Future farmers may collect urine, not milk

The grandchildren who revamp Old MacDonald's Farm years from now may end up harvesting a product their forebear ignored. If so, they can thank the first researchers to genetically engineer animals that concentrate a pharmaceutical product in urine.

Robert J. Wall of the U.S. Department of Agriculture in Beltsville, Md., and his colleagues have developed transgenic mice that produce human growth hormone in their bladders. Although the mice produce only a tiny amount, Wall says they show that urine farming techniques work.

The notion of turning livestock into four-footed pharmaceutical factories has intrigued researchers for at least a decade, Wall's team notes in the January NATURE BIOTECHNOLOGY. So far, most of the effort has gone into developing cows, sheep, and goats that secrete commercially interesting proteins in their milk. No such products have yet reached the market, but Wall says several are now being tested in people. The furthest along, he estimates, is a milk-produced blood-clotting agent, antithrombin III, developed by Genzyme Transgenics Corp. in Framingham, Mass.

Despite the unappealing image, a drug company already sells natural horse estrogen from urine as a hormone replacement.

Urine could offer the drug farmer significant advantages over milk, says Wall. Both male and female animals urinate, starting soon after birth. The urine of large animals carries much less protein than their milk, which could cut the processing costs. "The really expensive part is actually the cost of purifying the drug," Wall explains.

Even though creating a transgenic animal is not cheap—$60,000 for a sheep or goat—standard breeding techniques can then produce an entire herd. "It's only that founder cost that is so staggering," he says.

The possibility of urine farming arose in 1995, when Tung-Tien Sun of New York University identified genes that are active only in the bladder. The genes encode proteins called uroplakins, which form part of the bladder lining. David E. Kerr, then at the Agriculture Department, attached the genetic sequence for human growth hormone to the uroplakin gene promoter, which controls where and when the gene switches on.

Mice engineered to carry the new gene have produced up to 500 nanograms of the hormone in each milliliter of their urine. Kerr, now at the University of Vermont in Burlington, does not recommend mice as commercial sources of drugs—although collecting their urine was easy. All he had to do was hold the mice over a piece of plastic wrap.

Whether urine farming turns out to be economically feasible remains to be seen, say Harry Meade and Carol Ziomek from Genzyme. In an accompanying editorial, they say the idea "deserves further investigation." However, they judge the yields to be "too low to make it a viable alternative at present (10,000 fold lower than in milk)." Pumping up yields may be tricky, since gene activity in the mice already seemed high. "This could mean that the secretory pathway of the bladder is very inefficient," they say.

Collecting urine from farm animals may also prove challenging, Meade and Ziomek warn. Drug farmers may have to keep their herds attached to catheters.

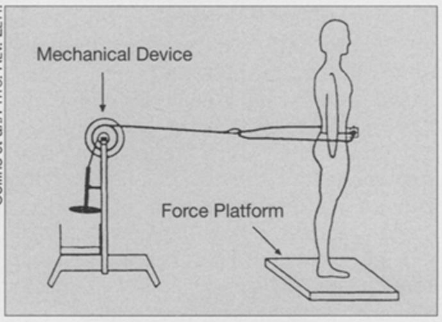
Wall acknowledges that the bladder does not compare to the mammary gland as a secretion powerhouse, but he suggests that bladder yields may improve and that the ease of processing urine might make up for the smaller amount of product.

It's too early to dismiss urine farming, says Henryk Lubon, who directs transgenic research at the American Red Cross laboratory in Rockville, Md. Some proteins might not be suitable for milk farming because they damage mammary tissue, he says, and he hesitates to compare the initial urine results to the more mature transgenic milk production. "Ten years ago," he says, "who knew that milk was going to work out?" —*S. Milius*

Posture control depends on balancing act

Even when standing still, the human body is in constant motion. That subtle swaying causes the center of pressure under an individual's feet to shift randomly within a radius of a centimeter or two.

Researchers have now shown that monitoring the path followed by the center of pressure of a quietly standing person furnishes useful information about the body's response to small impulses, or shoves. Such measurements may eventually help in diagnosing balance disorders in people, says mathematician Carson C. Chow of Boston University's Center for Biodynamics.



Collins et al/PHYS. REV. LETT.

Apparatus for measuring center-of-pressure displacements when a subject is pulled backward slightly.

Chow, biomedical engineer James J. Collins, and their coworkers at the center describe their findings in the Jan. 12 PHYSICAL REVIEW LETTERS.

Whether in studies of how infants learn to sit up and stand or in efforts to correct balance problems, human posture control has long been a subject of considerable interest. Although researchers sometimes measured gross characteristics of center-of-pressure fluctuations, until now they have paid little attention to the details of the overall pattern of movement.

Several years ago, Collins recognized that the location of the center of pressure, as measured on a sensitive apparatus known as a force platform, follows a specific type of random walk. Each successive step of the walk occurs in a randomly selected direction. The overall path is constrained, however, almost as if the wanderer were connected to the central point by an elastic band.

According to Chow, such fluctuations can be described by simple equations that also apply to a string or polymer strand glued flat to an elastic membrane. As random perturbations displace the strand, the membrane pulls it back to its straight equilibrium position.

In the mathematical model developed by Chow and his colleagues, the motion of the center of pressure corresponds to the movement of a single point of the strand. Experiments in which subjects stood still or were pulled backward by a mechanical device demonstrated that the observed movements fit the model quite well.

The model enables the researchers to link the body's intrinsic, random movements when standing still to its response when disturbed by a small impulse. It suggests that the same neuromuscular mechanisms control posture, whether fluctuations are random and intrinsic or caused by an external, perturbing force.

This finding may greatly simplify the tests that clinicians use to determine a person's susceptibility to falling. "All you have to do is stand on a force platform and do nothing for 30 seconds," Chow says. "By measuring the fluctuations, we can determine how you respond to perturbations."

He adds that "we want to come up with a software package that a clinician can use with a patient standing on a platform to characterize his or her body's stiffness or reaction time." —*I. Peterson*