Correspondence

Archives of Disease in Childhood, 1973, 48, 984.

Wilms's tumour—a correction and an apology

Sir,

My faith in the flawlessness of British medical writing has been shattered by the repeated misspellings of Professor Wilms's name in the paper by Evans and Holzel (*Archives* 1973, 48, 645).

Not only was poor old Professor Wilms's name misspelt throughout the body of the paper, but even more disrespectful to his memory was the diligent effort on the part of someone to change the correct spelling of Wilms's surname to the incorrect one in all the references cited in which Wilms's name is given.

Please restore my faith in medical editing on your side of the Atlantic.

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Dr. Cone is of course correct, and we apologize abjectly. We will try to do better in future, and to restore Dr. Cone's faith. *Editors.*

Effect of fatty acids on bilirubin conjugation

Sir,

We were interested in the article by T. Hargreaves (*Archives*, 1973) concerning the interaction between fatty acids and bilirubin conjugation *in vitro*. In an earlier study (Levillain *et al.*, 1972) we showed similar results with unsaturated fatty acids but also some inhibition of conjugation with saturated fatty acids. The discrepancy between these results could be due not only to a different concentration in incubation milieu (we used approximately a concentration of 2 mmol/l. for each saturated fatty acid), but essentially to a different relative concentration of fatty acid, bilirubin, and albumin. This possibility was tested in a recent study (Luzeau *et al.*, 1973a).

We also found (Levillain *et al.*, 1972; Luzeau *et al.*, 1973a) a relation between the inhibitory effect of mother's milk samples on the glucuronyl transferase activity *in vitro* and their concentration of free fatty acids. Milk samples from mothers whose infants had a prolonged neonatal jaundice inhibited the enzyme

activity and contained more free fatty acids than control samples. This difference cannot be detected in fresh milk samples but becomes obvious after storage, depending on duration and temperature conditions. An important liberation of fatty acids only takes place in pathological milks when they are kept at +4 °C or +20 °C while their *in vitro* inhibitory effect increases. Such liberation does not take place when the milk samples are preheated at +56 °C for 15 min immediately after the collection. The results obtained suggest the existence of an abnormal lipolytic activity in the milk of mothers whose infants have a prolonged jaundice. Lipoprotein lipase seems to be the enzyme responsible for the activity. These experimental data allowed us to feed 3 icteric infants with maternal milk after heating at 56 °C for 15 min: 3 or 4 days later the jaundice had disappeared. A simplified method for detection of these inhibitory milk samples has been recently described using Nile blue reaction (Luzeau *et al.*, 1973b).

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REFERENCES

- Hargreaves, T. (1973). Effect of fatty acids on bilirubin conjugation. *Archives of Disease in Childhood*, 48, 446.
Levillain, P., Odièvre, M., Luzeau, R., and Lemonnier, A. (1972). Possibilités d'inhibition de la glucuroconjugaison de la bilirubine en fonction de la teneur en acides gras libres du lait maternel. *Biochimica et Biophysica Acta*, 264, 538.
Luzeau, R., Levillain, P., Odièvre, M., and Lemonnier, A. (1973a). Demonstration of a lipolytic activity in human milks that inhibit the glucuroconjugation of bilirubin. *Biomedicine*. (In the press.)
Luzeau, R., Levillain, P., Odièvre, M., and Lemonnier, A. (1973b). Dépistage des laits maternels inhibiteurs de la glucuroconjugaison de la bilirubine par une réaction colorée. *Archives Françaises de Pédiatrie*, 30. (In the press.)

Dr. Hargreaves comments as follows:

The letter from Professor Odièvre and his colleagues emphasizes yet again the difficulties in elucidating the cause of breast milk jaundice (Arias *et al.*, 1964; Hargreaves and Piper, 1971). The observed differences between the effects of fatty acids are probably due to the concentrations used. I used a maximum concentration of 1 mmol/l. for the investigations of saturated fatty acids on bilirubin conjugation in rat liver slices (*Archives*, 1973, 48, 446) whereas Levillain *et al.* (1972) and Bevan and Holton (1972) used higher concentrations. In rat liver microsomes I found no inhibition of bilirubin conjugation by saturated fatty acids even at high concentrations. Bevan and Holton (1972) compared the effect of inhibitory breast milk and oleic acid on the bilirubin content of rat liver slices. They showed that the effect was similar except that high concentrations of

oleic acid increased the unconjugated bilirubin in the liver slices.

I cannot agree that it is only breast milks from mothers of children with breast milk jaundice which develop increased inhibition to bilirubin conjugation on storage. The original observation (Hargreaves, 1970) that this could occur in milk from mothers of nonjaundiced children has been confirmed (Bevan and Holton, 1972). These authors also showed that the increased activity was associated with an increase in the free fatty acid content of the milk. The observation was thought to have practical implications in that deep-frozen milk is used for feeding premature infants, but it was shown that the inhibitory activity does not develop in sterilized milk (Hargreaves, 1970).

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REFERENCES

- Arias, I. M., Gartner, L. M., Seifter, S., and Furman, M. (1964). Prolonged neonatal unconjugated hyperbilirubinemia associated with breast feeding and a steroid pregnane-3 α ,20 β -diol in maternal milk that inhibits glucuronide formation *in vitro*. *Journal of Clinical Investigation*, **43**, 2037.
- Bevan, B. R., and Holton, J. B. (1972). Inhibition of bilirubin conjugation in rat liver slices by free fatty acids, with relevance to the problem of breast milk jaundice. *Clinica Chimica Acta*, **41**, 101.
- Hargreaves, T. (1970). Breast-milk jaundice. *British Medical Journal*, **3**, 647.
- Hargreaves, T., and Piper, R. F. (1971). Breast milk jaundice. Effect of inhibitory breast milk and 3 α ,20 β -pregnanediol on glucuronyl transferase. *Archives of Disease in Childhood*, **46**, 195.
- Levillain, P., Odièvre, M., Luzeau, R., and Lemonnier, A. (1972). Possibilités d'inhibition de la glucuroconjugaison de la bilirubine en fonction de la teneur en acides gras libres du lait maternel. *Biochimica et Biophysica Acta*, **264**, 538.

Urinary diversion in children

Sir,

It is now 20 years since I performed my first operation for urinary deviation in a child. As the years passed I became less enthusiastic about the operation and, generally speaking, I prefer a colonic conduit to an ileal conduit. I can now present to Dr. S. R. Meadow (*Archives*, 1973, **48**, 657) a series of girls aged 8 to 12 years with normal upper urinary tracts whose neuro-pathic bladders have been emptied by manual expression. Cine-radiography has shown that reflux has not resulted from this manoeuvre.

With the enthusiastic co-operation of the parents, I propose to continue treatment of many of my patients in this way until Professor John Lenihan (Medical Physics and Bio-Engineering, University of Glasgow) can provide my patients with a suitable bladder pace-maker.

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Arteriohepatic dysplasia

Sir,

We were interested by the article recently published by G. H. Watson and V. Miller (*Archives*, 1973), as since 1956 we have observed almost similar facts. We studied our patients essentially for their chronic cholestasis. Among 30 children with hepatic ductular hypoplasia, 15 comprised a distinct, homogeneous, readily recognizable group (Alagille, Habib, and Thomassin, 1969; Alagille and Thomassin, 1970). This new syndrome is more complex than proposed under the 'arteriohepatic dysplasia' label.

The association of chronic cholestasis related to hepatic ductular hypoplasia (15/15), characteristic facies (15/15), and pulmonary arterial stenosis (11/15) is almost always present in this group. But other abnormalities are almost as frequent: vertebral arch defects (8/15), growth retardation (8/15), mental retardation (9/12), hypogonadism in males (6/7) with spermatogenic hypoplasia in the 5 testicular biopsies performed.

Watson and Miller probably emphasized the pulmonary arterial stenosis because they are interested in the field of heart diseases. However, we disagree with this point, as 2 of our 15 patients had no heart abnormality, and 2 others had a different abnormality. We also disagree with their suggestion about genetic transmission: in our group there was a family history *in sibs* for 5 of the 15 patients, *but never in parents* (Alagille *et al.*, 1968). This is why we suggest, as they do, the possibility of a genetic disorder which could either have autosomal recessive transmission or be due to chromosome abnormality. This last possibility is suggested by associated multiple congenital malformations. However, chromosomal and dermatoglyphic studies in our patients have yielded normal results. Nevertheless, infections or toxic agents transmitted *in utero* from the mother to one or more offspring may also produce the teratogenic effects observed.

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REFERENCES

- Alagille, D., Borde, J., Habib, E., Joannides, Z., Thomassin, N., and Kremp, L. (1968). Ictères cholestatiques familiaux de l'enfant. *Revue Internationale d'Hépatologie*, **18**, 701.
- Alagille, D., Habib, E. C., and Thomassin, N. (1969). L'atrésie des voies biliaires intra-hépatiques avec voies biliaires extra-hépatiques perméables chez l'enfant. In *Journées Parisiennes de Pédiatrie*, p. 301. Editions Médicales Flammarion, Paris.
- Alagille, D., and Thomassin, N. (1970). L'atrésie des voies biliaires intra-hépatiques avec voies biliaires extra-hépatiques perméables chez l'enfant. *Revue Médico-Chirurgicale des Maladies du Foie, du Pancréas et de la Rate*, **45**, 93.
- Watson, G. H., and Miller, V. (1973). Arteriohepatic dysplasia: familial pulmonary arterial stenosis with neonatal liver disease. *Archives of Disease in Childhood*, **48**, 459.

Dr. Watson replies as follows:

We are glad to comment on the letter from Professor Alagille, which clearly relates to the same syndrome as