LETTERS TO THE EDITOR

Intravenous Injection of Dextrose, 5 per cent.

SIR,—It is common knowledge that on heating solutions of dextrose in an autoclave they become markedly acid in reaction. This phenomenon was noted by Hudson and Tarlowski[1] who suggested that such solutions should either be buffered before autoclaving or be sterilised by filtration. The fact that large quantities of dextrose solution are used and that all the commercial preparations we have examined have had a low *p*H suggest that the acidity is not widely regarded as a very serious matter. The *p*H is usually in the region of 4·2 to 4·5. Recent experience (especially with infants) of venous thrombosis following prolonged intravenous administration of 5 per cent. dextrose solution has caused us to re-examine the matter. So far as we are aware no explanation of the phenomenon has been put forward. The following notes give the gist of our findings, which are incomplete. (1) *Addition of Phosphate buffer.* The addition of sufficient sodium phosphate buffer to prevent the *p*H falling below 6 during autoclaving brought about discolouration of the solution to a degree which rendered it unfit for use. (2) *Saturation with nitrogen.* Saturation of the solution with nitrogen and displacement of the air above the solution with nitrogen gave solutions of slightly higher *p*H than the controls, viz. controls of 4·2, nitrogenated solutions 4·5. This was consistent over a number of experiments. (3) *Addition of Sodium Ascorbate.* 20 mg. of ascorbic acid as sodium ascorbate solution (*p*H 7) was added to each 100 ml. of dextrose solution. This was then nitrogenated. After autoclaving the *p*H was 5·5. 100 mg. of ascorbic acid in a similar experiment gave a *p*H of 6·0. (4) *Irgalon (ethylenediamine tetracetic acid).* As the solution salt (*p*H 7), in a concentration of 10 mg./100 ml. of dextrose solution this substance gave *p*H 5·2 and 100 mg./100 ml. gave *p*H 6·0. As with the ascorbic acid solution, the solutions were nitrogen saturated. Irgalon is used as a sequestering agent for trace metals and as an anti-oxidant for fats owing to its property of sequestering peroxide oxygen. (5) *Hydrazine Hydrate.* Hydrazine hydrate 10 mg. was added to each 100 ml. of nitrogenated dextrose solution. After autoclaving *p*H 6·0 was given. It appears to us that the above findings suggest a dual oxidation taking place in the dextrose solutions, viz. (a) an "external" oxidation using dissolved atmospheric oxygen: this is to some extent prevented by saturation with nitrogen and (b) an "internal" oxidation of the dextrose molecule. This appears to be prevented or retarded by the addition of reducing substances as shown. The processes appear to be addition, since non-nitrogenated solutions treated with reducing agents give lower *p*H readings than the nitrogenated ones. In view of the serious difficulty of prolonged intravenous administration of dextrose to infants, we investigated the effect of the "stabilised" solutions on red cells, expecting to find them less damaging than the unadjusted, acid reacting fluids. Both the ascorbic acid and the irgalon-treated samples brought about a marked *in vitro* auto-agglutination and hæmolysis at 37 per cent. Slight agglutination was also found in the unadjusted control but hæmolysis was not noticeable. The hæmolysis may be due to fact that our solutions were approaching the critical *p*H for hæmolysis noted by Hendrie[2]. There was, however, no apparent correlation between the degree of hæmolysis and the degree of agglutination. The latter phenomenon could well be associated with that of venous thrombosis and since in infants especially the volume of injected fluid is high in relation to blood volume and moreover,

since little or no dilution with blood takes place for some distance along the vein it seems possible that such a connection exists. We believe the matter to be worthy of fuller investigation. We are particularly impressed by the fact that plain dextrose solution is not free from the agglutination property.

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REFERENCES

1. Hudson, T. A., and Tarlowski, L., *Pharm J.* **158,** 1947, 451.
2. Hendrie, E. B., *Edin. med. J.,* 1948, **40,** 427.

ABSTRACTS (*continued from page* 470)

stimulated the growth of human tubercle bacilli. The possibility therefore arose that Ungar and Muggleton's results were due to retarded growth because of lack of oxygen in the controls as compared with the test cultures in which the containers were frequently opened for the assay and replacement of penicillin. To test this possibility, 3 sets of cultures were set up, the bottles containing the controls and those containing the test cultures being opened at the same time. One set of bottles was a control; no penicillin was used in them and the bottles were not opened. A second set were identical with the first but they were opened for the same periods as the test set. The test cultures contained 5 I.U./ml. of penicillin, the antibiotic level being maintained by assay at 48-hour intervals and adjustment by addition of more penicillin as found necessary. The results showed that the greater growth in set 3 than in set 1 could be due to the greater oxygen supply. The penicillin disappears completely in a few days and by assaying at 2-hourly intervals it was found that it was destroyed by the culture at a rate of about 5 units per ml. in 2 hours. A 2-months' culture, in which a considerable amount of lysis had occurred, centrifuged until free from cells, destroyed 50 units of penicillin per ml. per hour at 37°C.; the crude culture fluid destroyed the antibiotic at the same rate. Tubercle bacilli therefore produce a penicillinase and further experiments showed that the enzyme loses its activity after 1 hour at 60°C., that it is adsorbed by a bacterial filter, that it is destroyed by shaking and that it is most active at *p*H 6·0. The lower activity of tubercle penicillinase as compared with other varieties may be due to the presence of iron in the medium used, this metal having been previously reported to inhibit penicillinase. Since young cultures show little penicillinase production it is probable that the enzyme is intracellular in the living organism and liberated only on its death and lysis. H. T. B.

Phenylmercuric Acetate, as Preservative in Antigens. I. Williams and G. Piness. (*J. Allergy,* 1949, **21,** 45.) On the basis of laboratory and clinical studies covering a period of 3 years, the authors recommend a 1:25,000 dilution of phenylmercuric acetate as the most satisfactory preservative for use in antigens. The bacteriostatic and fungistatic efficiency in this dilution was demonstrated by *in vitro* tests employing cultures of *Staphylococcus aureus, Staph. albus, Bacterium coli, Bacillus subtilis* and *Aspergillus.* Skin tests conducted on a number of patients, using a 1:25,000 dilution in buffered saline solution, showed that intracutaneous injections gave rise to no pain or irritation. Comparative skin tests also showed that phenylmercuric acetate in this dilution neither destroys nor inhibits antigenic potency. S. L. W.