informally and applicable only to the very few compulsorily detained in hospital or under guardianship.

The terms subnormality and severe subnormality as descriptions of human beings are inaccurate, hideous, and revolting. They were not introduced into the Scottish Act; the composite term was sensibly rejected by the Mental Deficiency Section of the Royal Medico-Psychological Association, by the *Journal of Mental Deficiency Research*, and by other organizations. As clinical descriptions of our patients they should be rejected now and for ever. The older term "defective" did not collect much opprobrium, but if some find it offensive what is wrong with "mental retardation"? Mental retardation is a term in general use in this country and America; it is acceptable; it holds out a measure of hope. Let anyone say to himself which he would rather disclose: "I have a subnormal child" or "I have a retarded child." Nurses who find the term subnormal so offensive and degrading would much rather be called a nurse of the retarded, and even we doctors who practise in this branch of psychiatry could call ourselves retardologists. A further disadvantage of the terms severe subnormality and subnormality is that they divide the patients into two classes, whereas they have always been divided into three, and their introduction has made chaos of statistics and other work. If the term mental retardation is to be adopted then patients could be classified as severely retarded, moderately retarded, and slightly retarded, or as in American practice as untrainable, trainable, and educable.—I am, etc.,

JOHN GIBSON.

St. Lawrence's Hospital,
Caterham, Surrey.

Haemagglutination in Virus Hepatitis

SIR,—Your annotation (July 13, p. 69) refers to our studies,¹ among others, in a discussion of the diversity of observations relating to haemagglutination in viral hepatitis. Although all who have looked have indeed seen this effect in some form, there remains an important difference of opinion concerning the significance of the phenomenon. To be resolved is the matter of whether the virus itself is required to produce the haemagglutination or if it is entirely the effect of some physical or biochemical change produced by the disease process. Also to be considered is whether differences in the technique of performing the test are important.

I would like to describe some recent observations that might help to explain the disparate views. In a comparison of several reported techniques I found that the method of Hoyt and Morrison² was insensitive to the point of uselessness. Solvent treatment of the test sera, which Havens found useful,³ is derived from techniques designed to prevent interference with virus effects.^{4,5} Our method of using rhesus monkey erythrocytes gives

significantly higher titres and more discrimination than do chick cells, provided great care is taken to keep everything cold.

Using this preferred technique, the sera of 28 hospital patients with acute hepatitis were tested as soon as a diagnosis was made, and weekly thereafter. Of these patients, 19 had brief but sharp rises in titre, persisting for two or three weeks at peak values of 256 to 2,048. The levels then dropped gradually during a period of three to four weeks to stable, low levels of 8 to 32. Of these 19 there were five in whom the maximum titre occurred in two to four weeks, nine in five to eight weeks, four in eight to twelve weeks, and one in 22 weeks. The last patient died in the 24th week as his titre was dropping.

Of the remaining nine patients, one died in the midst of a sharp rise during the 14th week. In five of the others, titres rose slightly in the fourth to sixth week and remained constant but at a fairly low level (16 to 32). In three patients there was no change in haemagglutinating titre during the period of observation.

Considering the variations in diagnosis, symptoms, time of admission, etc., the haemagglutinating responses were quite reproducible for most of the cases. A somewhat similar progression of changes has been described by Turner *et al.*⁶; and I have been informed by Dr. Rightsel, of Parke-Davis Laboratories, that patients given viral hepatitis experimentally and tested by means of our preferred technique have shown a similar temporal pattern of rising and falling haemagglutinating response.⁷

It is evident that if one examines hepatitis patients at different times in their illness there may be great variations in the proportions with positive responses, depending not only on the time after the diagnosis of the disease but also upon its severity. It is also clear that this is not the usual form of virus haemagglutination as it is seen in the classical pattern of influenza, etc.

From the concomitant biochemical studies it appears that peak haemagglutination titres occur when the disease and the serum transaminase values are first beginning to regress. Therefore, one view of the mechanism could be that this phenomenon of cold haemagglutination requires not only virus but also specific antibody; and when the antibody levels are high enough to suppress the virus the phenomenon disappears.

In support of this view is our previous observation¹ that the haemagglutinating titre can be destroyed in hepatitis serum with β -propiolactone, an agent known to inactivate the hepatitis virus. Antiserum produced in animals to rhesus monkey cells, to serum of "normal" people, or to pooled human gamma globulin with measurable haemagglutinating titres cannot be affected by this chemical treatment. The occasional case of hepatitis in which the titre fails to disappear or where it never occurs might be explained either by faulty diagnosis or by the per-

sistent carrier state that is well known in hepatitis—where one might imagine that antibody production would be deficient.

There is no protracted disease that is characterized by a biochemical change that appears only briefly. Indeed, it would be difficult to conceive of a metabolic change that was detectable neither during the most acute phase of a disease nor during the period of resolution, but only in the interval between the two stages. Nor is it likely that a pathological manifestation would be delayed (but not abolished) where the disease was more severe—as seen in our two fatal cases.

An explanation that is completely compatible with our understanding of infectious disease processes (and with the present situation) is the simultaneous presence of an infectious agent and its antibody. These do occur together, though only briefly, when the disease begins to regress.

The observation that the serum of a normal person can cause the haemagglutination of rhesus monkey or chick cells is not surprising. Non-specific inter-species haemagglutination, as well as haemagglutination inhibitors, have frequently been reported. Although there are many ways of producing haemagglutination non-specifically, such phenomena cannot rule out the possible effect of viruses, and it may be possible to distinguish the source of the agglutinating activity by the judicious use of β -propiolactone.—I am, etc.,

B. A. RUBIN.

Research and Development Division,
Wyeth Laboratories, Inc.,
Radnor, Pennsylvania, U.S.A.

REFERENCES

- Rubin, B. A., Kemp, H. A., and Bennett, H. D., *Science*, 1957, 126, 1117.
- Hoyt, R. E., and Morrison, L. M., *Proc. Soc. exp. Biol. (N.Y.)*, 1956, 93, 547.
- Havens, W. P., *New Engl. J. Med.*, 1958, 259, 1202.
- Porterfield, J. S., *Trans. roy. Soc. trop. med. Hyg.*, 1954, 48, 261.
- Casals, J., Olitsky, P. K., and Anslow, R. O., *J. exp. Med.*, 1951, 94, 125.
- Turner, P., Jha, V. N., Crowley, N., and Sherlock, S., *J. clin. Path.*, 1962, 15, 491.
- Rightsel, W. A., Ketsch, R. A., Taylor, A. R., Boggs, J. D., and McLean, I. W., *J. Amer. med. Ass.*, 1961, 177, 671.

Gas Mixtures

SIR,—The preliminary communication by Dr. M. E. Tunstall (October 12, p. 915) describes a number of experiments upon the cooling of pre-formed nitrous oxide: oxygen mixtures, some of which are in part based upon those of Cole.¹ It might appear from Dr. Tunstall's observations that a chilled "condensed" cylinder containing some liquid nitrous oxide and gaseous oxygen would always give warning of its dangerous state to a would-be user by appearing "frosted" on the outside when brought into a warm room. I think it likelier that a cold cylinder, whether below its N_2O condensation temperature or not, would merely show moisture condensation on its surface. This would give no information about the state of the cylinder gases. "Inverting briskly three times,"

which appears effectively to restore a homogeneous mixture when the cylinder is above its condensation temperature, would have no effect if it was not. At the present time it must be accepted that these cylinders may spend a part of their working lives out of doors in cold weather, and a very small but definite risk to the subsequent user develops every time the outside temperature falls below the condensation temperature of the gas mixture used.

The $N_2O:O_2$ 60:40 mixture condenses at about the freezing point of water (actually $-1^\circ C.$). There was ground frost last winter on 128 nights at Aberdeen (Dyce airfield), 111 nights near Portsmouth (Thorney Island airfield), and 139 nights at Boscombe Down, Wiltshire,¹ and on each of these nights any 60:40 cylinder stored outside would have been at risk. Two of these places are near the sea, where extremes of temperature are rare.

The $N_2O:O_2$ 50:50 mixture condenses at $-8^\circ C.$ The grass temperature fell below $-7^\circ C.$ over the same period on 27 nights in Aberdeen, 30 nights on Thorney Island, and 32 nights at Boscombe Down.² The 50:50 cylinder would therefore have been at risk about four times less frequently in these places than the 60:40 cylinder, and incidentally in a milder winter the grass temperature may not reach $-8^\circ C.$ at all in many places.

There are obviously many more cogent factors to consider when the adoption of pre-mixed gases is considered by the Central Midwives Board, but my recent experience of gas-air machines in this part of the Wessex region leads me to believe that the use of 50:50 $N_2O:O_2$ cylinders would be as safe in practice; and safer in theory, than the many mal-adjusted gas-air machines which lurk about in this country. If 50:50 mixtures are shown by experience to be too weak,³ and warm storage can be guaranteed, then the 60:40 mixture may in time be preferred, but not yet.—I am, etc.,

R. C. NAINBY-LUXMOORE.

Southampton.

REFERENCES

- ¹ Cole, P. V., and Nainby-Luxmoore, R. C., *Anaesthesia*, 1962, 17, 505.
- ² Daily Weather Reports of the Meteorology Office from September 1, 1962, to May 30, 1963. H.M.S.O., London.
- ³ McAneny, T. M., and Doughty, A. G., *Anaesthesia*, 1963, 18, 488.

Immunological Pregnancy Tests

SIR,—In his recent letter (October 5, p. 869) discussing laboratory tests for the diagnosis of pregnancy Dr. A. J. N. Warrack rightly points out that some of the so-called "false-positive" results may be due to a very early abortion being mistaken for an abnormally heavy period. He suggests that a greater number of "false positives" are obtained with the haemagglutination inhibition tests because they are more sensitive than the biological test. Two of these immunological tests

for pregnancy, given a comprehensive trial in this laboratory, are said by the makers to give a positive reaction when the urine contains 2,500 or more international units of chorionic gonadotrophin (i.u. C.G.) per litre. The toads used in this laboratory for the diagnosis of pregnancy are so selected that they respond by laying eggs when there is between 2,500 and 3,000 or more i.u. C.G. per litre of urine. The immunological and Hogben tests are similar in their sensitivity. However, other laboratories doing the Hogben test may not use such sensitive animals.

In our experience urines from some women with a threatened abortion do produce a positive reaction in the immunological test when the Hogben test is negative. In similar cases it is not uncommon for the immunological test to give a negative reaction when the Hogben test is positive. A positive or negative result in cases of threatened abortion will depend upon the sensitivity of the test, and the result obtained will indicate that more or less than a certain amount of C.G. is being excreted. When the Hogben test was compared with the haemagglutination inhibition tests the equivocal results, which were obtained with the urines from women with a threatened abortion, were not included in the calculation of the accuracy of either of these tests (June 15, p. 1606), and we must look for some other explanation of the false-positive inhibition reactions.

Wide¹ has pointed out that human pituitary luteinizing hormone will cross-react in the haemagglutination inhibition test and produce an inhibition reaction indistinguishable from that produced by C.G. Wide has also shown, and his observations have been confirmed in this laboratory, that if the sensitivity of the immunological test is increased then urines collected during the normal menstrual cycle or from men will produce a positive reaction. It is known that the amount of pituitary gonadotrophin, both follicle-stimulating and luteinizing, excreted by women at the menopause is considerably in excess of that excreted during the normal cycle, and half the false-positive reactions in our investigations came from women who were subsequently diagnosed as being menopausal. Some makers of immunological tests for pregnancy now recognize that pituitary luteinizing hormone may be responsible for some of the "false-positive" reactions and recommend that tests for women over 40 years old should be done on half the amount of urine normally used.

Dr. Warrack says that false-positive and false-negative results are equally deplorable, but my clinical colleagues, who use the services of this laboratory, are unanimous in agreeing that false-positive results would cause more trouble than false negatives. However, Dr. Warrack and I would agree over the importance of the overall accuracy of the test.

When I wrote about the reliability of the Hogben test for pregnancy I men-

tioned three laboratories which used this test and which obtained *good consistent results*. I did not include the Sheffield Centre because at that time I had no exact information about the accuracy of their Hogben tests. It would appear from a recent publication² that the overall accuracy of the test at Sheffield is 80%. There may have been some peculiar and unfortunate reason for the accuracy being so low in this series, but if there was it was not given in the paper.—I am, etc.,

B. M. HOBSON.

Pregnancy Diagnosis Laboratory,
Department of Obstetrics and
Gynaecology,
University of Edinburgh.

REFERENCES

- ¹ Wide, L., *Acta endocr. (Kbh.)*, 1962, Suppl. 70, 1.
- ² Shuttleworth, E. M., *Lancet*, 1963, 2, 699.

Tetanus Prophylaxis in Industry

SIR,—Not surprisingly the subject of tetanus immunity frequently appears in your correspondence columns. Since most people are not actively immunized, doctors treating casualties are often faced with a dilemma over administration of antitetanus serum. On one hand serum has a bad reputation for allergy; on the other tetanus, though uncommon, is a serious disease. Happy is the doctor, especially outside hospital, who deals with a tetanus-prone wound¹ and finds his patient has been immunized. Possibly more important is the certainty that many minor wounds inflicted in the garden never receive adequate medical attention.

At present tetanus toxoid is offered to young children and members of the Forces. This leaves the majority of adults unprotected. Doctors working in industry could help to rectify this, since they are in a favourable position to conduct immunization campaigns with their employees. In my experience, 90% of persons in industry are not immunized as recommended²; of these, 90% will accept a course of tetanus toxoid when offered. Immunized persons should of course be given a record card, to avoid risk of unnecessary serum subsequently.

It is only fair to add that tetanus toxoid, which has an exemplary reputation regarding allergy, can cause reactions.^{3,4} I have found a local reaction in 3–5% of subjects. This lasts two to three days, and can usually be controlled by antihistamine.⁵ It will be interesting to see whether adsorbed tetanus toxoid proves less troublesome.—I am, etc.,

R. G. ORR.

Atomic Energy Research Establishment,
Didcot, Berks.

REFERENCES

- ¹ Parish, H. J., and Cannon, D. A., *Antisera, Toxoids, Vaccines and Tuberculin in Prophylaxis and Treatment*, 5th ed., 1961, p. 59. Livingstone, Edinburgh and London.
- ² *Brit. med. J.*, 1962, 1, 585.
- ³ Brindle, M. J., and Twyman, D. G., *ibid.*, 1962, 1, 1116.
- ⁴ Frankland, A. W., *ibid.*, 1960, 1, 1733.
- ⁵ *Ibid.*, 1961, 2, 1036.