

the meeting was bacterial production of human proinsulin. This natural precursor of insulin contains both chains of the amino acids that are joined to make the hormone. In previous work, Genentech-sponsored scientists had modified separate bacteria to make each chain (SN: 9/16/78, p. 195). Production of insulin from proinsulin is an alternative strategy that may be technically simpler than the combination of two separate chains and purification of the insulin product. The company also requested authorization to scale up new procedures for producing the two separate insulin chains and the human hormone somatostatin (SN: 11/12/77, p. 310). Genentech had been authorized previously for large-scale production of those three substances and also for human growth hormone.

At the closed session of the advisory committee meeting, the pharmaceutical company Eli Lilly also asked for further scale-up authorization for insulin. In addition, Schering-Plough pharmaceutical company requested authorization to scale up bacterial production — probably of interferon (SN: 1/26/80, p. 52).

In other action, the advisory committee decided that a set of safety guidelines written for large-scale recombinant DNA operations would be published in the FEDERAL REGISTER for public comment, and the members argued whether industrial authorizations should be handled through the Occupational Safety and Health Administration, instead of through the NIH committee. □

Interferon bandwagon

Although interferon is still too scarce and too expensive to be proved an effective drug, hints that the substance can fight both viral infections and cancer have led the drug industry to invest millions of dollars in pursuit. Among the latest announcements are those from Abbott Laboratories of Chicago and G.D. Searle and Co. of Skokie, Ill. Abbott says it will use a tissue culture technique developed for another drug to produce fibroblast-type interferon. Searle announced it also has new technology for growing fibroblast cells in tissue culture for interferon production. Searle says it plans to construct a \$12 million pilot plant in England to make interferon and other biological therapeutics. This month Searle will begin supplying scientists at the University of Texas with interferon for the first large-scale (30-patient) evaluation of fibroblast interferon as cancer therapy. While stepping up their tissue culture methods, both Searle and Abbott claim to have the resources and expertise to convert, if it becomes expedient, to recombinant DNA techniques, which have already been demonstrated capable of making small amounts of another type — leukocyte — interferon (SN: 1/26/80, p. 52). □

Kinetics: Enter laser, spectrometer

Lasers have performed in a number of analytical duets over the years: They have teamed up with cloud (SN: 5/26/79, p. 343) and combustion (SN: 9/15/79, p. 188) chambers, for example, for the study of various chemical processes. Now, John T. Herron and colleagues of the National Bureau of Standards are experimenting with another useful partner for the laser — a mass spectrometer.

Herron and co-workers recently coupled an infrared-laser to a mass-spectrometer to study the kinetics — or rate — of complex chemical reactions in real time. "Most chemical processes of importance are controlled by kinetic factors [such as temperature or concentration of reactants]," explains Herron. Furthermore, these processes all involve intermediates: "You don't just go from A to C; you go from A to B to C, where B is the intermediate." The laser in Herron's system breaks the A molecules into the B's, or free-radical intermediates — molecules with an odd number of electrons in the

outermost principal energy level.

But, says Herron, "You not only have to be able to make the free radicals using an infrared laser, you also have to have a way of following them in real time. In this case we are using a mass spectrometer."

Mass spectrometers, the "watchdogs" of chemical reactions, continually monitor which free radicals are formed and how fast they disappear. The instrument capitalizes on a molecule's unique mass to charge (m/e) ratio: The m/e signals received by the spectrometer from a particular reaction chamber identify the free radicals in that chamber and the intensity of the signals indicate the abundance of free radicals.

Coupled with a laser, the spectrometer becomes part of Herron's new chemical kinetics technique — infrared-laser photolysis/mass spectrometry — which he hopes to apply to the study of photochemical smog formation, chemical reactions of the stratosphere and combustion. "We're getting into an era of chemistry in which we have to understand biomass and coal processes, for example, and those are very complicated," Herron says. "That's the kind of chemistry we're interested in attacking." □

Disease carriers and lowered IQ

It's not surprising that victims of certain inherited metabolic diseases suffer brain damage as one of their symptoms. But what is surprising is the apparent finding that carriers of at least one of these disorders also suffer brain damage on occasion and, even more intriguing, that the damage the carriers incur sometimes consists of subtle drops in IQ. So report Mark L. Batshaw of Johns Hopkins Medical Institutions and his colleagues in the Feb. 28 NEW ENGLAND JOURNAL OF MEDICINE.

Males who inherit an X chromosome-linked deficiency in the enzyme ornithine transcarbamylase are unable to correctly metabolize protein and as a result suffer vomiting, coma and even death. Females who carry one gene for the enzyme deficiency and one normal gene, sometimes, but not always, show symptoms of the disease as well, notably mental retardation. Batshaw and his team have now tested the hypothesis that even largely asymptomatic carriers of this enzyme deficiency may suffer some subtle brain damage as a result of their carrier state.

The researchers zeroed in on four generations of a Mormon family in which 12 males had died of an ornithine transcarbamylase deficiency. They tested 18 females in the family to see whether they were carriers of the enzyme deficiency and found that seven were. Then they examined the seven women and six of their sisters neurologically and psychologically. Results were analyzed for evidence of cerebral dysfunction by four psychologists who were unaware of the purpose of

the study and thought it was set up.

The psychologists found no significant differences between the carriers and their sisters on visual perception, memory and academic performance tests. In addition, the carriers' neurological exams were within normal limits. Their IQs, however, were an average of 5.6 points lower than those of their healthy siblings — a statistically significant difference. In fact, the carrier with the lowest IQ showed the most pronounced indication of enzyme deficiency (high levels of ammonia after eating protein), while the carrier with the IQ closest to those of the healthy subjects showed the least indication of enzyme deficiency. So it appears that carriers of ornithine transcarbamylase deficiency may suffer lower IQ because of excesses of ammonia in their bodies.

"This is particularly interesting," Steven Matthyse, a physician with McLean Hospital in Belmont, Mass., writes in an accompanying editorial, "because almost nothing is known about the role of metabolism in differences in IQ within the normal range of scores." It is possible, he says, that carriers of other metabolic disorders may also suffer cerebral dysfunction — say a drop in IQ or even psychosis. In 1966, in fact, a researcher reported a high frequency of psychotic disturbances in families that included some members afflicted with the inherited metabolic disease homocystinuria. That carriers of the inherited metabolic disorder phenylketonuria are at an increased risk of schizophrenia has also been proposed. □