

level of disturbance. A partial correlation, however, holding age constant, increased the correlation between lead level and the behaviour rating from 0.029 to only 0.031 (still well below a statistically significant level).

The level of disturbance shown in this sample was high but not "astoundingly" so to anyone acquainted with comparable surveys carried out in London. Indeed, the incidence of disturbance among the children in our sample with blood-lead levels of 40 μ g. and above was strikingly similar to that found in another London borough—18.6% compared with 19.1%.⁷ The fact that the children in our sample with blood-lead levels below 40 μ g. were more disturbed than the others did not make us think that a high lead level is associated with normal behaviour; it did indicate that factors other than lead ingestion should be considered. We did not imply that there was a difference in social class between the families who had recently moved into the area and those who had been living there since their children were very young; we noted the differences in behaviour and intelligence and reported anecdotal evidence that there were differences other than those crudely measured by the Registrar-General's classification. We agree though that a further analysis of family factors would have been desirable.

We see no reason to reconsider our main conclusion at this stage. In our view it is just not possible to incriminate lead as a cause for the clinical manifestations described in the lengthy quotation cited by Bryce-Smith and Waldron in the absence of clear evidence of lead encephalopathy. Confident assertions to the contrary can only be sustained if the evidence supporting them is based on studies which are methodologically sound. The reasons for regarding social factors (both extra-familial and intra-familial) as important in the causation of behaviour disorders in city children do not, of course, lie merely in our own anecdotal evidence, but in a number of other excellent studies beyond the scope of the present discussion.

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CONGENITAL HEART DEFECTS AND PRENATAL SEX HORMONES

SIR,—Two retrospective case-control studies have suggested an association between prenatal use of sex hormones and subsequent congenital heart-disease, especially transposition of the great vessels (T.G.V.).^{8,9}

We examined this possible association by identifying 88 patients with T.G.V. who were less than 5 years old when first seen in the Children's Cardiac Center, Johns Hopkins Hospital, from January, 1968, to April, 1973. In obtaining the cases from a computer index of all patients, we included embryological variations of conal defects, such as single ventricle and corrected transposition. Demographic data were abstracted as well as information on the history and outcome of pregnancy, including birth defects. In taking the medical history, various clinicians had used a standard questionnaire that included specific questions on hormones and other drugs, but the responses were not independently verified. As controls, charts of patients with only ventricular septal defects (V.S.D.) and with normal hearts (usually functional murmurs) were chosen and matched for sex and race, and as closely as possible for year and age at first visit.

The 3 groups of patients each had 58 males (50 White, 8 Black) and 30 females (22 White, 8 Black). Of the patients

with conotruncal defects (63 T.G.V., 19 single ventricle, and 6 corrected transposition), 4 cases, all with T.G.V., had prenatal exposure to sex hormones during the first trimester (2 for maintenance of pregnancy, 1 for inadvertent birth control, and 1 for fertility). 2 of the 4 also had congenital idiopathic microcephaly and mental deficiency, but shared no other dysmorphic features.

Among controls, 3 with V.S.D. and 3 with normal hearts were exposed to prenatal sex hormone during the first trimester. In addition, in 2 with V.S.D., time of exposure was not specified and, in 1 normal control, was in the last 2 trimesters only. 1 of the V.S.D. patients had microcephaly, another had pectus excavatum; no birth defects were recorded among the normal controls. Hormones were given to the controls (a) to maintain pregnancy (5 cases); (b) as birth control (1 case); and (c) for unclear reasons (3 cases).

These results, obtained retrospectively, fail to support the suggested association between transposition complexes and prenatal exposure to sex hormone. Rather, they point to the need for further studies of different design.

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METABOLIC AND HORMONAL RESPONSE TO ACUTE MYOCARDIAL INFARCTION

SIR,—Dr Vetter and others (Feb. 23, p. 284) have made it difficult to evaluate the full significance of their findings on the initial metabolic and hormonal changes after acute myocardial infarction by the lack of matched controls. The rituals of admission to a hospital have been shown to significantly increase urinary 17-hydroxycorticosteroids in healthy adults.¹ To state that individuals after admission to a modern coronary-care unit for suspected myocardial infarction have elevated plasma-cortisol, catecholamines, sugar, and free fatty acids might be saying little more than that the patients are undergoing severe psychological stress. Before any statements can be made from this study regarding the systemic response to acute myocardial infarction, might it not be helpful to study control levels from patients who underwent a similar ordeal, but did not have a detectable infarct?

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* * We showed this letter to Dr Vetter and his colleagues, whose reply follows.—ED. L.

SIR,—Your correspondent makes a legitimate point of which we are, of course, aware. But who shall be the controls? One has to identify a group of individuals, apparently well and going about their usual work, who are suddenly and unexpectedly confronted with a crisis associated with severe pain and are then admitted to an intensive-care unit *within an hour*. Probably the only comparable groups are patients with burns or trauma, and in both situations^{2,3} the metabolic responses are comparable to those described by us in patients with myocardial infarction. Patients with acute myocardial ischaemia will not do as controls, since their initial metabolic response is likely to be similar to those with myocardial infarction.

1. Mason, J. W., Sachar, E. J., Fishman, J. R., Hamburg, D. A., Handlon, J. H. *Archs gen. Psychiat.* 1965, **13**, 1.
2. Birke, G., Carlson, L. A., Liljedahl, S.-O. *Acta med. scand.* 1965, **178**, 337.
3. Johnston, I. D. A. *Adv. clin. Chem.* 1972, **15**, 255.

7. Rutter, M. L. *Proc. R. Soc. Med.* 1973, **66**, 1221.

8. Levy, E. P., Cohen, A., Fraser, F. C. *Lancet*, 1973, **i**, 611.

9. Nora, J. J., Nora, A. H. *ibid.* p. 941.

Certainly, the changes which we have recorded in plasma substrate and hormone concentrations could be due to "severe psychological stress", but to determine whether they were initiated by the heart-attack itself or by the psychological reaction to it or by the psychological reaction to intensive care would be very difficult. A similar study in the earliest hours of home care might resolve the last possibility. It is our experience that anxiety occurring in a coronary-care unit is not related to the severity of the physical reaction to the attack,⁴ and yet in our study many of the changes were. Therefore it seems unlikely that psychological factors played a major part in altering the plasma concentration of substrates and hormones. As a point of further information, we have examined 15 patients with myocardial infarction within 30 minutes of admission to the coronary-care unit and have measured plasma-total-catecholamine concentrations, anxiety using the Neuroticism Scale Questionnaire,⁵ and clinical severity measured by prognostic indices and serum-enzyme changes. There was a close correlation between plasma-total-catecholamines and severity ($r=0.78$, $P<0.001$), but no correlation between anxiety and either plasma-catecholamine concentrations or severity.

Finally, Dr Pallor misses the purpose of our report, which is to define and delineate the earliest changes in the plasma concentrations of substrates and hormones so that the response of the myocardium to ischaemia is better understood and metabolic, therapeutic, or preventive intervention can be rationalised.

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mortality of patients with myocardial infarction, seen within three hours of the onset of symptoms, is due entirely to the "medical" intervention of the mobile unit.

It is extremely unlikely that the whole of this 9% difference in mortality derives from initiating therapy at the beginning of the ambulance journey rather than at the end. Would not some difference in mortality still have been apparent even if medical therapy was deferred until hospital was reached? Let us also not forget the contribution of the coronary-care unit to reducing mortality amongst those patients who would have reached hospital before three hours without the help of the mobile unit.

Furthermore, Dr Webb fails to mention that the Brighton service would also have got a large number of myocardial-infarct patients to hospital, and thereby specialised care, within three hours. A reasonable estimate of this number would be 300 cases annually (50% of the myocardial-infarction cases seen), which, using his argument, would mean that the Brighton service could also claim to have prevented a further 27 deaths, giving a rate of 8.25 "lives saved" per 100,000 population served—a figure very similar to the Belfast estimate of 8.6.

On present evidence, therefore, it seems that, so far as the contribution of the mobile units is concerned, a Belfast domicile is no more advantageous than a Brighton one in reducing mortality from myocardial infarction, and that any disadvantage that might arise from not having a doctor on the ambulance is balanced by the gaining of hospital admission some 86 minutes earlier by using the 999 system.

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FOOD ANTIBODIES AND MYOCARDIAL INFARCTION

SIR,—As babies, most of us had antibodies to milk which could well return rapidly after the passage of traces of milk protein through the lungs or across an inflamed oesophagus. This might happen in patients who have vomited a lot; who have lain long on their backs or been fed in that position; or who have suffered oesophageal reflux while shocked, sedated, or supine. Thus milk antibodies are perhaps more likely to appear after a severe than after a mild cardiac infarction. Could this be a factor in their association with death, which Dr Davies and his colleagues report (May 25, p. 1012), irrespective of any response of the body to their formation? It would be interesting to know which of their controls drink heavily, have hiatus hernias, or sleep on their backs.

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MOBILE CORONARY CARE

SIR,—In reply to Dr Webb's interesting letter (March 30, p. 559), may I make the following comments? Whilst it is certainly true that the correction of ventricular fibrillation is not the sole benefit of mobile coronary-care units, it is the only available direct evidence of life-saving peculiar to these units, and is therefore the most appropriate index by which to compare them.

Secondly, Dr Webb's estimate that the medically staffed unit saved six times the number of lives that the Brighton Ambulance Service did is almost certainly a gross exaggeration, for he appears to assume that the 9% lower hospital

NOMENCLATURE AND ABBREVIATIONS FOR VITAMIN D METABOLITES

SIR,—The most notable advance in our understanding of the mechanism of action of the fat-soluble vitamin D has been the elucidation of the complex structural modifications of the parent seco-steroid which are associated with the metabolism to its biologically active form.¹ To date, at least seven different hydroxylated modifications of cholecalciferol (D_3) [25-OH-D_3 ; $1,25\text{-(OH)}_2\text{-D}_3$; $1,24,25\text{-(OH)}_3\text{-D}_3$; $24,25\text{-(OH)}_2\text{-D}_3$; $25,26\text{-(OH)}_2\text{-D}_3$] and ergocalciferol (D_2) [25-OH-D_2 ; $1,25\text{-(OH)}_2\text{-D}_2$] have been chemically characterised. More recently, efforts have been directed at synthesis of clinically useful analogues, such as 1-OH-D_3 .^{2,3} Unfortunately, there is no agreement among workers (who include chemists, biochemists, and clinicians) as to what are acceptable and unambiguous abbreviations for these compounds. Thus, in recent publications 25-hydroxycholecalciferol has been abbreviated as 25-H.C.C.,⁴ 25-H.C.C.,⁵ 25-OH-D_3 ,⁵ 25-OH-CC ,¹ while 1,25-dihydroxycholecalciferol has been abbreviated as 1,25-DHCC,⁶ 1,25-D.H.C.C.,⁴ 1,25-diOH-CC, 1,25-(OH)₂-CC,¹ or 1,25-(OH)₂-D₃.¹ In my opinion, there is no basis in the rules of chemical nomenclature for abbreviating a hydroxyl with an H or indicating the number of hydroxyls with capital letters, such as a D for di, T for tri (or tetra?), and so on. Also, no obvious benefit accrues to the reader by insertion of the plethora of periods as in 1,25-D.H.C.C. Many of these notations undoubtedly were originally laboratory jargon. But in view of the increasing number of these calciferol metabolites and analogues, it is now appropriate to propose

4. Cay, E. L., Vetter, N., Philip, A. E., Dugard, P. *J. psychosom. Res.* 1972, **16**, 437.

5. Keer-Calwell, J. J. *Br. J. soc. clin. Psych.* 1965, **4**, 214.

1. Norman, A. W., Henry, H. *Clin. Orthopæd. rel. Res.* 1974, **98**, 258.
2. Barton, D. H. R., Hesse, R. H., Pecket, M., Rizzardo, E. *J. Am. chem. Soc.* 1973, **95**, 2748.
3. Okamura, W. H., Mitra, M. N., Norman, A. W., Pirió, R., Sine, S. M., Wing, R. M. *Fedn Proc.* 1974, **33**, 1574.
4. Kodicek, E. *Lancet*, March 2, 1974, p. 329.
5. Haddad, J. G., Hahn, T. J. *Nature*, 1973, **244**, 515.
6. Frolik, C. A., DeLuca, H. F. *Archs Biochem. Biophys.* 1971, **147**, 143.