of phenylalanine and tyramine and, in the absence of the enzyme, accumulates in large quantities in the plasma and urine. In patients with alkaptonuria, a second enzyme, homogentisic acid polyphe-
noloxidase, present in mammalian tissue, catalyzes the oxidation of the accumulated homogentisic acid in vivo to an ochronotic pigment that has a high affinity for cartilage and connective tissues, forming fragile complexes. The clinical manifestations of the disease — dense, coal-black pigmentation of costal, tracheal and laryngeal cartilages, blue-grey pigmentation of the ears and sclera, and extensive early degenerative arthritis of the spine and large joints (due to the breakdown of the cartilage-pigment complexes) — are the result of this pigment deposition. The excess homogentisic acid also appears in the urine, where it may undergo oxidation on exposure to atmospheric oxygen, particularly in an alkaline environment. This

oxidation results in a characteristic gradual darkening of the urine downward from the surface on standing.¹

To appreciate the relation of this to photography, we need a (somewhat simplified) explanation of the processes involved in the creation of a photographic image. The photographic emulsion consists of microscopic crystals of silver bromide embedded in a gelatin matrix. Photons striking the crystals dislodge electrons, resulting in the formation of metallic silver atoms and bromine. The latter is trapped by the gelatin matrix, leaving the silver atoms. At this stage the number of silver atoms is relatively small, creating what is termed a latent image. If this image is now "developed," by placing it in a solution containing a relatively strong reducing substance, the crystals in which the process of conversion to metallic silver has been initiated rapidly seize the electrons donated by the reducing substance, multiplying the original generation of metallic silver atoms by a factor of roughly 10 000. The developed image is now formed of crystals of metallic silver wherever light struck it, interspersed with unaltered crystals of silver bromide. The latter are then rendered soluble and washed out of the emulsion,

leaving only the areas of dark metallic silver to form the photographic image.²

The connection between this process and alkaptonuria becomes clearer when one examines the molecular structures of hydroquinone (a widely used developer present, for example, in Kodak D11 and D76) and homogentisic acid (Fig. 2).

As a developer, the paired hydroxyl (OH) groups on the benzene ring serve to reduce the silver ions. The effectiveness of homogentisic acid in this process was noted as early as 1942 by Fishberg, who proposed its use as a specific test for “the instantaneous diagnosis of alkaptonuria on a single drop of urine.”³ It should be noted that, although the fundamental requirement for a developer is that it be a reducing substance, the process is rendered more efficient in the

usual commercial developers by the addition of a number of other chemicals. These obviously are lacking in urine, which probably accounts for the restricted range of contrast evident in Fig. 1. An intriguing speculation is the role played by the pigment formed as the homogentisic acid oxidizes, either in contributing to the overall cast evident in the photograph or to the image itself.

My father never published this experiment, but the same concept was applied by Scott Williams and his students in the 1995 Technical Photographic class at the Rochester Institute of Technology.⁴ They used coffee as a developer, affording a new use for the cold dregs at the end of a long day. One of Williams’ students subsequently extended the concept, using an infusion of mint, which proved to be an even more effective de-

veloper, in addition to producing olfactorily enhanced prints,⁵ perhaps an advantage over the urine of ochronotic patients.

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IN THE LITERATURE

Is there a role for estrogen in the prevention and treatment of urinary incontinence?

Hendrix SL, Cochrane BC, Nygaard IE, Handa VL, Barnabei VM, Igesia C, et al. Effects of estrogen with and without progestin on urinary incontinence. *JAMA* 2005;293:935-48.

Background: The role of estrogen in the treatment of urinary incontinence is unclear. Given that the lower urinary tract shares a common embryologic origin with the genital tract, it has been theorized that urinary incontinence may be related to atrophy associated with estrogen loss. However, epidemiologic and trial evidence has shown both beneficial and harmful effects of estrogen on urinary incontinence.^{1,2}

Design: This study included 23 296 healthy, postmenopausal women aged 50–79 years enrolled in the Women’s Health Initiative hormone replacement therapy (HRT) trial and for

whom baseline and 1-year data on urinary incontinence (defined as self-reported involuntary urine leakage of any amount in the past year) were available. Women were randomly assigned to receive either placebo or HRT in the form of conjugated equine estrogen (0.625 mg/d) with or without medroxyprogesterone (2.5 mg/d) based on their hysterectomy status. Participants, clinic staff and outcome assessors were blinded to group allocation. Primary outcomes were incident urinary incontinence at 1 year among women without baseline incontinence (N = 8255) and severity of incontinence among those with urinary incontinence at baseline

(N = 15 041). Urinary incontinence was further subdivided by type (stress, urge or mixed). Measurements of severity included self-reported frequency, amount, associated limitations in daily activities and “degree of bother.”

Result: HRT was associated with an increased 1-year incidence of all types of urinary incontinence among women who were continent at baseline (Table 1). It was also associated with an increase in the severity of urinary incontinence among women who were incontinent at baseline (Table 2).

Commentary: This large, well-designed, multicentre, randomized trial appears to resolve the controversy around estrogen and urinary incontinence. The