phenomenon was not detectable and the actual differences between A₁ and O were in fact the other way round from those found in the other villages.

Although regional differences in the frequency of ABO genes certainly occur, there is no evidence in the data of Kopec¹ for micro-differentiation between neighbouring Oxfordshire groups from which most of the non-local individuals came. Further the migration matrix analysis of movement into the Otmoor populations² not only predicted that there would be no between-village heterogeneity but that the genetic composition of the villages should be the same as those in the surrounding neighbourhood. It therefore seems unlikely that the differences in ABO frequencies between locals and non-locals arise from their being two primary populations. (We should perhaps add here that further analysis of other polymorphic systems indicates genetic heterogeneity between the Otmoor villages, but this is not shown by the ABO system.)

An overall analysis of the IQ variance according to the ABO status reveals significant heterogeneity. In the four groups, local males, local females, non-local males and non-local females the IQ variance is always smaller for O subjects than for A₁ ones. Although these differences do not reach individual significance, an analysis of variance of logarithms of variances according to blood group status, sex and origin, indicate significant differences by AO status and sex ($t = 2.23$ and 2.03 respectively with 629 d.f.). (This variance analysis includes additional information to that previously reported, but the same trends are present in the original data.) The two-population model cannot account for variance differences but selective migration can. If, for example, high IQ individuals tend to out-migrate from Otmoor, which seems likely, and if these outmigrants tend to have a relatively high frequency of blood group O, then one would find a comparatively low variance of IQ in those O individuals who remained and were tested. Selective migration of this form could also explain the differences in the ABO frequency of the locally and non-locally born groups and particularly, the unusually low frequency of the O gene in the locally born males.

It is perhaps also worth mentioning that in some of the village groups a significant difference in the IQ of A and O people also exists among the non-locals.

Department of Genetics,
University of Cambridge, and
Departments of Human Anatomy
and Biomathematics,
University of Oxford, UK

Dantrolene sodium and 'skinned' muscle fibres

HAINAUT and Desmedt¹ have reported the results of their work with Dantrolene sodium (1- {[5-(*P*-nitrophenyl) furfurylidene] amino} hydantoin sodium hydrate salt) and skeletal muscle. In single fibres of frog semitendinosus muscle they showed a greatly reduced twitch force and a shift in the dose-response curve for potassium contractures. These results in general agree with those already obtained with whole muscle². Other workers³ have shown that Dantrolene sodium has no effect on sarcolemma resistance or capacitance, and all evidence²⁻⁴ points to the intracellular Ca²⁺ control mechanisms as the level at which Dantrolene sodium produces its effect.

If the contractile proteins themselves are not involved, the twitch tension following a single release of Ca²⁺ from the sarcoplasmic reticulum may be reduced in two ways: less Ca²⁺ may be released, and also the rate of uptake of Ca²⁺ may be raised. Hainaut and Desmedt¹ show a reduction of 30% in the aequorin luminescence of barnacle fibres, following treatment with high concentrations of Dantrolene sodium, thus demonstrating that Ca²⁺ release is certainly reduced in this muscle. In the frog, however, the twitch may be reduced by 75% with 15 μ M Dantrolene sodium and it is possible that several mechanisms may be involved. A good method for detecting changes in Ca²⁺ uptake into the sarcoplasmic reticulum is the Ca²⁺-gel pipette technique of Gillis⁵, which can be used for frog muscle. Here, controlled local contractions are produced by a short contact with the Ca²⁺-containing gel on an area of the muscle fibre from which the sarcolemma has been mechanically removed. Thus Ca²⁺ is introduced from an external source, and relaxation follows with the uptake of these ions into the sarcoplasmic reticulum. Drops of Dantrolene sodium in aqueous solution were added to the fibre under paraffin oil. The concentration of Dantrolene sodium was about 15 μ M, a saturated solution in 120 mM KCl. In this 'skinned' preparation with no membrane it may be expected that the concentration of the negatively charged Dantrolene ions within the sarcoplasm is much higher than that inside an intact fibre. The volume of Dantrolene sodium solution given was roughly twice the volume of the 'skinned' region of the fibre, so it would be expected that the concentration at the point of the test contractions remained high for some time.

Contraction-relaxation cycles before and after Dantrolene sodium treatment were recorded on cine film and compared for speed and distance of contraction, spread of activation and rate of relaxation.

There was absolutely no change in any of these parameters, either a few seconds after Dantrolene sodium or several minutes later. In view of the undoubted effects of Dantrolene sodium on the intact muscle it would seem that it acts uniquely on Ca²⁺ release—the event bypassed using the Ca²⁺-gel pipette. It is clear that sliding filament reactions and Ca²⁺ uptake are not altered in the 'skinned' fibre. Also, as the spread of activation was not reduced it seems likely that the regenerative release of Ca²⁺ from the reticulum is not inhibited. This aspect of the possible actions of Dantrolene sodium has been discussed previously⁴ in relation to other results.

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LYDIA BROCKLEHURST

Department of Physiology,
University College, London, UK

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DRS HAINAUT AND DESMEDT REPLY—Studies on single muscle fibres have demonstrated that Dantrolene sodium reduces the Ca²⁺ release from the sarcoplasmic reticulum during a twitch¹. The finding that Dantrolene sodium does not accelerate the myoplasmic Ca²⁺ uptake studied in skinned muscle fibres² is in line with our observations on intact barnacle muscle fibres injected with aequorin. Figure 2d–e from our paper¹ indeed showed that the calcium transient, though markedly reduced in size, was not significantly changed in its time course by Dantrolene sodium. The half time of the exponential falling phase of the luminescence transient studied for different depolarisations in six different fibres was 38.9 ms (s.d. = 1.8 ms) before and 38.4 ms (s.d. = 2.9 ms) in presence of Dantrolene sodium. These and other data (K. H., and J. E. D., unpublished) confirm that Dantrolene sodium depresses the Ca²⁺ release but does not affect the rate of reuptake of Ca²⁺ in intact muscle fibres.

University of Brussels,
Brussels, Belgium

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