Notes

1. Weinberg seems to disagree, as he states, "Some scientific issues can be unequivocally answered by science, others . . . cannot—either because science has not progressed sufficiently (as in the debate on depletion of the ozone layer) or. . . ."
2. Examples of persistent misunderstandings and lobbyists' half-truths include the following. If ozone is reduced at one level in the stratosphere, it will reform at lower elevations. The atmosphere is a robust system that has successfully coped with volcanic eruptions, atomic bombs, and the impact of current military and civil flying without measurable effect. Ozone has been increasing since 1957 (sometimes earlier or later dates are cited). Early prophecies assumed the stratosphere to be completely static. The theory is based on a chemical reaction that has been demonstrated in the laboratory but never observed occurring naturally in the stratosphere. When some computer jockeys take their giant machines and feed them material designed to prove a preconceived idea, they come up with what they want, not what is valid. It is just a theory. To undo the effect of ozone reduction, all one must do is to move north by x miles. Proposed man-made reductions of ozone are of no consequence because ozone naturally undergoes greater variation from time to time and place to place. If SST's reduce ozone, it can be replaced by release of man-made ozone.
3. These four items correspond respectively to: (i) a reasonable model for the NO_x emission of the formerly proposed Boeing SST based on the number of SST's proposed in 1971 and on the properties they were said to have then; (ii) a reasonable model for a financially successful SST fleet in the future *if* the NO_x emissions remain at the value for current Concordes; (iii) the fact that Concordes burn less fuel per mile and fly at lower altitudes than the formerly projected Boeing SST (the indicated ozone reduction by the Concorde is only about one-half of the formerly projected U.S. SST on an equal fuel consumption basis); and (iv) the biological effect of reduced stratospheric ozone that has received the most nearly quantitative investigation. A 1 percent ozone reduction would be expected to increase the three types of skin cancer by 2 percent or more.
4. In legal matters, *probable cause* is sufficient for a grand jury to recommend that a case be tried in a court of law, rather than be dismissed. *Preponderance of evidence* is the degree of proof required in civil cases, and *proof beyond reasonable doubt* is the degree of proof required in criminal cases. In law, as in science, there is no such thing as *absolute proof*—except after the fact.

I am pleased to learn that certain elements of the ozone problem have been proved "beyond reasonable doubt." Since there remain aspects of the ozone depletion theory that are still unresolved, I agree with Johnston that this may be a very good opportunity to test Kantrowitz's quasi-judicial scientific court.

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Hepatitis B Vaccine: Tests in Humans

Witold J. Brzosko (Letters, 7 Nov. 1975, p. 510) reports that material containing hepatitis B surface antigen (HB_sAg) prepared in Poland has been tested for immunogenicity in patients with hepatitis and that additional batches will soon be "checked in humans in HBV [hepatitis B virus] endemic areas." This situation can only be viewed with considerable alarm.

The possibility of using purified, spherical HB_sAg particles 16 to 25 nanometers in diameter from the serums of asymptomatic chronic carriers as an immunogen seems attractive. Such experimental vaccines, containing no detectable nucleic acid, have been prepared (Research News, 11 April 1975, p. 137) and subsequently have been shown to protect a limited number of chimpanzees susceptible to HBV infection. These preliminary studies, although encouraging, were by no means comprehensive, and further results of experiments in which many more animals were used are urgently awaited. Meanwhile, further physicochemical and immunochemical analyses of these HB_sAg preparations indicate that they may induce harmful immunological reactions to host proteins if used as immunogens (*1, 2*). Several independent studies have shown a close association between HB_sAg and a number of serum proteins. These may be tightly bound as nonspecific contaminants during the purification procedure (*3*) or may be integral components of HB_sAg (*4*). The complexity of the HB_sAg small particle structure was also illustrated by Brzosko and his colleagues in 1972 (*5*). They found that ribonuclease treatment may destroy the morphological integrity of the core of these particles. The same laboratory has consistently reported RNA to be closely associated with HB_sAg (*6*). While these findings have not been widely accepted, a recent study (*7*) in which a chimpanzee was experimentally infected has shown RNA to be closely associated with HB_sAg, although the nature of the association remains obscure.

To our knowledge, studies of the cell-mediated immune response after use of the candidate vaccines have not been carried out. Similarly no account has been taken of liver-specific lipoprotein, a macrolipoprotein which is thought to be a normal constituent of the hepatocyte plasma membrane. Recent studies (*8*) are consistent with the hypothesis that the progressive liver damage of active chronic hepatitis is due to an autoimmune reaction to a hepatocyte surface lipoprotein which is initiated in many cases by infection with HBV. Many observations indicate that immunological mechanisms and the presence of antibodies reacting with various tissue components may well be involved in the pathogenesis of liver damage. It may therefore be undesirable to employ preparations of HB_sAg which contain host cell components or host proteins for immunization.

An aspect which is generally overlooked is the potential use of antigenic polypeptides for immunization. A number of laboratories are investigating the subunit structure of purified HB_sAg, and it has been shown that such subunits consist of polypeptides. It was recently shown (*9*) that the polypeptides may elicit a vigorous antibody response in guinea pigs. The use of immunogenic HB_sAg polypeptides was validated by the finding of a cell-mediated response to intact HB_sAg after inoculation of the guinea pigs with certain polypeptides. Although there was no response to normal human serum, immunization with a component of low molecular weight did elicit a cell-mediated response to normal human serum, suggesting at least one integral component may contain an antigenic determinant related to a human serum protein. In other studies (*10*) it was also demonstrated that the structural polypeptides of the surface antigen are immunogenic. Each polypeptide was found to contain within its structure the group-specific surface antigen determinant. Efforts are being made (*2, 11*) to determine whether such preparations are suitable for use as hepatitis B vaccines.

At a recent meeting of the World Health Organization Scientific Group on Viral Hepatitis it was recommended (*12*) that

> A study should be made of criteria for the safety and effectiveness of the experimental hepatitis B vaccines under development both before the initiation of clinical testing and during subsequent monitoring. The virus has not been cultivated by conventional laboratory techniques, but there is a growing body of evidence to suggest that immunization can be achieved by the use of hepatitis B surface antigen or one of its polypeptides or glycolipids. Although the viral subunit preparations, when pure, are free of nucleic acid and therefore non-infectious, the fact that the starting material for their preparation is human plasma means that extreme caution must be exercised to ensure their freedom from all harmful contaminating material—this vaccine is therefore unique.

We can only hope that this recommendation will be generally accepted.

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