Chlorpropamide-alcohol flushing, aldehyde dehydrogenase activity, and diabetes complications

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standards. This sounds logical enough, but what does it mean in reality? Firstly, it does not mean what Lord Mottistone meant when he introduced his original amendment to the Transport Bill. This would have required *all* visors to be clear. At present the law requires only visors supplied with new helmets to be clear. Replacement visors can have any density of tint and can be worn both during the day and at night. The Government asked Lord Mottistone to withdraw his amendment so that it could replace it with its own. The Government's amendment means that regulations can now be brought in so that instead of all visors having to be clear, as Lord Mottistone proposed, those worn during the day can be tinted. The Department of Transport seems to believe that a motorcyclist who sets off in good weather wearing a tinted visor will also carry a clear substitute in case the British weather changes during his trip or before he returns home at the end of the day if he is riding to work. The department cannot really believe that he will not ride in the dark in a tinted visor because it proposes fines for doing so. After dark the police would be expected to detect the illicit use of tinted visors, a task which visually might prove difficult.

Optically, even with a clear visor the motorcyclist is at a disadvantage at night. He is trying to see the hazards ahead with a single headlamp, which at best has only half the power of the pairs of headlamps of oncoming vehicles. More often his single headlamp has an inferior performance; sometimes it is woefully weak. There are no minimum performance requirements for motorcycle headlamps. What evidence does the Department of Transport have that shows that if the stylists employed by the motorcycle clothing industry are permitted to tempt motorcyclists into buying fashionably tinted visors more motorcyclists will not run into obstructions and into potholes which they have failed to see in time?

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Myocardial disarray revisited

SIR,—I was interested to read the article by Dr E G J Olsen (9 October, p 991) in which he reviews observations which support those that I made in 1976 that disarray of myocardial fibres is a common feature of congenital heart disease.

I found that in addition to disarray of muscle fibres all the other histological features accepted as specific for hypertrophic cardiomyopathy are commonly seen in congenital heart disease.[1 2] The finding of classic echocardiographic and myocardial histological features of hypertrophic cardiomyopathy in a patient with congenital bicuspid aortic valve stimulated me to investigate the myocardial histology in 11 postmortem heart specimens from patients who had congenital heart disease and whose echograms during life had shown symmetrical or asymmetrical septal hypertrophy. In four hearts histological examination of the myocardium showed generalised disarray of myocardial fibres with whorled patterns, large bizarre nuclei, and fibrosis. Considerable hypertrophy and abnormal branching of muscle fibres were also evident in these cases. In the remaining seven hearts similar but patchy myocardial changes were present. When these histological sections were shown to the late Professor R D Teare, who had no knowledge of the underlying cardiac disorder, he confirmed that they were all unequivocally compatible with hypertrophic cardiomyopathy. The unexpectedly high incidence of myocardial cell disorganisation in this small series of patients with congenital heart disease with both symmetrical and asymmetrical septal hypertrophy raises the possibility that hypertrophic cardiomyopathy may be an integral part of congenital heart disease. There is no doubt that isolated hypertrophic cardiomyopathy occurs. My findings led me to speculate, however, that when the two conditions coexist the myopathy and the anatomical defects may result from the same abnormal stimulus. It is possible that the extent of the anatomical defects depends on the timing and dose of insult during embryogenesis.

These observations must have been considered too revolutionary at the time because they were not accepted for presentation at the British Cardiac Society meeting nor for publication by two international journals of cardiology. They were, however, presented and subsequently published in the Ultrasonics International conference proceedings,[3] and included in my MD thesis.[4]

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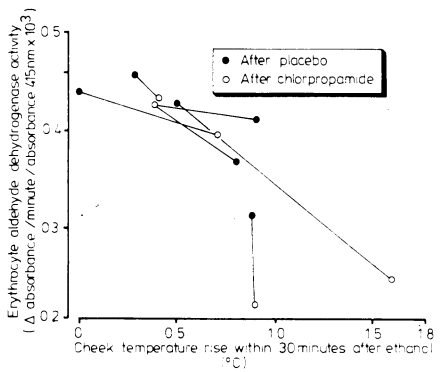
[4] Feizi O. MD Thesis, University of London, 1979.

Chlorpropamide-alcohol flushing, aldehyde dehydrogenase activity, and diabetic complications

SIR,—In their interesting paper (25 September, p 838) Dr H Öhlin and others showed that erythrocyte homogenates from diabetic chlorpropamide-alcohol flushers eliminated acetaldehyde more slowly than those from non-flushers, suggesting a difference in the activity of erythrocyte aldehyde dehydrogenase between those two groups. This difference in acetaldehyde elimination was apparent in the absence of chlorpropamide. Chlorpropamide has been shown to inhibit aldehyde dehydrogenase activity,[1 2] and might thus be expected to decrease further any genetic or permanently acquired reduction in aldehyde dehydrogenase activity.

We have conducted a study in which six fasting non-diabetic subjects attended twice for an ethanol test: the first time, unknown to the subjects, having taken placebo tablets; and the second having taken 500 mg chlorpropamide four hours previously. They rested in a room with ambient temperature kept at 20±SD 0·3°C. When cheek temperature was steady they drank 0·2 ml/kg body weight of 90% ethanol in two volumes of water, and temperature measurement was continued for 30 minutes. Immediately before drinking the alcohol a venous blood sample was taken for estimation of plasma chlorpropamide concentration and erythrocyte aldehyde dehydrogenase activity. Plasma chlorpropamide levels were measured by high performance liquid chromatography using ultraviolet detection.[3] Erythrocyte aldehyde dehydrogenase activity was measured by spectrophotometric monitoring of reduced nicotinamide adenine dinucleotide production and expressed as change in absorbence/minute/absorbence at 415 nm $\times 10^3$ (units).[4]

Two subjects noted facial warmth (both on placebo), two flushed visibly in both tests, and one flushed only after the placebo. Cheek temperature rise above baseline during 30 minutes was from 0 to 0·9°C, median 0·5°C, during the placebo test, and from 0·4 to 1·6°C, median 0·7°C, during the chlorpropamide test. Median erythrocyte aldehyde dehydrogenase activity was 0·426 (range 0·308 to 0·454) unit in the placebo tests and not significantly different at 0·396 (0·222 to 0·434) unit in the chlorpropamide tests. In each of the five men cheek temperature rise was greater at lower erythrocyte aldehyde dehydrogenase activity, whether or not the subjects had taken chlorpropamide (figure), the change in cheek temperature rise correlating inversely with the change in erythrocyte aldehyde dehydrogenase activity (Kendall's $\tau = -0{\cdot}8$, one-tailed $p < 0{\cdot}05$). In the one woman cheek temperature rise was the same in both tests. Erythrocyte aldehyde dehydrogenase activity did not differ significantly in those with or without symptoms or those with or without visible flushing. Plasma chlorpropamide concentrations after the single dose of 500 mg ranged from 10 to 66 μg/ml, median 50 μg/ml, and did not correlate with erythrocyte aldehyde dehydrogenase activity. These chlorpropamide concentrations are below those seen in many patients on long-term chlorpropamide treatment; results from a group of such patients will be available shortly.



Erythrocyte aldehyde dehydrogenase and cheek temperature rise with ethanol in six non-diabetics after placebo or a single 500 mg dose of chlorpropamide.

The results from this small group of non-diabetic subjects suggest that erythrocyte aldehyde dehydrogenase activity influences cheek temperature rise after ethanol in men but provide no evidence to implicate the enzyme in the chlorpropamide component of chlorpropamide-alcohol flushing.

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