Carter's lofty win: India gets A-fuel

The U.S. nuclear-nonproliferation stance was weakened Sept. 24 when the Senate failed to block shipment of fuel for India's Tarapur nuclear reactor. By not backing the House, which last week voted an overwhelming (three to one) condemnation of the proposed nuclear-fuel sale, the Congress failed to halt Carter in one of their most significant recent challenges of his foreign policy. The win is particularly important for Carter as a sign of his strength as the election nears.

In May, Carter had promised the Ghandi government that, although it was in violation of the U.S. Nuclear Antiproliferation Act (SN: 10/8/77, p. 231), its bid to buy 40 tons more fuel for Tarapur, near Bombay, would be approved. (The act clarified for the first time conditions — such as the refusal to adopt international safeguards on all its nuclear facilities — under which the United States would be forced to stop sales with nuclear-importing powers. A two-year grace period that was offered nuclear-importing nations for achieving compliance with the act expired last spring.) When the Nuclear Regulatory Commission refused several days later to approve the Indian fuel purchase — NRC's sanction is required for all U.S. nuclear exports — Carter overrode them with an executive order (SN: 5/31/80, p. 344).

Among the reasons Carter offered for his request to exempt India from having to comply with provisions of the act were:

- That India has threatened to view an interruption of fuel supplies guaranteed under its contract with the United States as absolving it from having to abide by that contract's clauses (such as those requiring that Tarapur remain under international safeguards and that U.S. approval be obtained before any extraction of weapons-grade plutonium is attempted from spent fuel now stored at Tarapur).
- That owing to India's strategic military importance to the United States, its "friendship" must not be jeopardized.

After apparently giving up any hope of swaying House intentions, the Carter administration had in recent weeks mustered an intensive pro-Tarapur lobbying campaign of Senate members. Although the Senate vote this week was close, the outcome of Senate deliberations — which included nearly 10 hours of floor debate prior to the polling — is surprising.

First, their ultimate consensus rejects the decisions of not only the five nuclear regulatory commissioners, but also both the House and Senate foreign-relations committees. Second, a refusal to ship India any more nuclear fuel could be interpreted as the United States' only legal contractual recourse (since the contract promising India fuel contains the statement that India must "comply with all applicable laws, regulations and ordinances of the United States"). Third, India has not exactly courted the friendship of the United States while these sensitive deliberations by the Congress have been underway: According to the chairman of the Senate's subcommittee on energy, nuclear proliferation and federal services, John Glenn (D-Ohio), since the President's decision in May to send it fuel, "India concluded a $1.6 billion arms deal with the Soviet Union, became the only noncommunist country to recognize the pro-Soviet regime in Kampuchea and signed a long-term trade agreement with Iran that undercuts our ability to apply pressure for the release of our hostages."

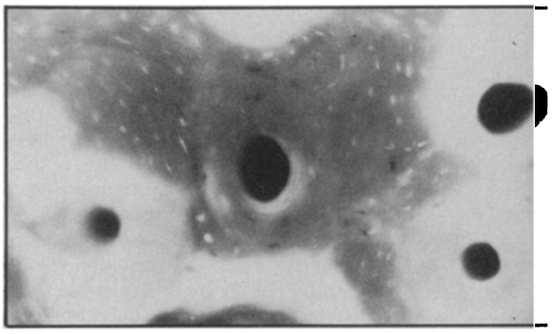
Most important, the Indian fuel sale could threaten the U.S. nonproliferation efforts ongoing around the world. It could, for example, undermine negotiations with nations that have not yet signed the Nuclear Nonproliferation Treaty (NPT) — most notably Pakistan, Argentina, Brazil, Israel and South Africa — in adopting full-scope safeguards on any nuclear facilities they have or intend to build. It could also cause other nuclear-supplier nations that now require importers to apply safeguards to their facilities to reassess their own policies. Switzerland, for example, which has such policies, is already bristling over the threatened refusal by the United States to license the Swiss sale of nuclear fuel — originally purchased from the United States — to Italy. The reason U.S. diplomats gave this week is that the Swiss contributed to Pakistan's obtaining supplies it needed to produce a clandestine nuclear reprocessing plant.

Among possible last-minute swing factors influencing the Senate vote was the announcement in the Sept. 23 Washington Post that India's combative and worrisome neighbor, Pakistan, had resumed construction of a small, clandestine, nuclear-fuel reprocessing plant near Rawalpindi to produce bomb-grade plutonium. The story reports "U.S. intelligence experts" as claiming that the Pakistanis could generate "enough fissionable material to stage an initial atomic test in the fall of 1981."

India has already detonated a bomb and even flaunted defiantly its perceived right to conduct further bomb testing. Pakistan's actions now offer India even greater incentives to put off signing the NPT — which would have required that all its nuclear facilities become subject to international safeguards.

Blocking the U.S. sale of fuel for Tarapur would not necessarily have stalled development of an Indian nuclear arsenal, since some of India's nuclear facilities are not now "protected" — as Tarapur is — by adherence to international safeguards monitoring. It would have removed, however, the opportunity for others to interpret the sale as tacit endorsement of India's recalcitrance in adopting international safeguards. □

Ancient bone glow: Is it tetracycline?



Light rings indicate fluorescence.

Debra L. Martin got more than she bargained for in a routine check of the thickness of bone sections taken from an ancient Sudanese cemetery. The optical light microscope normally used by researchers to examine such bone samples already was in use; so Martin — of the University of Massachusetts at Amherst — turned to a fluorescent microscope. There, under the ultraviolet light of the fluorescent scope, the bones glowed an intense yellow-green identical to the signal produced in modern bones by the widely used antibiotic tetracycline. Expecting only to gather data for an anthropological study on bone aging, Martin now had evidence that an ancient Sudanese people ingested fairly large doses of tetracycline about 1,400 years before common medical use of the antibiotic began.

Martin and her colleagues at Amherst, along with Antonio R. Villanueva of Henry Ford Hospital in Detroit, Mich., tell the tale of this fortuitous discovery in the Sept. 26 SCIENCE. The researchers recovered the bones from a cemetery that holds the remains of an agricultural population, the Sudanese Nubians, who cultivated flood plains of the Nile, about 600 miles south of Cairo, from about A.D. 350 to A.D. 550.

A source of tetracycline for the Nubian population may have been the mold-like bacterium *Streptomycetes* — a natural producer of the antibiotic — that grew on the wheat, barley and millet the Nubians stored in mud bins. Each time the Nubians ate bread or drank beer made from this mud-bin grain, they also — most likely unknowingly — received a dose of naturally occurring tetracycline, Martin and coworkers report.

Intentional use of tetracycline as a broad-spectrum antibiotic began in the 1950s. At that time, researchers noted that, in a process similar to the stain-causing incorporation of the drug in tooth enamel, the antibiotic causes staining and fluorescence in other calcifying tissues. In bone, for example, tetracycline can bind to the surfaces of osteons (cylindrical bone units) that are actively mineralizing, or laying down calcium. A yellow-green

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fluorescence in bone sections under ultraviolet light at a wavelength of 490 angstroms is evidence of such a phenomenon, Martin and colleagues report.

But Henry Dion of Parke, Davis & Co., a pharmaceutical firm, is not convinced that the fluorescent material in the Nubian bones is tetracycline: The observed yellow-green glow could be the fluorescence of other chemicals with the same structural core as tetracycline — four hexagonal carbon rings linearly fused. National Institutes of Health researcher Walter W. Stewart, who has developed fluorescent dyes, adds that more objective and definitive evidence could be provided for the tetracycline theory by obtaining an emission spectrum, in which the light emitted by the fluorescent material is analyzed to determine the amount of energy given off at each wavelength.

Should the fluorescence that Martin and colleagues observed be due to large doses of tetracycline, it could explain the extremely low rates of infectious disease, which can be detected by the incidence of certain bone inflammations, found among the Sudanese Nubians. In addition, it could also explain the known evolution of R (resistance) factors — cytoplasmic elements responsible for the spread of drug resistance among bacteria — among several ancient populations that lived before the antibiotic era. □

Diet danger detailed

The Last Chance diet may have lost its last chance.

Researchers from the University of Rochester in New York recently placed six healthy, obese volunteers in a clinical research center on a liquid diet and carefully monitored their health. The findings support what has long been suspected — the diet can be fatal. Three of the six volunteers suffered "potentially life-threatening" heart arrhythmias, or irregular heartbeats, as early as 10 days after they began a 300-calorie-per-day, vitamin- and mineral-supplemented liquid protein diet, the scientists report in the Sept. 25 NEW ENGLAND JOURNAL OF MEDICINE. "Use of the liquid protein diet should be terminated pending further investigation of the causes and prevention of cardiac toxicity," they recommend.

Liquid protein diets have been used widely since the publication in 1976 of a book called *The Last Chance Diet*. But in 1977 when about 100,000 people went on the diet, at least 60 unexplained deaths occurred. While heart arrhythmias have been implicated in protein diet-related deaths (SN: 7/29/78, p. 70), this study is the first clinical demonstration of such problems. The researchers caution that 24-hour heart recordings, rather than routine, periodic electrocardiograms, are required to detect serious problems during the course of the diet. □

'Me generation' of cancer cells

Self-sufficiency may explain why some cancer cells outstrip their neighbors and proliferate beyond control. All cells require a variety of hormones or growth factors to prosper, but George J. Todaro suggests that certain cancer cells are able to produce regulatory chemicals for themselves. While normal cells are kept in bounds by a dependence on hormones produced by other cells in the body, those cancer cells can be oblivious to that restriction on growth.

Epidermal growth factor is one compound often required for cell proliferation. This string of 53 amino acids is produced in the mouse salivary gland and other as-yet-unidentified tissues. Some cancer cells do not bind epidermal growth factor (EGF), Todaro told the International Symposium on Aging and Cancer last week in Washington. He suggests that those cells make their own growth factor and use it to boost their proliferation.

In experiments at the National Institutes of Health, Todaro has purified a growth factor from mouse cells made cancerous by murine sarcoma virus. When that factor, which Todaro calls sarcoma growth factor (SGF), is added to some types of cells growing in laboratory culture, it gives them some properties of cancerous cells. The cells revert to their normal characteristics when the factor is washed out of the culture.

Although SGF binds to the same cell membrane receptor as EGF, the two are clearly distinguishable, Todaro finds. The factors differ in size and electrical charge and bind different antibodies and binding proteins. In addition, mouse sarcoma cells do not make EGF, and EGF does not make normal cells act as if they are cancerous.

Some human cancers appear to behave in a similar self-promoting style, Todaro finds. Todaro has isolated from human tumor cells a growth factor that can bind to the EGF receptor and shares other characteristics with mouse SGF.

Todaro sees EGF as one of a family of factors necessary for cell growth. It is not clear whether the tumor-produced factors are absent in normal tissue; Todaro suggests they might be active normally during embryonic growth. Todaro envisions the growth stimulating compounds as being one of the factors in the progression of events that, triggered by a viral or chemical carcinogen, allow normal cells to become cancerous. He says the "inappropriate" hormone production by tumors, observed clinically, may overcome growth restrictions and thus be quite appropriate from the tumor's point of view.

Recognition of the importance of growth factors and hormones in supporting cell proliferation has come largely from attempts to grow cells in laboratory media in which all the components are known (SN: 12/3/77, p. 377). The search for appropriate growth media facilitates discovery of new hormones and unexpected hormonal requirements, Gordon Sato of the University of California in San Diego told the Washington symposium.

By looking at the growth requirements of human cancer tissue, Sato hopes to find clues for therapies. He recently has identified five factors, including insulin and EGF, necessary for growing cells of a type of human lung cancer. He has also determined conditions under which the cancer cells differentiate into normal epidermal cells. If such terminal differentiation could be induced in patients, the cancer would be defeated, he says.

So far, most types of cells in the body cannot be grown in a chemically defined medium. As the growth requirements are worked out for more cells, comparisons between normal and cancer cells will become possible. Todaro predicts that tumor cells will be found to be independent of some factors needed by their normal counterparts, because the cancer cells will be found to produce the growth-permitting factors themselves. □

Toxic shock culprits

Medical discoveries, like whodunits, often unfold in bits and pieces, and identification of the culprits behind the toxic-shock syndrome is no exception. The latest installment came last week from the Center for Disease Control in Atlanta.

The toxic-shock syndrome was first described in 1978 by James K. Todd of the University of Colorado and colleagues. It usually strikes women younger than age 30 and is characterized by high fever, vomiting, diarrhea, severe prolonged shock and low blood pressure. It can be fatal. Although the incidence of the syndrome is low — about three victims per 100,000 persons — it appears to be increasing, the CDC announced last May (SN: 5/31/80, p. 343). In July, the syndrome was linked to the use of tampons (SN: 7/5/80, p. 6). And now it has been associated with the use of a particular brand of tampon called Rely, the CDC reported last week.

The CDC researchers studied tampon use among women who contracted the syndrome during July and August. They found that Rely tampons were used twice as often by those women as were other tampon brands. In response to the study, Proctor and Gamble, the manufacturer of Rely, has removed the product from the market until the Food and Drug Administration, which oversees the safety of medical devices, can review the data to determine if regulatory action against Rely or any other brand of tampon is warranted. The researchers suspect that the syndrome is caused by a bacterium that is introduced into the body via a tampon. □