Bumpers bill that has alarmed researchers.

All three bills give the Department of Health, Education and Welfare responsibility for regulation, and the administration bill and that introduced by Sen. Howard M. Metzenbaum (D-Ohio) promulgate the NIH guidelines as at least initial interim standards. Under the administration bill HEW would license research facilities and register individual projects.

The subcommittee has yet to meet in executive session to decide how to handle the bills. However, there is some time pressure. If the final bill authorizes money, for example for inspection of facilities, it must have action on the floor of at least one house by May 15. □

# Switching cancer cells back to normal

More and more evidence is accumulating to show that cancer is not necessarily stable, but can be reversed and modulated, according to a variety of evidence reported at the annual meeting of the Federation of American Societies for Experimental Biology in Chicago last week. Under a variety of laboratory conditions, cancer cells lose their malignant characteristics and revert to normal, researchers from five laboratories reported. These results suggest clinical methods might be sought to return cancer cells to normal control.

The most dramatic experiments were those in which one type of tumor cell that had been grown by transplantation from mouse to mouse for eight years was injected into early mouse embryos. The embryos were then implanted into surrogate mothers. The cells derived from the tumor could, in the embryo, differentiate normally into the many types of mouse tissue. The healthy tumor-free mice that resulted often had cells from both the tumor and the original embryo. "The father was a tumor," jokes pathologist Henry C. Pitot. Genes, such as the one for fur color, that had not been expressed during the eight years of the tumor's existence were once again operating in an orderly and controlled manner. Although other types of tumors may arise by changes in the genes, the malignancy in this type of tumor, called a teratoma, is apparently not due to a mutation of the DNA but to a reversible loss of control of normal gene expression, researcher Beatrice Mintz concludes.

Mintz first performed these experiments at the Institute for Cancer Research in Philadelphia. Now M. W. McBurney of the University of Ottawa also reports experiments showing normalization of cancer cells transplanted into early mouse embryos.

Another method of switching cells between cancerous and normal states was described by Selma Silagi of Cornell University Medical College. Silagi adds small amounts of the chemical 5-bromodeoxyuridine to the culture medium of cells from a pigmented mouse tumor. That chemical is incorporated into the cells' DNA in place of the natural component thymine. Cells derived from the tumor, after three cell divisions in the presence of 5-bromodeoxyuridine, are incapable of forming tumors in adult mice. The reverted cells also lose other characteristics of tumor cells, such as production of pigment and of a protein-destroying enzyme. But if the chemical is removed from the medium and is eventually replaced with thymine in the DNA, the cells resume their tumor characteristics and again cause tumors when injected into mice.

An aspect of this work that may have great clinical relevance is that the treated cells, which no longer cause cancer, can prevent untreated cells from inducing tumors. If the two cell types are mixed together before they are injected into mice, the mouse's immune response to the treated cells kills the tumor-causing cells as well. Inoculation with treated cells will also prevent a later injection of cancer cells from causing tumors. Now the researchers are isolating components of treated cells' membranes that will provoke the immune response, so as to avoid having to inject living cells. Silagi believes this research will lead both toward a better understanding of malignant cells and toward a method for immunizing patients after surgery to prevent recurrence of their tumors.

Reversion of cancer cells, although shown in animals only recently, has been observed in plant cells for over 20 years, Frederick Meins Jr. of the University of Illinois points out. Research on plant tumors revealed that their uncontrolled growth can result from inappropriate production of a substance called cell division factor. Researchers have devised ways to manipulate how much of this factor is produced by cells grown in culture outside of a plant. The most recent work by Meins shows that the change of a plant cell from normal to a tumor is progressive. There is a gradual increase of the growth factor production. The change is also reversible. The researchers find that if a tumor cell's production of the cell division factor is momentarily blocked, the cell returns to normal control. These findings indicate that the tumor cells retain their potential for normal growth and development.

Finally Pitot, of the University of Wisconsin, suggests on the basis of research on liver cancer that very early in cancer development cells may be converted to normal tissue, whereas later, when the cells exhibit marked alterations in their chromosomes, the cells may be irreversibly transformed into cancer. The prevailing hypothesis had been that initiation, the first stage in cancer development, is irreversible.

The researchers told a news conference that finding cancer is not always irreversible is no panacea, but it is one ray of light that in the future may be important.

The ability of cancer cells to become normal is also providing a new tool for experimental study of human genetic diseases. Mintz and co-workers are deliberately producing mutations in tumor cells growing in culture. The researchers then select cells with specific biochemical changes known to be involved in certain diseases. These cells are injected into mouse embryos where they participate in forming the body tissues. Sperm and eggs derived from the altered cells can create a mouse model of the corresponding human disease. □

# A functioning artificial penis

To date, penis construction in female-to-male transsexual operations has left massive scarring and awkward-appearing organs with little or no sexual functions. A first-time combination of several known techniques and some novel techniques by surgeons at the University of Missouri Columbia Medical Center has led to the creation of a more aesthetic and sexually functioning artificial penis.

The nine-month procedure, performed by Charles L. Puckett and Joseph Montie of the medical center on a female transsexual wanting to become a male, was reported last week at the 23rd annual Urology Seminar in Kansas City, Mo. Urologists at the meeting described the results as "beautiful" and "fantastic."

Prior to penile construction, the patient underwent four years of hormone treatment, mastectomies and removal of female reproductive organs. A groin skin flap from the patient was then used to form a penile shaft. The groin flap, often used in other plastic surgery, has many advantages over the abdominal and chest skins used for earlier sex organ construction. It is quite similar to the actual penile tissue, eliminates disfiguring scars and the need for grafts and is hairless.

In earlier penile constructions, no attempts were made to sculpture a realistically shaped penis. In Puckett and Montie's operation, however, tucks were made at the tip of the penis to imitate a glans. Tactile sensations were also achieved by moving the clitoris, much enlarged by hormone treatment, and placing it at the exterior base of the penis. This step provided sensations not achieved in past operations. As in earlier procedures, though, a scrotum and artifical testes were constructed.

In past female-to-male operations, sexual function of an artifical penis was attempted by inserting a permanent semi-rigid prosthesis in it. This approach was not always successful. Puckett and Montie reached a more satisfactory solution by inserting an inflatable prosthesis in their patient's sculpted penis. The patient is thus able to have intercourse, although ejaculation is not possible. The device, developed about three years ago at Baylor University in Texas, has been used for men impotent because of disease or surgery.

A liquid-filled reservoir in the patient's abdomen is connected to two small cylinders in the penis. Erection is achieved when a small bulb in the scrotum is pumped and the cylinders are filled with liquid. Pressing a valve in the scrotum refills the reservoir in the abdomen and deflates the penis.

In similar operations, the urinary tract has been rerouted. In this case, the doctors decided against it because of risk of infection and possibility of interference with the implanted cylinders.

The value of the procedure in transsexual operations is obvious. But the doctors say the techniques are also adaptable for treating men whose organs have been amputated, disfigured or injured. □

# RNA tumor viruses: More insights

Because tumor viruses cause various kinds of cancers in animals and may possibly do so in humans as well, there is great need to learn more about how they can trigger disease in cells. For instance, during infection of a cell, an RNA tumor virus (a virus with a core of RNA as its genetic material) makes a DNA copy of its RNA. This DNA then becomes a closed circle and integrates into the cell's DNA before the life cycle of the virus can continue. A crucial question is: How can a linear RNA result in a circular DNA molecule?

A partial answer is provided in the March PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES by two separate research groups at Harvard Medical School and Harvard University. The investigators are William A. Haseltine, Allan M. Maxam and Walter Gilbert, and Dennis E. Schwartz, Paul C. Zamecnik and H. Lee Weith. They have found that the bases (chemical building blocks of nucleic acids) at both the left and right ends of viral RNA are virtually identical. Such identical sequences may help explain how a DNA copy of RNA can become circular.

When an RNA tumor virus enters a host cell, it carries two copies of linear viral RNA and several copies of the reverse transcriptase enzyme that it needs to make DNA copies of its RNAs. Also, attached to the left end of each RNA to help in transcription is a host-cell transfer RNA. As an enzyme starts to transcribe a viral RNA strand into a DNA copy, the tRNA primer is elongated into DNA. Then the enzyme goes on to make a DNA copy of some 100 bases at the extreme left end of the RNA. Using a new method that Maxam and Gilbert designed (SN: 4/2/77, p. 216), Haseltine, Maxam and Gilbert determined the sequence of this 100-base stretch. Meanwhile, Schwartz and his colleagues determined the sequence of bases at the right end. It turns out that the 21 bases at the extreme left end are also at its extreme right end. The only difference is that the stretch at the right end is followed by several A (adenine) bases.

So how do these identical ends help a linear DNA copy of a viral RNA to become circular? When DNA copying begins at the left end of the viral RNA, only one percent of the RNA is made into DNA. So how is a DNA copy of the other 99 percent made, since it must be made from the right, not from the left, end? Because the DNA transcription starts at the left end, the growing DNA chain must jump to the right end and then continue copying the rest of the RNA. And this is where the identical bases at the left and right ends probably come into use.

For instance, the growing DNA chain could float away from its RNA at the left end and pair up with another viral RNA at the right end for further elongation. Or a reverse transcriptase enzyme might digest some of the RNA from the RNA-DNA hybrid containing the 100 bases at the left end, revealing that DNA so that it can pair with the repeated sequence at the right end. Thus, as the DNA is brought around from the left end of the viral RNA to the right end, it also creates DNA circles. □

# Astronomers urge 25-meter telescope

The largest optical telescope in the world, located in the Crimea, has a mirror 6 meters in diameter. The next largest is at Mt. Palomar in California (5 meters or 200 inches). These represent about the ultimate technological limit for the casting of a single mirror.

These large single telescopes give a view that goes billions of light years into the distance and past of the universe and records objects as dim as 23rd magnitude, but they have been surpassed in distance and discrimination by the antennas of radio astronomy. Optical and radio astronomy work in tandem, and for best results astronomers would like to have optical equipment that can match the best available for radio, which in the not too distant future will be greatly improved by the Very Large Array now under construction in New Mexico. And so a study group assembled under the aegis of the Kitt Peak National Observatory and led by KPNO staff members Donald N. B. Hall, R. C. M. Learner and L. D. Barr now proposes a ground-based optical telescope with a 25-meter aperture.


Kitt Peak National Observatory

*One of four concepts for giant telescope.*

Consideration of such a project is made possible in general by two recent developments. Work on multiple-mirror telescopes has shown that it is possible to coordinate the movement of a number of separate mirrors (by using reflected laser beams) so that they all throw their image to the same point. The development of speckle interferometry, a technique whereby numerous snapshots of a given object are combined by computer into an image that has the effects of atmospheric turbulence (twinkling) removed, has circumvented what was the effective limitation on the resolving power of optical telescopes.

A 25-meter telescope would thus be made of a number of separate mirrors. At least four possible designs are under consideration; the optimum one from an engineering and economic point of view remains to be chosen. A telescope of this size would have 25 times the light-gathering power of the big one on Mt. Palomar. Its limiting magnitude would be about 27 for fairly wide band (1,000-angstrom) observations and fainter for certain narrow portions of the spectrum.

If such a scope were built in a dry location it would be particularly useful for infrared observation.

This kind of a telescope could see faint and small objects and effects such as dark dwarf stars, planets around other stars, stellar motions in other galaxies and weather changes on large planets of the solar system. Because of its complexity the telescope would require more technical support than most. Hall says the siting would probably be a trade-off between dryness and support. Kitt Peak is one obvious choice; Mauna Kea is another possibility. Cost would run to about $250 million, about as much as the current generation of particle-physics laboratories or a quarter of an aircraft carrier. □