Permanent Discoloration of Primary Dentition by Nitrofurantoin

We record the case history of an infant whose erupting teeth have been stained a permanent bright yellow by orally administered nitrofurantoin. This undesirable effect of the drug does not seem to have been reported before. Our findings suggest that there is a risk of permanent staining whenever nitrofurantoin is allowed repeatedly to contact erupting teeth.

CASE HISTORY

A male infant aged 16 days was admitted to the Royal Hospital for Sick Children, Edinburgh, on March 29, 1960, because of increasing pallor. The haemoglobin was only 4.8 g./100 ml., and tests on mother and child proved the diagnosis of haemolytic disease due to rhesus incompatibility. The infant had shown only slight jaundice between the third and sixth days of life. Blood transfusions were given on March 29 and April 20, but at 3 months of age the infant was readmitted because of anaemia (Hb 8.3 g./100 ml.), pyrexia, and increasing enlargement of liver and spleen. No infection could be found, but a fine nodular rash and enlarged peripheral lymph nodes developed. Polymorphonuclear leucocytosis, thrombocytopenia, and purpura were present. Various antibiotics (including tetracycline for 14 days) were without effect. A skin biopsy (August 1) showed "infiltration of the same type as in Letterer-Siwe disease" (Dr. A. R. Macgregor).

There was a dramatic response to prednisolone (10 mg. b.d.) started at the age of 5 months and continued in smaller dosage until the age of 17 months. However, the early phase of recovery was marred by two urinary infections. On both occasions enterococci, sensitive only to chloramphenicol and nitrofurantoin, were cultured from the urine. The first infection responded to chloramphenicol, but when relapse occurred nitrofurantoin was begun on October 24 in a dose of 12.5 mg. six-hourly (8 mg./kg./day) orally as crushed tablets. The urinary infection was controlled within seven days, but it was then thought wise to continue the nitrofurantoin prophylactically in a dose of 12.5 mg. b.d. in view of the previous relapse and the special need to keep this infant free of infection. The total period of administration was 68 days between the seventh and ninth months of life.

At the age of 1 year the baby no longer showed any clinical or haematological abnormality. However, when seen at the age of 14½ months it was noticed that his four upper incisor teeth and the two lower central incisors were a bright yellow. The two most recently erupted teeth, the lower lateral incisors, were white.

Dental examination at the age of 20 months showed: Teeth present erupted were $\frac{DCBA}{DCBA}/\frac{ABCD}{ABCD}$. The $\frac{BA}{A}/\frac{AB}{A}$ were discoloured bright yellow. There was some yellow staining in the cervical region of $\frac{C/C}{CB/BC}$. The $\frac{C/C}{C/C}$ showed a 1-mm. horizontal band of more translucent enamel at approximately one-third crown height. No roughness or breach of surface enamel was detectable to a probe. There were no signs of attrition. The $\frac{A/A}{A/A}$ had begun to erupt at 7 months, the time of readmission to hospital, and were then apparently normal in appearance. No further eruption details were remembered.

The crowns of $\frac{BA}{A}/\frac{AB}{A}$ were opaque and evenly pigmented on all visible surfaces. This pigmentation was deep and resisted scaling with sharp instruments.

The enamel of the $\frac{C/C}{CB/BC}$ was more translucent, and yellow only in the cervical third. This pigmentation was removed by scaling, leaving an intact colourless enamel surface.

Differential Diagnosis.—Rare causes of intrinsic pigmentation of deciduous teeth are amylogenesis and dentinogenesis imperfecta. These conditions were excluded here by the bright-yellow pigmentation, the absence of wear of the teeth, and the fact that only part of the dentition was affected. Pigmentation caused by jaundice at birth was excluded by the following observations: (1) the colour was distributed throughout the crown, and was not confined to a band in the neonatal area; (2) the neonatal jaundice had been very mild; and (3) the dental discoloration was bright yellow and not green. Tetracycline could be excluded as the colouring agent because the affected incisor crowns were formed before the administration of tetracycline, which is incorporated specifically in the developing hard tissues of the teeth. It at once seemed likely that nitrofurantoin was to blame. The incisors had started to erupt soon after the drug was commenced orally, and only those teeth which had erupted during the period of its administration were discoloured yellow.

As an experiment carious deciduous teeth that had been erupted for several years were immersed on extraction in a proprietary paediatric suspension of nitrofurantoin. The pigment was taken up by the cementum and by early carious lesions in the enamel, but not by the intact enamel. However, the composition of newly erupted enamel changes by absorption from its environment, its mineral content progressively increasing (Sognnaes and Shaw, 1952; Sognnaes *et al.*, 1955). It was during this post-eruptive period of ionic absorption that nitrofurantoin had been given.

COMMENT

In paediatric practice nitrofurantoin has a limited but useful application in the treatment of urinary-tract infection by organisms resistant to other drugs. In lower dosage it is sometimes used prophylactically in children prone to recurrent urinary infections because of congenital abnormalities of the renal tract. Thus, Marshall and Johnson (1959) reported favourably on its prophylactic use in 100 children for periods ranging from 6 to 27 months, in doses ranging from 1 to 5 mg./kg./day. The only side-effects encountered were variable degrees of gastro-intestinal intolerance, occasional temporary rashes, drowsiness in one patient, and patchy alopecia in two.

No previous reports have been found of dental staining caused by nitrofurantoin. Here, repeated contact between the drug and the deciduous incisors during the eruptive and post-eruptive periods of absorption has resulted in their permanent discoloration. The rather prolonged administration of the drug no doubt accounts for the severity of the dental staining, but it is possible that much shorter periods of administration of the crushed tablets or the suspension to teething infants might result in appreciable permanent discoloration. For this reason it seems advisable not to administer nitrofurantoin orally to infants during the period of eruption of their front teeth. When the second dentition is erupting, tablets might be preferable to a paediatric suspension which would contact the teeth.

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