Correspondence

Archives of Disease in Childhood, 1976, **51**, 242.

Schilder's disease: cholesterol metabolism in cultured fibroblasts

Sir,

Among the heterogeneous group of cerebral demyelinating disorders there is a specific form of Schilder's disease with adrenal insufficiency and an X-linked mode of inheritance (Hoefnagel *et al.*, 1967; Forsyth, Forbes, and Cumings, 1971). It has been reported (Burton and Nadler, 1974) that abnormalities in cholesterol metabolism previously noted in brains of patients with Schilder's disease (Forsyth *et al.*, 1971; Eto and Suzuki, 1971) may also be shown in cultured fibroblasts. Thus, after 10-12 days' exposure to labelled cholesterol, cultured fibroblasts from 3 male patients with Schilder's disease and varying degrees of adrenocortical insufficiency or unresponsiveness to ACTH accumulated more cholesterol than did normal cells. Moreover, after a 24-hour exposure to labelled cholesterol, Schilder's disease fibroblasts retained significantly more of the label than did the control fibroblasts.

On the basis of these results the authors speculated that Schilder's disease related to a generalized defect in cholesterol metabolism or transport. The possibility was also raised that in families at risk it might be possible to detect the abnormality in cultured fibroblast-like amniotic fluid cells and thus establish the diagnosis prenatally. The results of our studies on cultured fibroblasts from a patient with familial Schilder's and Addison's disease, however, do not support the above observations.

The patient is the survivor of 2 affected brothers, the elder having died at 9 years of age. Neurological features included cortical blindness, dementia, ataxia pyramidal signs, and seizures, and there was laboratory evidence of adrenocortical insufficiency.

Skin fibroblasts from the patient and 3 control subjects were cultured in HEPES-buffered Dulbecco's modified Eagle's minimum essential medium containing 15% heat-inactivated fetal calf serum. All cells had undergone 6-15 passages in culture at the time of our study.

Studies of the uptake and disappearance of radioactivity were carried out as described (Burton and Nadler, 1974) with the exception that radioactive media were prepared by adding the 4- (^{14}C)-cholesterol as

a solution in ethanol (final ethanol concentration 0.1% v/v). Initial activities of the media used in disappearance and uptake studies were 3.2×10^4 and 2.6×10^4 dpm/ml, respectively.

The uptake of labelled cholesterol after 24 hours (day 1) and the rate of loss of radioactivity over the next 5 days were similar for the patient and 3 controls (Fig). Moreover, in a separate experiment we observed

FIG.—Disappearance of (4- ^{14}C) cholesterol in fibroblasts from a patient with Schilder's disease (— — —), and 3 control subjects (—).

similar uptake of ^{14}C -cholesterol in Schilder's disease and control cells when cultured in labelled medium for 13 days.

The difference between our results and those of Burton and Nadler (1974) are unexplained. Clearly more studies are required.

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Intramuscular versus oral phenytoin

Sir,

The use of intramuscular phenytoin was recommended for seizures in the review article on bacterial meningitis by Hambleton and Davies (*Archives*, 1975, **50**, 675).

Prior reports comparing oral versus intramuscular administration have shown conflicting results. Recent evidence (Serrano and Wilder, 1974; Serrano *et al.*, 1973) has shown that a portion of injected phenytoin is released immediately and the remainder is released over a prolonged period; the half-life is prolonged and drug levels are low. In addition, experimental studies (Wilensky and Lowden, 1973) have shown crystallization of diphenylhydantoin and haemorrhage in the injection site. Serrano and Wilder (1974) showed this to be a variable finding but with chromatographic analysis phenytoin was retained at the injection site at 24 hours.

In seriously ill or unconscious patients in whom adequate levels are required, phenytoin must be given *intravenously* with its recommended caution. There appears to be little place for the use of intramuscular

phenytoin because of variable blood levels and potentially harmful effects on muscle. Should it be necessary, the duration of intramuscular injections should be short and blood levels should be monitored to achieve the desired therapeutic range.

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We showed the letter from Dr. D'Souza to Dr. Davies and Dr. Hambleton, who replied as follows:

We are grateful to Dr. D'Souza for drawing our attention to the fact that release of a portion of intramuscularly injected phenytoin may occur gradually over a prolonged period. This makes it, as he says, an unsuitable drug for the immediate treatment of fits. However, we suggested either intravenous diazepam or intramuscular paraldehyde for this, to be followed by short-term anticonvulsant therapy such as phenobarbitone or phenytoin. If oral treatment is not possible, as is so often the case in the very sick infant or child, then intramuscular phenobarbitone would be the drug of choice after the initial treatment.

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Blood urea levels in artificially-fed infants

Sir,

Dale *et al.* (1975) report high levels of blood urea in artificially-fed infants, confirming the results of a previous study by Davies and Saunders (1973). This finding was a surprise to us, for it is in disagreement with our daily experience in hospitalized infants fed on artificial milk, and prompted us to check plasma urea, sodium, and protein in 22 consecutive infants (14 male, 8 female) aged between 14 days and 3 months. All were convalescent from benign, nondigestive, disorders, and were fed on powdered half-skimmed cow's milk formulae prepared at the usual 15% concentration, either alone (15 infants), or with additional cereals and infant food (7 infants).