Suxamethonium Sensitivity

SIR,—The occurrence of rare individuals who show a marked sensitivity to suxamethonium ("scoline") has led to the discovery of inherited variation in serum pseudocholinesterase. Recent work has shown that the genetics of this condition is complex. There appear to be at least four allelic genes for this human enzyme:

- (1) The "normal" gene (N).
- (2) The gene for the atypical variant (D) (recognized by an altered response of the enzyme to the inhibitor dibucaine).
- (3) A gene for an enzyme with an altered sensitivity to fluoride inhibition (F).
- (4) A "silent" gene determining a complete absence of enzyme activity (S).

Since each individual possesses two allelic genes, these four give rise to the ten possible genotypes shown in the table.

Possible Genotypes Determined by the Four Pseudocholinesterase Genes: Normal (N), Atypical or Dibucaine-resistant (D), Fluoride-resistant (F), and Silent (S)

Genotype	Suxamethonium Sensitivity	Comments
<i>Homozygotes</i>		
N-N	Not sensitive	The normal population Frequency = 1:2,800
D-D	Markedly sensitive	Rare. Frequency not known
S-S	" "	Rare. Frequency not known
F-F	Moderately sensitive	Rare. Frequency not known
<i>Heterozygotes</i>		
N-D	Not sensitive	3.8% of the population
N-S	Probably not sensitive	
N-F	Probably not sensitive	
D-S	Markedly sensitive	3 cases of apnoea described
D-F	Moderately sensitive	Frequency unknown
F-S	Expected to be moderately sensitive	Not yet described

The evidence for the relationship between this complex polymorphism and suxamethonium apnoea is still scanty. The paper by Dr. A. B. M. Telfer and his colleagues in your 18 January issue (p. 153) is therefore a valuable contribution to the subject. Several points appear to merit further comment.

Dr. Telfer and his colleagues report that two patients with suxamethonium apnoea (Nos. 1 and 7) appear on dibucaine testing to be heterozygotes for the normal and atypical genes (genotype N-D in table). It has been our experience that such individuals are not sensitive to suxamethonium. We have been fortunate in the past few years in having the close collaboration of our anaesthetist colleagues, who have told us of all cases of apparent suxamethonium apnoea in our hospitals (St. Bartholomew's Hospital, London, and United Oxford Hospitals). During this period approximately 50,000 patients have been given suxamethonium and 3.8% of these, or 1,900 individuals, must have been heterozygotes of the N-D type. Yet we have never seen suxamethonium sensitivity in persons of this genotype. Possible explanations of the suxamethonium sensitivity of Cases 1 and 7 is that they are either heterozygotes for the genes for the typical and fluoride-resistant enzymes (D-F), or homozygotes for the latter enzyme (F-F). However, the fluoride numbers reported for these two cases do not fit in

with this theory. It may be, therefore, that other genetic or environmental factors played a part in the suxamethonium sensitivity of these patients.

Case 6 is of interest in that an individual who appeared to be an atypical homozygote had one offspring with a normal dibucaine number. This suggests that the parent is, in fact, a heterozygote for the atypical and silent genes (D-S). Such a person would appear phenotypically to be an atypical homozygote, but on mating with a normal person could produce offspring with the genotype N-S. Such children would have normal dibucaine numbers but enzyme levels around the lower limit of normal.

Lastly, we should like to state, as has been done before, that the use of test papers for spotting low pseudocholinesterase activity in sera has, in our experience, not given satisfactory results.—We are, etc.,

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Tuberculosis in Developing Countries

SIR,—Dr. W. Fox's article (18 January, p. 135) has caused us some misgiving. The paper relates particularly to Asia, but that the views expressed are meant to encompass other areas is plain, and there is a danger that they may be accepted as something of a blueprint for underdeveloped tropical Africa, for example.

So far as West Africa is concerned we do not agree that "little attempt has been made to adapt current knowledge. . . ." Much effort has been devoted to this very matter in various centres there over the last decade, and that Commonwealth Governments are very conscious of the gravity of the problem of tuberculosis is evidenced by the fact that the disease has been a State concern for many years, that treatment is free to all, and that antituberculosis drugs are imported duty free.

The great mass of patients in tropical Africa live in scattered rural communities, faced by paucity of clinical facilities, great distance often of home from clinic, and inability to leave rural occupations at will. The problems are very different from those experienced by the Madras Chemotherapy Centre, upon whose work Dr. Fox would appear to base many of his views.

The work quoted by Dr. Fox in support of out-patient chemotherapy was undertaken in centres with first-class facilities (we include here the Madras Chemotherapy Centre) at a level and of a quality unheard of in tropical Africa or elsewhere in the underdeveloped world. There is ample evidence that good chemotherapy is effective in the treatment of pulmonary tuberculosis in the African, but our own work in West Africa, undertaken at a field level with facilities little different from normal, to determine what could realistically be achieved in rural and semi-rural communities, showed that the rules which govern its application cannot be observed under existing conditions or those likely to apply for many years. This is evidenced by the failure of out-patient chemotherapy in the clinical sense and by very disturbing levels of bacterial resistance. The situation in West Africa¹⁻³ is little different from that in East Africa.^{4,5} The reasons for development of resistance in patients under treatment may

relate to a number of factors around the central one, which is that patients do not take drugs in the dose or form prescribed, regularly and for a prolonged period.

Good out-patient chemotherapy can only be achieved if strict control measures are brought to bear, but the "minimum facilities" given by the Madras Chemotherapy Centre⁶ as being necessary for the "satisfactory organization of an efficient domiciliary service based on a tuberculosis clinic" are wholly unrealistic in the context of underdeveloped Africa. If Dr. Fox's views gain credence and if therefore uncontrolled out-patient chemotherapy becomes the order of the day we can expect further deterioration of an already lamentable situation—in Africa certainly, and possibly in other parts of the underdeveloped world.

It is our view that control can only be achieved by a form of therapeutic detention, at least for a period. For this purpose hospital beds must be made available. Construction costs for Nairobi, quoted by Dr. Fox, would appear to relate to formal hospital buildings in a city which in sophistication is almost unique in tropical Africa. The need is for simple shelters built of local materials at the village level, where patients may rest or work under control. Upkeep is minimal and the only staff required need be para-medical personnel, who can ensure that adequate regular treatment is applied; their work can be complemented by periodic visits from a physician.

With regard to bacteriology, much certainly can be learned from the sputum smear, which is a useful index of progress. The smear does not, however, give any indication of bacterial sensitivity of the new case—a knowledge of which is the prerequisite to good chemotherapy. If we consider streptomycin, P.A.S., and isoniazid: of patients presenting in Ghana and denying previous chemotherapy 23% can be expected to be resistant to one or more drugs.⁷ Whether these are instances of true primary resistance or not is irrelevant; what matters is that the clinician is faced with giving drugs to many patients whom he knows are likely to be resistant to one or another of the drugs available. This can only result in a situation similar to that in Ghana, where 60% of patients receiving chemotherapy are resistant to one or more drugs (27% to one, 24% to two, and 9% to three drugs).⁸ Equipping and staffing laboratories capable of undertaking culture and sensitivity work, at least for new patients, need not be costly as Dr. Fox suggests,⁷ and if *in-vitro* sensitivity testing means anything the need for them in tropical Africa is obvious.—We are, etc.,

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REFERENCES

- ¹ Bell, W. J., and Brown, P. P., *Tubercle (Lond.)*, 1960, 41, 247.
- ² ——— *Brit. J. Dis. Chest*, 1961, 55, 192.
- ³ ——— *W. Afr. med. J.*, 1963, 12, 181.
- ⁴ Pepys, J., Mitchison, D. A., and Kinsley, B. J., *Tubercle (Lond.)*, 1960, 41, 32.
- ⁵ Short, G. M., *ibid.*, 1961, 42, 535.
- ⁶ *Bull. Wild Hlth Org.*, 1959, 21, 51.
- ⁷ Bell, W. J., *W. Afr. med. J.*, 1959, 8, 258.

Future Organization of Psychiatry

SIR,—At its meeting on 12 February 1964 the Council of the Royal Medico-Psychological Association gave careful consideration to the agreed ballot of all its members on the