

Honing a diagnostic weapon

A hoary old ally of laboratory technicians is being refitted for new roles, including, perhaps, a routine test for detection of breast cancer

by Faye Marley

The time may come when urinalysis as a test for breast cancer may become as common—and effective—as the Pap smear for early diagnosis of uterine malignancy. A number of biochemists have shown that women with breast cancer have different patterns of hormone excretion in the urine than non-cancerous women. Some have gone so far as to say that proneness to this disease can probably be detected in individuals even before the disease attacks.

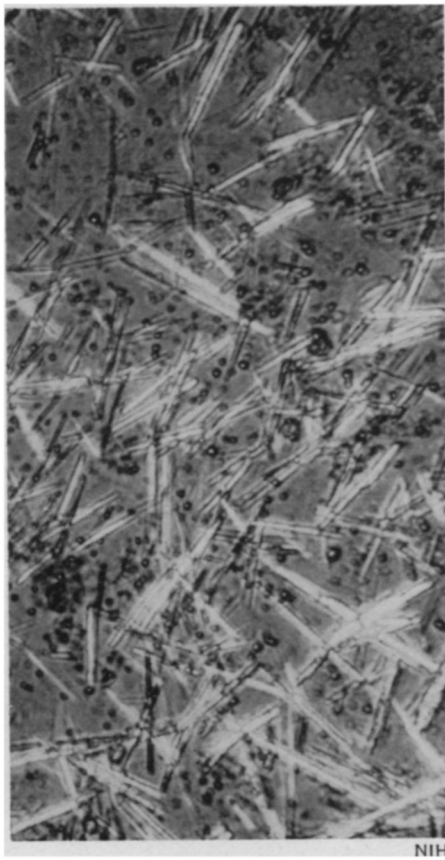
But obviously the methods of urinalysis used by the average technician today are inadequate. He is looking chiefly for glucose to indicate diabetes or for protein, pus and bacteria as signs of other disease conditions.

Dr. Ian E. Bush of the Medical College of Virginia, who is working under a grant from the National Institute of General Medical Sciences, points out that to make full use of the possibilities of urinalysis, speeding up the measurement of complex biochemicals on a large scale is essential.

To study cancer of the breast, for instance, through the study of steroids in the urine or blood, would require sampling between 5,000 and 8,000 women, he estimates.

"We would face the prospect of handling between 40,000 and 64,000 blood or urine samples a year, or between 160 and 256 samples per working day," he says.

While Dr. Bush was senior scientist at the Worcester Foundation of Experimental Biology in Shrewsbury, Mass., he outlined the need for automation of steroid analysis, describing his work in developing a machine for the precise direct photometric measurement of paper chromatograms. He calls his machine CASSANDRA, for Chromato-



Urate crystals

gram Automatic Soaking Scanning and Digital Recording Apparatus. (Cassandra, in the Greek myths, was a prophetess who predicted doom.)

Researchers would rather see development of a simple dip-stick screening test to help technicians detect millions of undiagnosed urinary tract infections. And that is the purpose of at least one research contract, awarded recently to Georgetown University in Washington, D.C., by the Public Health Service's National Center for Disease Control.

Dr. Robert Melville, program administrator in the National Institute of General Medical Sciences, believes that wider use of urinalysis would greatly improve medical diagnoses. He says urine is the most obvious and prolific commodity the human being produces for diagnostic use.

It was some 140 years ago that routine urinalysis was introduced by Dr. Richard Bright, an English physician after whom Bright's disease was named. Bright's disease is any one of a group of kidney diseases attended with edema—the accumulation of excess fluids in the tissues—or with albuminuria—the presence of serum albumin or serum globulin in the urine.

Urinary tract infections occur more often than any except those of the respiratory tract. Studies indicate that

more than three million undetected urinary tract infections, a large majority of them in women, exist at any given time in the United States.

Urinalysis checks the output of the body's vital filters, the kidneys. For their small size, they do a huge filtration job, with their million filter tubes, or nephrons, per organ. As much as one-fourth of the blood supply has been estimated to be passing through them at any given moment. Short arteries carry the blood to the kidneys from the aorta.

Proteinuria is probably the best single piece of evidence for the presence of kidney disease, specialists say. It is often the first sign of toxemia of pregnancy. When proteinuria appears, the dangerous condition called preeclampsia, a toxemia of late pregnancy, should be suspected. This is why fairly frequent urinalyses should be taken so the diagnosis can be made as early as possible.

A great deal of attention has been given to another urine test, that for PKU, short for phenylketonuria, which causes severe mental retardation in infants. Urinalysis is important along with serum tests for finding excess phenylpyruvic acid and other phenyl derivatives. PKU is an inborn disease in which there is metabolic failure to convert phenylalanine, an important amino acid, into tyrosine, another.

Maple Sugar Urine Disease is also associated with abnormalities of brain function due to a metabolism defect. A mother first brought to the attention of physicians the fact that the urine of affected children has a characteristic odor similar to that of maple syrup. When the urine was examined in the laboratory, an abnormal concentration of organic acids was found. Further examination revealed that these were keto acids derived from the branched-chain amino acids leucine, valine and isoleucine, which accumulate as the result of an enzyme deficiency.

The severe brain damage in such instances is being prevented by treatment with a synthetic diet low in these branched-chain amino acids. Some victims have come through the treatment with normal intelligence.

Stressing the importance of urinalysis, specialists have just ended a meeting (Dec. 2) at Oak Ridge, Tenn., co-sponsored by the Oak Ridge National Laboratory and the National Institute of General Medical Sciences. Topic of the symposium was urinary constituents of low molecular weight. A machine has been developed at Oak Ridge that will identify 130 different components of low molecular weight in the urine—opening further possibilities of diagnosis. At this time only 30 constituents can be identified, Dr. Melville says.