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. Schmid2 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 pH 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 pH 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 pH, seems to involve the distal part of the renal tubules.


Skin Disease from Photographic Colour Developers

Since 1958, when two independent papers appeared from France1 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—thus 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.3

Isolated cases have been shown at meetings in Great Britain (for example, by E. L. Rhodes4), and now Lionel Fry5 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 paraphenylenediamine. 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. Buckley6 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. Paraphenylenediamine 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% paraphenylenediamine, 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 says 25% if no precautions are taken, but this figure can be

3 Canizares, G., ibid., 1959, 86, 119.
reduced to 1% with adequate precaution. With the increasing use of colour developers, especially among amateur photographers who may be unaware of the hazards, we can expect a steady rise in the number of persons developing either the eczematous or the lichenoid type of eruption, and it would be well to be on the look-out for them.

**Survival in Hodgkin’s Disease**

It is usually taught that a diagnosis of Hodgkin’s disease is tantamount to a sentence of death. Even if the disease is first confined to a group of lymph nodes it soon becomes generalized, and death usually occurs within five years. While the initial response to treatment is excellent, it is assumed that recurrence is inevitable and that the lesions ultimately become resistant both to radiotherapy and to cytotoxic agents.

This grim picture has been modified in recent years. In about 12% of cases the affected tissue shows a predominant infiltration with lymphocytes and there are fewer abnormal reticulum cells than in the classical lesion, though many Sternberg-Reed giant cells are present. This variant is called paragranuloma, § or benign Hodgkin’s disease, § and is associated with a ten-year survival rate of 85%.  

About a quarter of these patients develop the classical disease in the course of time. If paragranuloma is treated energetically with radiotherapy cure is possible; otherwise recurrences are likely to occur even after many years of quiescence.

But even in the remaining 88% of cases of classical Hodgkin’s disease the prognosis is extremely variable. The period of survival is related to the extent of the disease. In one series of cases 50% of patients were alive after five years when the lesions were confined to a single group of lymph nodes or to two adjacent groups. When the disease was generalized the five-year survival-rate was almost nil.  

in another series 58% of patients with localized disease survived for ten years without recurrence after effective radiotherapy. 

E. C. Easson and M. H. Russell found that 42–45% of treated patients with localized disease survived ten years without recurrence, but when the disease was generalized only 13% survived this length of time.  

They showed too that among patients with localized disease the rate of mortality declined with time, and the death rate among those who survived ten years was no greater up to the fifteenth year than in the general population. Their conclusion was that patients surviving this length of time without recurrence were probably cured. In a recent review of 42 cases of Hodgkin’s disease occurring in childhood F. Kelly has once again shown that with effective radiotherapy the outlook is not hopeless. 

Of 39 children with the classical disease ten are still alive, seven having survived over five years and three over ten years. The disease runs a somewhat slower course in children than in adults, and at all ages the prognosis is better in females than in males. Kelly believes that as long as the disease remains localized cure is possible after adequate radiotherapy.

While many observers will require a longer period of remission before conceding cure, there can be no doubt that the energetic treatment of localized Hodgkin’s disease is often extremely rewarding. The concept that all cases are multifocal in origin is seriously questioned by the excellent results of local irradiation. It is important to be aware that these patients may enjoy many years of complete relief, and that an attitude of fatalistic resignation is no longer necessary.

**Beneficent Influence**

The valuable work carried out at the London School of Hygiene and Tropical Medicine is once again the subject of its Annual Report.  

From this it appears that the number of students (696) was considerably higher than in the previous year (595), which the Dean, Dr. E. T. C. Spooner, attributes mainly to an increase in the number of courses being offered by the School. For the first time in several years students from the United Kingdom outnumbered those from overseas. There were 364 of them, an increase of 58% over the previous year. Nine lectureships established by the Ministry of Overseas Development have now all been filled, and six of the lecturers are working abroad—one in Nigeria, two in Kenya, one in Tanzania, one in Geneva, and one in Singapore.

Many individuals, associations, and industrial firms have given generous support to the School, but a specially notable gift this year is £1,000 from Lady Jameson in memory of her husband, the late Sir Wilson Jameson, who was dean of the School from 1931 to 1940. In this capacity and as professor of public health there he won the highest esteem for his influence on the education of students from all parts of the world and enjoyed the affection of all who met him. The donation is to finance five fellowships enabling past D.P.H. students to visit European countries and study their public health services. Like most academic institutions the School is short of money and accommodation. The housing of its students presents a special problem in that many of them are older than is usual in a university school. Consequently it has joined a company promoted by the London School of Economics with the aim of acquiring properties to let to students on a non-profit-making basis.

At a time when many overseas peoples are becoming sharply conscious of their national identity the School exerts a beneficent influence that reaches beyond textbook education. Members of all creeds and races join there, whether as teachers or as learners, in an endeavour to bring better health to mankind.

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