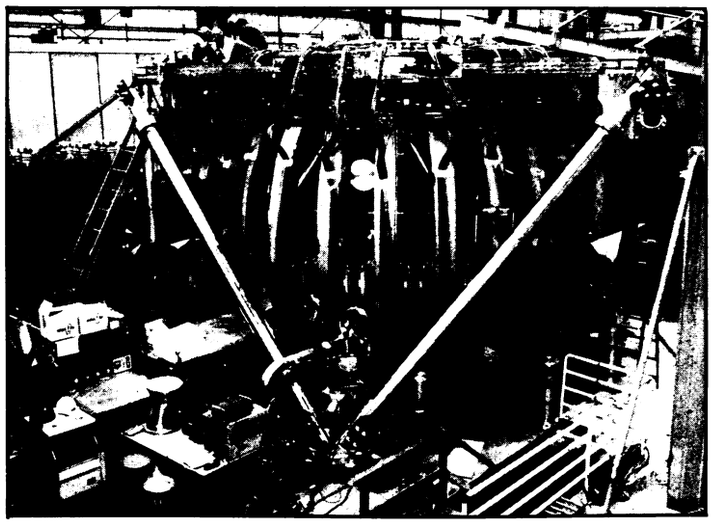
tween 58,000 and 75,000 are "associated with" asbestos. However, because exposure to more than one carcinogen may increase one's chances of getting cancer far more than might be expected from the individual risk factors, projecting cancer incidence from all factors combined becomes quite complicated. For example, many of the cancer cases will be associated with smoking as well as with some industrial carcinogen. For this reason, a rather artificial term — "excess cancers" — is used to compare the potential danger to workers from various industrial substances. (The quantity reflects the number of cancers that would result from a given length of exposure in a group of workers of the same age who didn't change jobs.) For asbestos, the number of expected "excess cancers" a year is 13,900 — far less than the number actually expected to be associated with asbestos exposure, but a useful figure when comparing risks. The excess cancers expected annually from five other common industrial substances — arsenic, benzene, chromium, nickel oxides and petroleum fractions — is 33,000, leading the researchers to conclude that "the five other agents together pose hazards similar to or greater than those posed by asbestos."

And that's just the beginning. Some 221 substances have been identified as causing cancer in animals, but for most not enough occupational exposure data have been gathered to allow projections like those above. To compensate for this handicap, the report presents a list of occupations known to involve high cancer risks, but where no single agent can be identified. Furniture workers, for example, experience three or four times the number of cancers in the nasal cavity and sinuses than would ordinarily be expected. Other high-risk occupations: shoe workers, miners, tire workers, newspaper pressworkers and chemists.

Predictably, industry representatives strongly disagreed with the conclusions of the report. "If the vinyl chloride estimates are any indication of the accuracy of the rest of the report," said Ralph L. Harding Jr., president of the Society of the Plastics Industry, "the document must stand convicted as an embarrassment to medical science and to the government agencies that produced it." The study has estimated an excess cancer rate from vinyl chloride of 1,940 cases annually. Harding called the estimate "ludicrous to the point of absurdity," saying that only 23 confirmed fatalities from the chemical had been seen in the last 16 years.

Other industry sources were more cautious, preferring to wait until company scientists had had a chance to analyze the data carefully. More specific challenges will certainly follow, and the whole issue of how the public should be protected from hard-to-predict risks is likely to heat up when new proposals for regulations result from this report. □

Doublet III pulls up its hosen



General Atomic

The vertical coils look a little bit like stays, and somewhere inside them is the chamber where Doublet III's plasma is expected to hold its hourglass figure as it slithers toward the day of breakeven.

Of American experiments aimed toward controlled thermonuclear fusion, the series called Doublet, which has been operated by General Atomic in San Diego, is unique for its shape. The Doublet series is made up of magnetic confinement experiments in which a magnetic field is used to confine a plasma of atomic nuclei and electrons until the nuclei fuse. There are many other varieties of magnetic confinement experiment. The vacuum chamber in which Doublet's magnetic fields do their confining is a toroid. That, too, is not unusual; there are many toroidal experiments.

The unusual quality is the cross-sectional shape of the plasma, which is bilobar, or figure-eight shaped. Most plasmas are held in circular or elliptic cross sections, but it has been General Atomic's conviction, or rather the conviction of Tihiro Ohkawa, vice president and head of General Atomic's fusion division, that the Doublet shape would provide savings in magnetic field strength that would mean less power needed to keep a fusion reactor going, and therefore a more economical reactor system than other options (SN: 1/22/77, p. 61).

Now General Atomic has dedicated Doublet III, the biggest in the series, 500 tons, 16 feet tall, 19 feet in diameter. In it they hope by the early 1980s to reach "breakeven," the situation in which energy generated by fusions equals the energy expended to get the fusions going. To them this means temperatures near 100 million degrees for up to a second and a density of 300 trillion nuclear particles per cubic centimeter. □

Self and non-self chemicals of immunity

Cancers might be attacked more successfully and flu vaccines might be more effective if the body's immune system could be thrown into high gear at a physician's command. Two chemical approaches that may rev up disease-fighting ability are: imitating a natural invader and imitating a signal normally sent between the defense troops. Drugs that result from investigations of these mechanisms, also could aid patients with immune system deficiencies and with auto-immune diseases.

The first approach, imitating a natural invader, is based on the established use of dead bacteria and bacterial extracts to stimulate a general immune response. This technique took a step forward in 1974 when Edgar Lederer of Orsay, France, isolated a small bacterial molecule, a sugar attached to two amino acids, that contained much of the immune stimulating activity. The molecule, called a muramyl peptide, is as potent as but less toxic than a complete bacterial extract.

At the recent meeting of the American Chemical Society in Miami Beach, Peter Dukor of Ciba-Geigy Limited in Basel, Switzerland, discussed research on the muramyl peptide. It has been synthesized chemically, along with analogs that have even greater activity than the natural molecule. Dukor suggests that these peptides act by stimulating macrophages. In the body, the macrophages release chemicals that act at several places on the immune system. Thus, the single peptide can boost proliferation of the T and B lymphocytes and also can act to stimulate precursor cells to mature into additional macrophages. The first application of the bacterial component, Dukor expects, will be as an ingredient to enhance the effect of vaccines.

A second approach to enhancing disease-fighting ability involves imitating body chemicals that stimulate the immune system. Researchers have identified

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several thymus hormones that can signal immune system cells. These factors, when injected into mice whose thymuses were surgically removed, stimulate immunity. Jean-François Bach and colleagues in Paris are studying the nine-amino acid circulating thymic factor, whose sequence they have determined. Chemical synthesis yields a compound as active as the natural product, and synthesis of more than 20 has helped locate the site of biological activity on one part (the carboxy terminal end) of the molecule.

Bach reports that he and co-workers have demonstrated that the factor is present in the normal thymus, but is absent from blood of animals lacking a thymus. The factor is also seen in human blood, but not in blood from patients with certain immune diseases, such as lupus and congenital immunodeficiency.

It is difficult to predict the action of treatments using this thymic factor, Bach says. The factor induces T lymphocytes, but those cells have diverse functions. Some stimulate the B cells to make antibodies, while others repress antibody formation.

Clinical trials have already begun on crude extracts containing several thymus hormones, and Bach reports that pharmocological and toxicological studies of the pure, synthesized circulating factor are in progress. He predicts that the first clinical trials of the pure factor will begin in a few months.

The expectation that thymic factors will play a role in the treatment not only of obvious deficiencies but of autoimmune disease as well is a "new and important concept," according to Bach. A condition where the immune system is overactive, attacking even cells of the body, may be caused by deficiencies of the T cells that repress antibody production. Thus, in some situations, restoring a deficiency should help restrain an immune system active beyond its normal control. □

Shuttle aimed for 9/28/79

Friday, Sept. 28, 1979, is the new official target date on which the National Aeronautics and Space Administration hopes to send the space shuttle into orbit for the first time. The date, announced to a House subcommittee this week by NASA associate administrator John Yardley, represents a six-month delay from earlier plans, due primarily to problems in tests with the shuttle's engines. Recent tests have been more successful, but about two-thirds of the required test-firing time has yet to be accumulated, and the target date could slip still further. As now set, however, it may still be in time to let astronauts from the second or third flight raise the orbit of the slowly descending Skylab, which has been maintaining its low-atmospheric-drag orientation of late in response to ground commands. □

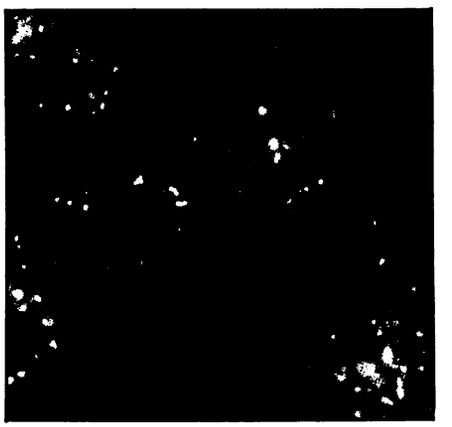
Histocompatibility antigens as double agents

Fascinating proteins called histocompatibility antigens are sprinkled over all human cells (except red blood cells). Each person has four varieties of these proteins — two inherited from each parent. Thus, each person's histocompatibility antigens are as individual as eye color or nose shape — which is why the antigens play a major role in organ transplant rejection. In other words, if an organ is transplanted into a patient, and antigens on the organ do not match those on the patient's cells, the patient's immune system views the transplanted organ as a foreign object and attempts to destroy it.

Now, histocompatibility antigens have been found to do something even more intriguing — they serve as handles for viruses to hook onto when they infect cells, according to Ari Helenius of the European Molecular Biology Laboratory in Heidelberg, Germany, and his colleagues in the August PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. Such a finding is ironical, to say the least, because while the antigens are helping keep certain alien objects, such as transplanted organs, out of the body, they are allowing other foreign objects — viruses — in. What's more, the discovery that histocompatibility antigens serve as a cell entry point for viruses provides the first characterization ever of an animal virus cell receptor (SN: 2/19/77, p. 120).

The research narrative that unfolds in PNAS includes as its principal characters histocompatibility antigens from both humans and mice and the Semliki Forest virus, a simple virus capable of infecting many different kinds of vertebrate cells. First, protein spikes from Semliki Forest viruses were shown to bind to the cells of interest (see illustration), suggesting that the spikes were attaching to certain receptors on the cells' membranes. Then, strong evidence was obtained suggesting that histocompatibility antigens on the cells were receptors for the virus. For instance, histocompatibility antigens taken from the cells were found to interact in solution with Semliki Forest viruses. Complexes between the viral protein spikes and histocompatibility antigens were isolated from cell surfaces. When coupled to an insoluble matrix, the viral protein spikes selectively bound to histocompatibility antigens in solution, although they had the option of binding to other cellular proteins as well. And so on.

Thus, histocompatibility antigens appear to be handles by which Semliki Forest viruses attach to host cells, the researchers conclude. But does a virus grab only a few antigens on a cell at first, then recruit more, since they're mobile? Or does it attach to only a few antigens? And once a virus hooks up with histocompatibility antigens, how does it slip into the cell? Finally, why are Semliki Forest viruses able to use histocompatibility antigens as ports of entry into host cells? Do the antigens have some special reason to accommodate them? Or have the viruses evolved some trick of exploiting the antigens? The latter hypothesis seems more likely, because histocompatibility antigens from different vertebrates are strikingly similar chemically, and the virus can infect cells from all of them. In other words, the virus has probably evolved some means of recognizing certain chemical sequences in many different histocompatibility antigens and thus latches onto these sequences. □



Helenius et al./PNAS

Viral protein spikes attached to cell surfaces, probably to cell receptors.

The 'schizophrenics' who aren't

Diagnosing schizophrenia is somewhat akin to investigating the properties of antimatter: Theoretically, the phenomenon exists and has a tremendous impact on its environment — but no one is quite sure of its exact nature. The immediate consequences of such vagueness in psychiatry — unlike physics — go far beyond theory. A person who is not schizophrenic, but who is diagnosed as such — and vice-versa — may receive inappropriate treatment, including administration of drugs, that could carry adverse effects for many years, or permanently.

Estimates abound on the "widespread" nature of psychiatric misdiagnosis (SN: 7/9/78, p. 28). Now, a comprehensive documentation of substantial overdiagnosis of schizophrenia in state hospitals has been reported in the August AMERICAN JOURNAL OF PSYCHIATRY.

Psychiatrists Michael Alan Taylor and Richard Abrams of the University of Health Sciences at the Chicago Medical School report a "five-fold overdiagnosis of schizophrenia" at a university psychiatric inpatient unit in a suburban-rural area in New