children had some genetic factor which modifies the intrauterine environment and thus predisposes the embryo to these malformations. Such a hypothesis opens up interesting possibilities, but before accepting it one would have to be satisfied that the higher incidence in maternal relatives is not merely due to the fact that the history is obtained in most cases from the mother.

Renal Excretion of Urobilinogen

Estimation of the urobilinogen in the urine either by the Schlesinger test or by the Ehrlich aldehyde reaction is helpful in reaching a diagnosis. The results are interpreted on the concept that there is an entero-hepatic circulation for urobilinogen (actually three closely related compounds), which is formed by reduction of conjugated bilirubin by bacteria in the large bowel.[1] The recent studies of R. Lester, W. Schumer, and R. Schmid[2] have established that in man a small proportion of the urobilinogens formed undergoes reabsorption in the terminal ileum and colon and is then re-excreted in the bile; the exact form in which it appears in the bile has not, however, been elucidated.

In health only minimal amounts of urobilinogen are present in the urine, but in cases of liver disease or partial biliary obstruction an increased amount of the reabsorbed urobilinogen may be diverted to the kidneys. Lester and colleagues postulated that in liver disease urobilinogen may also be reabsorbed from the small bowel, owing to invasion of it by bacteria from the colon. In haemolytic disease excessive catabolism of haem causes an increased production of bilirubin and thus in the amount of urobilinogen available for reabsorption and excretion in the urine; in this condition there may be some liver dysfunction which limits the excretion of urobilinogen in the bile, but this has still to be established.

The investigations of Dr. E. Bourke, Professor M. D. Milne, and Dr. G. S. Stokes, published at page 1510 of the *B.M.J.* this week, draw our attention to a new aspect of the factors controlling the urinary excretion of urobilinogen. They show that, even in the healthy person, making the urine alkaline greatly increases the renal excretion of urobilinogen, while acidification diminishes it. The diurnal variation in urinary urobilinogen that has been noted may therefore be related to changes in urinary *p*H as well as to the concentration of urobilinogen in the plasma. The authors' recommendations that analysis of urobilinogen in urine should be performed on specimens collected between noon and 4 p.m. and that a correction for urinary *p*H should be made are therefore worth following if these determinations are to be used to assess haemolytic states or hepatic dysfunction.

Our understanding of the mechanism of the excretion of urobilinogen is still limited by a lack of adequate techniques for estimating this substance, whose level in the blood is only about 5.3 μg. per 100 ml. The chromogen is more than 80% bound to plasma proteins, and it appears that the unbound pigment undergoes glomerular filtration. Tubular secretion may also occur,[3] though further studies are needed to prove this point. Another mechanism, which is dependent on *p*H, seems to involve the distal part of the renal tubules.

[1] Watson, C. J., *J. clin. Path.*, 1963, **16**, 1.
[2] Lester, R., Schumer, W., and Schmid, R., *New Engl. J. Med.*, 1965, **272**, 939.
[3] Milne, M. D., Schribner, B. H., and Crawford, M. A., *Amer. J. Med.*, 1959, **24**, 709.

Skin Disease from Photographic Colour Developers

Since 1958, when two independent papers appeared from France[1] and the United States,[2] there have been several reports of a lichenoid eruption in persons coming in contact with developers of colour films. This eruption is in many ways similar to lichen planus, and even Wickham striae have been reported[3]—that is, characteristic greyish lines in a network on the surface of the papules. The lesions last for months and the residual pigment may last a year or more. The mucous membranes are reported as being spared. In addition to this subacute condition an acute eczematous eruption may also occur, and either type may progress into the other.[2 3]

Isolated cases have been shown at meetings in Great Britain (for example, by E. L. Rhodes[4]), and now Lionel Fry[5] reports a series of twenty cases seen at St. John's Hospital for Diseases of the Skin. The patients had come into contact with Kodak, Agfa, or Ilford colour developers. Unlike the earlier reports, the majority (namely, thirteen) of Fry's cases showed the eczematous pattern of the reaction, while the remainder were lichenoid. In all cases the rash was present on the hands and forearms, a distribution suggesting that direct contact with the developer was the cause of the eruption; in two patients the eruption was also present at other sites. The active chemical in the colour developers is a substituted *para*phenylenediamine. Patch tests with the type of colour developer used by the patient were positive in all but three of the patients; two of the patients with a negative patch test had a lichenoid eruption and the other an eczematous one. All the patch-test reactions were of an eczematous nature, but W. R. Buckley[2] reported that patch tests in his patients progressed to a typical lichenoid pattern.

Although the location of the eruption suggests that contact with the developer is the cause of either type it is not certain, and the possibility of absorption through the mouth or by inhalation cannot be ruled out. Lichenoid eruptions closely simulating lichen planus can be produced by many drugs taken internally, including arsenic, gold, and mepacrine. The question whether this type of eruption is in fact lichen planus has yet to be decided. Fry considers the histological changes in his cases were not truly those of lichen planus.

It is not surprising that eczematous eruptions occur in patients handling colour developer. The *para*-grouping is very frequently found in sensitizing agents. *Para*phenylenediamine itself is responsible for most cases of hair-dye dermatitis and may also be the cause of dermatitis from clothing. The *para*-grouping is found in some common local anaesthetics (procaine, amethocaine), sulphonamides, and some antihistamines, and all these medicaments are responsible for cases of dermatitis when applied topically. Moreover, cross-sensitization of one to the others is frequent. It is surprising, therefore, that in Fry's cases only one is reported as also being sensitive to 2% *para*phenylenediamine, though several were sensitive to more than one of the developers. The incidence of skin reactions in persons exposed to colour developer can be very high—Buckley[2] says 25% if no precautions are taken, but this figure can be

[1] Graciansky, P., Boulle, S., Quercy, P., and Cardot, J. L., *Bull. Soc. franç. Derm. Syph.*, 1958, **65**, 498.
[2] Buckley, W. R., *Arch. Derm.*, 1958, **78**, 454.
[3] Canizares, O., ibid., 1959, **80**, 119.
[4] Rhodes, E. L., *Brit. J. Derm.*, 1963, **75**, 258.
[5] Fry, L., ibid., 1965, **77**, 456.