

Further studies are being undertaken to examine the histology of the tattooed skin to see if that would throw light on the reason behind the peculiar response of the tattooed skin.—We are, etc.,

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1 Grolnick, M., *Annals of Allergy*, 1970, 28, 395.

### Multiple Sclerosis among Immigrants

SIR,—With the co-operation of the Multiple Sclerosis Society of Great Britain and Northern Ireland I am undertaking a study of the prevalence of multiple sclerosis (M.S.) among immigrants to England both from areas of the world where the disease is common, such as Ireland and Europe, and from areas of the world where the prevalence is thought to be low—Africa, Asia, and the West Indies. If immigrants from low-prevalence countries are immune to M.S. they should keep their low risk; if on the other hand they are not immune they should have a greatly increased risk of developing M.S. on immigrating to England. Most of the immigrants from low-prevalence areas have settled in Greater London and the Central Midlands and in these areas, with the permission of the research committees of the hospitals, over 9,000 M.S. case-folders have now been studied in order to ascertain the birthplace of the patients. This study has proved to be very successful, but some immigrants from low-prevalence countries have no doubt been missed.

I am very anxious to ask doctors who know of any M.S. patient who was born in a low-prevalence part of the world if they would co-operate with this study by informing me about the patient, with the patient's permission. I am, etc.,

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### Suicidal Attempts with Beta-adrenoceptor Blocking Agents

SIR,—Drs. P. Karhunen and G. Härtel (21 April, p. 178) reported a case of attempted suicide with 9,000 mg of practolol. Apart from very modest reductions in blood pressure and heart rate, no effects were observed and no special treatment was necessary. The highest measured plasma concentration of practolol was 58.6 µg/ml. More recently Drs. W. Wermut and M. Wójcicki (15 September, p. 591) reported a case of attempted suicide with 2,000 mg of propranolol. No signs of cardiac disturbance were observed after what is described as a "massive" dose of propranolol. The authors concluded that "the effect of propranolol on the healthy heart needs to be reconsidered."

We have recently reported<sup>1</sup> the effects of beta-adrenoceptor blocking agents in healthy human volunteers. Maximally tolerated doses were administered intravenously over five minutes. These were: practolol 1,280 mg, propranolol 120 mg, oxprenolol 160 mg, sotalol 160 mg, and pindolol 16 mg. Effects on supine blood pressure and heart rate were slight and

certainly represented no clinical hazard. There was, of course, marked antagonism of any induced increase in heart rate. Plasma levels of the drugs were not measured, but on the basis of the work of Aellig *et al.*<sup>2</sup> it is estimated that the peak plasma level of practolol in our lightest subject (62 kg) was approximately 100 µg/ml.

Doses of beta-adrenoceptor blocking agents required to achieve therapeutic effect cover a wide range. Zacharias and Cowen<sup>3</sup> found that more than 15% of hypertensive patients required 1,000 mg or more of propranolol daily. Kincaid-Smith *et al.*<sup>4</sup> report using propranolol in doses up to 2,000 mg daily and Prichard<sup>5</sup> up to 4,000 mg daily. Of course these doses have been achieved after gradual titration, and it is appreciated that in patients with incipient cardiac failure it is the starting dose that is likely to precipitate overt failure. However, even this hazard might well be prevented by prior digitalization.

When maintenance of resting cardiac output relies on sympathetic drive, administration of a beta-adrenoceptor blocking agent might, by antagonizing that drive, precipitate cardiac failure. The healthy subject when resting supine maintains cardiac output and blood pressure in the absence of sympathetic drive, and so in this situation beta-adrenoceptor blocking agents, even in "massive" dosage, are not likely to represent a hazard.—We are, etc.,

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<sup>1</sup> Boakes, A. J., Boeree, B. H., and Prichard, B. N. C., *Naunyn-Schmiedeberg's Archiv für experimentelle Pathologie und Pharmacologie*, 1973, 279, Suppl., R42.

<sup>2</sup> Aellig, W. H., Prichard, B. N. C., and Scales, B., *British Journal of Pharmacology*, 1970, 40, 573P.

<sup>3</sup> Zacharias, F. J., and Cowen, K. J., *British Medical Journal*, 1970, 1, 471.

<sup>4</sup> Kincaid-Smith, P. Fang, P., and Laver, M. C., *Clinical Science and Molecular Medicine*, 1973, 45, 75S.

<sup>5</sup> Prichard, B. N. C., *British Journal of Hospital Medicine*, 1973, 10, 45.

### Depression of Cellular Immunity in Pregnancy due to a Serum Factor

SIR,—The article by Dr. C. A. St. Hill and others (8 September, p. 513) is a wonderful example of how to hoodwink a venerable journal with statistical "t's and "P's, even when wrongly applied and irrelevantly theorized.

Consider that the *t* test was used to compare, within the same experiment, five groups of data: (A+B) with (C+D), (C) with (D), and (A+B+C+D) with (E). The correct method of analysis here would be analysis of variance, and I would guess that if anything were significant in the experiment by analysis of variance, only the last grouping might be. Of course, we don't even know how good the technique is, since the authors don't give us their normal values of lymphocytes in autologous serum with standard deviations thereof—it might discourage us from pursuing the paper.

Finally, to add insult to injury, the theorization is done not on the allegedly significant differences, but those which are insignificant (namely, (C) against (D), or "fetal serum has a greater depressive action than maternal serum").

Please, if we are to have statistics, let them be correctly planned, expertly presented, and judiciously edited.—I am, etc.,

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\*\* We showed Mr. Munster's letter to Dr. St. Hill and his colleagues, whose reply is printed below.—ED., *B.M.J.*

SIR,—If there had been no prior reason for testing the difference between the pregnant (C+D) and non-pregnant (A+B) sera, the significant result ( $P < 0.01$ ) might have been dismissed as an effect of multiple comparisons, but the investigation was concerned with a difference of this kind. To report an analysis of variance, as a process of unguided statistical exploration, would have been superfluous. Moreover, the most important of the possible comparisons, that of (E) with (A+B+C+D) is too highly significant to be dismissed in this way. The choice of the comparative transformation rate for the statistical analysis is an orthodox use of standard statistical techniques.

Mr. Munster is guilty of quoting out of context. Our statement that "fetal serum has a greater depressive action than maternal serum" was heavily qualified. Thus it was immediately preceded by the phrase: "Our results raise the possibility that . . .," and in the results section we noted that the difference in the suppressive action of fetal and maternal serum was statistically not significant. We therefore thought that we had made it sufficiently clear that this was only a suggestion; moreover, it only constitutes an unimportant part of our thesis.

Some years ago an eminent professor of orthopaedics who was opposed to, and probably ignorant of, the value of statistical analysis used to teach his students that statistics were not essential and that "if it's important, laddie, it will hit you in the eye." The kernel of our paper was the difference shown in the figure between (A+B+C+D) and (E). This surely "hits one in the eye," and statistical wrangling, however elegant, cannot possibly obscure this observation.—We are, etc.,

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### Making Hospital Geriatrics Work

SIR,—May I reply to Dr. R. V. Boyd (3 November, p. 298), who comments on the paper by Dr. P. M. Jefferys and myself (2 December 1972, p. 536)?

Dr. Boyd found that an 11% bed reduction suddenly imposed on his active department at Greenwich resulted in a catastrophic fall in admission rate and the accumulation of a large waiting list. One sympathizes with him on this unfortunate occurrence, but he does indicate that there were some unusual circumstances. In his well-bedded days he took on "a high long-stay commitment to help out other agencies under stress." In contrast to the Greenwich experience, other active departments have found it possible effectively to reduce their