restore the cerebral tissue: it can only arrest the disease. Arrest as rapidly as is consistent with safety is the only first requirement. It seems that the syphilitic processes are inhibited by penicillin before malaria could even come into operation, although further experience is necessary to show whether that inhibition is complete enough in all kinds of cases.

It is fallacious to say that clinical recovery occurs more quickly or more completely after this or that method of treatment, provided only that the treatment is effective—i.e., that it eradicates the disease. After any sufficiently effective treatment the extent of clinical recovery depends on the amount of the cerebral tissue that is capable of recovery; and that is not a function of the treatment but of the viable cerebral tissue. Similarly, the period of clinical recovery is the time required for the recovery of such cerebral tissue as is capable of restored activity. The final results cannot vary between one effective method of treatment and another, provided the treatments themselves are innocuous and reasonably prompt in their actions; and if an effective treatment has once been given no greater or quicker improvement can possibly be obtained by a multiplication of therapies. The practical results that have been reported are in general agreement with this conclusion.

Secondly, to ensure its permanence. Here our only criterion is the serological reactions. After the disease is arrested these take time to become normal, and if the cerebrospinal fluid is of the "inactive" type after three or four months, and normal, apart from the colloidal gold reaction, within a year, we may be satisfied. Such results are obtainable with penicillin as with malaria, and there seems no reason why they should not be as permanent. Though serological relapses must be watched for, they are likely to be few.

Conclusions

As a result of my observations I draw the following conclusions—tentative because longer observation is necessary.

1. Penicillin alone is sufficient in most cases of neurosyphilis. Whether it is adequate for the most acute cases of G.P.I. the experience of this series does not show.

2. If, with the possible exception of such cases, the patient can be kept under observation after treatment and penicillin repeated if necessary, malaria will seldom be called for, and the risk of it will seldom be justified.

3. Even if penicillin does not render malaria unnecessary it is a potent weapon and will make us much less dependent on malaria; and, if malaria is used at all, risks which were necessary before need not now be taken.

BIBLIOGRAPHY

- Callaway, J. L., *et al.* (1946). *Amer. J. Syph.*, **30**, 110.
 Dattner, B. (1947). *Arch. Neurol. Psychiat.*, **57**, 270.
 — Thomas, E. W., and Wexler, G. (1944). *Management of Neurosyphilis*. New York.
 Gammon, G. D., Stokes, J. H., and others (1946). *Ann. intern. Med.*, **25**, 412.
 Lescher, F. G., and Richards, H. R. M. (1947). *British Medical Journal*, **2**, 565.
 Nicol, W. D. (1946). *Brit. J. vener. Dis.*, **22**, 112.
 — (1948). *Post-Grad. med. J.* (Jan.).
 — and Whelan, M. (1947). *Lancet*, **1**, 559.
 Rose, A. S., *et al.* (1946). *Arch. Neurol. Psychiat.*, **55**, 428.
 — and Solomon, H. C. (1947). *J. Amer. med. Ass.*, **133**, 5.
 Smith, R. H. F. (1947). *Lancet*, **1**, 665.
 Worster-Drought, C. (1947). *British Medical Journal*, **2**, 559.

Two settlements in Bethnal Green, Oxford House and University House, are sponsoring schemes for studying social conditions there at first hand. The student is brought into intimate contact with the inhabitants, helping with the shopping or serving behind the counter, and studying the history and geography of the locality. The next course will be held on July 1–28. The fee is 4 guineas, and board and keep at one of the settlements is £2 a week. Further information may be obtained from the Vice-head, Oxford House, Mape Street, Bethnal Green, E.2.

A CASE OF ACUTE PORPHYRIA

BY

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"Acute idiopathic porphyrinuria is clearly recognized in Germany and elsewhere on the Continent; it is being increasingly reported in America, but even to-day it is scarcely mentioned in British literature." The above comment, made in 1939 by Chandler *et al.*, appears as true to-day as it did eight years ago. It has been suggested by clinicians (Rau, personal communication, 1947) who are familiar with the condition that the relatively large number of cases reported in Scandinavia and Germany was primarily due to a more widespread knowledge of the chief features of this rare metabolic disorder. This interest was particularly stimulated by the clinical investigations of Günther (1911), who first described the disease, and by Hans Fischer's elucidation of the chemical nature of porphyrin pigments. The comprehensive reviews of Mason, Courville, and Ziskind (1933) and Dobriner and Rhoads (1940) have recently served to stimulate in America an increased interest in the chemical and clinical aspects of this malady. A brief survey disclosed that no fewer than 36 reports have appeared in the literature in America since 1940, whereas only three indigenous cases have been recorded in British medical journals during the same period. A fourth British case, the chemical aspects of which were fully investigated, was recorded by Prunty (1946) in an American journal.

In man clinical porphyria occurs in the form of two distinct syndromes—congenital porphyria (Garrod, 1923), and acute porphyria.

Congenital Porphyria

This is a very rare disease that develops during foetal life. It is usually recognized in early infancy, and persists in the adult as a permanent disorder of metabolism. Transmission is thought to occur by the inheritance of a gene possessing recessive characteristics (Mackey and Garrod, 1926). Salient features are the excretion of burgundy-coloured urine and a disabling degree of photosensitivity of skin and exposed mucous membranes. Brown pigmentation of bones and pink discoloration of deciduous and permanent teeth have occasionally been recorded (Mackey and Garrod, 1926). Exposure to bright sunlight leads to blistering of unprotected skin and the formation of ulcers, indolent healing of which results in permanent disfigurement by scar tissue. Corneal ulceration due to similar actinic trauma may lead to seriously impaired vision. Both splenomegaly and hepatomegaly have been recorded as transient features in childhood. In this condition excess of uroporphyrin I is excreted.

Acute Porphyria

The symptomatology of this disease, which affects adults, differs entirely from that of the congenital variety. Acute porphyria occurs more frequently in women than in men and the onset is most often during the third decade. It is probable that the symptoms of acute porphyria are merely acute manifestations of a latent chronic metabolic disorder whose asymptomatic phase can be detected only by special investigation of the excreta. The acute and dramatic manifestations of the classical syndrome appear either spontaneously or as a result of prolonged ingestion of certain drugs, of which sulphonal is most commonly incriminated. It thereafter may pursue a prolonged and relapsing course, which often ends fatally. Most recorded cases have been sporadic examples, but recently

an increasing number of reports have indicated that the disease may occur as a familial condition (Nesbitt, 1944). There are factors in the case history recorded below which strongly suggest a familial incidence. It is thought that the inheritance of this disorder is by transmission of a dominant gene (Gates, 1946) whose degree of penetrance is small. Hence this undesirable characteristic may be acquired from a parent who discloses no clinical or metabolic abnormality.

The symptoms of acute porphyria tend to be remarkably stereotyped. The initial attack may be preceded by a prodromal period during which weight is lost and asthenia is pronounced. During this phase various *mental disturbances*—most frequently depression, irritability, or suicidal tendencies—have been notable features. *Abdominal symptoms* follow. There is usually severe para-umbilical colic or lower abdominal cramp-like pain, often associated with nausea and vomiting. Obstinate constipation amounting to a paralytic ileus is constantly present. The abnormal colour of the urine is usually noticed only after the onset of these symptoms, but frequently the significance of this observation is masked by the presence of concomitant icterus. Occasionally patients will admit having excreted dark urine intermittently long before the onset of the illness. A raised blood pressure is a consistent feature at this stage. It is often as high as 180/120, and its discovery in a young adult presenting severe abdominal pain without other localizing features should lead to examination of the urine for porphyrins.

Recovery may occur without further progression of the disease, but relapses are usual, and eventually in about half the cases evidence of *involvement of the central nervous system* appears (Waldenström, 1937). Coma, psychosis, delirium, amaurosis, and epileptic attacks are frequently associated with the more characteristic progressive impairment of motor function. Isolated cranial-nerve palsies, localized weakness of peripheral muscle groups, and more generalized motor involvement develop. Although paraesthesia is usually a marked feature, cutaneous sensibility remains intact. The intensity of the muscular weakness may fluctuate unaccountably, and spread of the paresis to the respiratory muscles, through bulbar involvement, usually terminates the illness. Although photosensitivity and pigmentation of the skin have been recorded in acute porphyria (Nesbitt and Watkins, 1942) they are both regarded as unusual features.

Excessive urinary excretion of uroporphyrin III characterizes most cases of acute porphyria (Waldenström, 1937). On occasion, however, the urinary uroporphyrin III is within normal limits, whereas uroporphyrin I (Prunty, 1946) or coproporphyrin III (Abrahams *et al.*, 1947, Watson *et al.*, 1945) is excreted in excessive amounts.

Case Report

A British soldier aged 26, who had served in the Mediterranean area since 1942, first observed symptoms of ill-health in December, 1946. He noticed that he was lacking in energy, that his limbs, previously very muscular, were now no longer so, and that his uniform had become too loose for him. In spite of increasing weakness, he remained on duty until March 2, 1947, when he was forced to take to his bed with symptoms which were then regarded as being due to "coryza." He was a little better next day and was able to get up, but three days later he was in bed again because of difficulty in standing.

He was admitted to a casualty clearing station seven days after the onset of these acute symptoms. His chief complaints were: central abdominal pain for 24 hours and constipation for three days, a generalized weakness, difficulty in concentration during the day, and sleeplessness at night. It is reported that when first examined at the C.C.S. the patient's condition was extremely poor. He was nauseated and very drowsy; pulse 120, temperature 97° F. (36.1° C.), respirations 20. He was severely

dehydrated. The abdomen was distended, epigastric tenderness was present, but there was no rigidity. Liver and spleen were not palpable. The respiratory system was normal, as was the cardiovascular system except that the blood pressure was 140/90. The pupils were constricted, but reacted normally to light and accommodation. All the tendon reflexes were obtainable and the plantar responses were flexor. In spite of obvious muscular wasting, power was good. There was no sensory loss. A generalized superficial lymph-node enlargement was thought to be due to the septic scabies present. The urine contained no sugar or albumin. Total leucocyte count, 22,400 per c.mm. (polymorphs 92%, lymphocytes 3%, monocytes 5%).

On re-examination the following morning a generalized pigmentation of the skin was noticed. The knee- and ankle-jerks and abdominal reflexes were now unobtainable. The left plantar response was equivocal. Lumbar puncture was performed. The pressure was normal and the fluid clear. Protein amounted to 35 mg. per 100 ml. There was no excess of globulin.

During the next few days the patient's condition, which remained critical, showed little change. Slight icterus of the conjunctiva was noticed on March 12.

On March 18 he was transferred to a British general hospital. The pulse was now 104, temperature 97° F., respirations 25, blood pressure 150/100. Lethargy was still marked, but the patient responded rationally to interrogation. Loss of power in all limbs was noted for the first time. All tendon reflexes were present except for the Achilles jerk. Plantar responses were both equivocal. There was no loss of cutaneous sensibility. The intense brown pigmentation of the skin was again a subject of comment, and it was suggested that it might be of pellagrous origin. With this in mind, and with the intention of demonstrating the associated excess porphyrin, two specimens of urine were allowed to stand exposed to the light for 24 hours, but no deepening of colour was observed. Owing to subsequent lack of response to nicotinic acid therapy, no further investigations into this aspect of the problem were made, nor were any pigmentary abnormalities detected during further routine laboratory examinations of the urine. By mid-April the gradually increasing weakness had proceeded to a stage in which limb movements were almost completely absent. Speech was slurred, but there was no dysphagia. The corneal reflexes were absent, as were all tendon reflexes, although cutaneous sensation was still unimpaired. Muscles were slightly tender to pressure. Lumbar puncture was repeated. Pressure was normal; protein totalled 70 mg. per 100 ml. with excess globulin; and there were 2 cells per c.mm. By this time an extensive series of investigations had been completed. Radiographs of the chest, repeated cultures of blood, urine, faeces, and throat, blood examinations for malaria parasites, and serum agglutinins disclosed no abnormality. Fasting blood sugar was 140 mg. per 100 ml., blood urea 90 mg. per 100 ml., serum protein 5.8 g. per 100 ml., van den Bergh reaction negative, haemoglobin 95%, and E.S.R. 32 mm. in 1 hour.

At this stage 10 ml. of "eucortone" was administered each day without any therapeutic response. "Prostigmin," 0.5 mg. intramuscularly three times a day, was equally ineffective in relieving the profound asthenia. During the first few days of April the patient remained extremely feeble. There was incontinence of faeces and urine; drowsiness during the day was increasing, whereas insomnia at night remained a troublesome feature in spite of sedation with barbiturates. At times attacks of tachycardia and breathlessness occurred. A slight improvement began in the second week of May, and his condition, although still very serious, permitted transfer to England.

The patient was admitted to Redhill County Hospital on May 18. He was a mentally alert individual showing very severe emaciation and extreme loss of muscle substance. The most striking feature, however, was a dusky pigmentation, which was most marked on the face but was also present on the arms and thorax, and to a less extent on the abdomen and legs. The hair was dark brown. (It was later established that his complexion had always been fair, and that when on leave in November, 1946, the dark colour of his hair and pigmented features had astounded his relatives.) The skin was scaly, and lesions of scabies were still present. There were hyperkeratotic patches on the flexor aspects of the fingers and on the palms and soles.

Central Nervous System.—Mentality normal. Amnesic for events occurring during early part of illness. Not aphasic, but could articulate only in a whisper. Pupils unequal, right larger than left; both reacting normally to light and accommodation. Fundi normal except that the arteries and veins were abnormally constricted. Eye movements were full and visual fields normal. No nystagmus. The muscles of mastication were of normal power. Extreme weakness present in all facial muscles, particularly frontales and orbiculares oculi, so that the cornea was always exposed, even during sleep. There was severe conjunctivitis and keratitis of both eyes. The palate moved normally and there was no dysphagia. The tongue, which was normally protruded, was wasted and deeply furrowed, with coarse fasciculation evident. Sensation of taste was not impaired. The right vocal cord moved normally, the left very sluggishly. The cervical muscles were of fair power, and the intercostal and diaphragmatic movements of normal range. All four limbs were flaccid and lay in positions dictated by gravity. There were weak movements of finger flexion in the left hand only. Except for ineffectual contractions of the upper fibres of both pectorales major, the muscles activating the shoulder-, elbow-, and wrist-joints were completely paralysed. The lower limbs retained fair power in the glutei, tensores fasciae latae, hamstrings, and posterior tibial muscles. Contractility of the quadriceps femoris, which were barely palpable as thin straps on the femur, was absent. Anterior tibial and peroneal groups likewise were totally paralysed. There was fair power of flexion of the toes. The deep and superficial reflexes were all unobtainable. The plantar responses, in the absence of contractility of the extensors of the toes, were necessarily flexor. There was no fibrillation of muscles other than the tongue. Complete faecal incontinence, but normal bladder control, was present. There was no sensory loss.

The pulse was regular 96, the blood pressure 110/80, and heart normal. There was no abnormality in the respiratory system. The liver and spleen were not palpable. The descending colon was palpable and spastic.

Investigations.—The combinations of inaugural abdominal symptoms with cerebral disturbances, evidence of lower-motor-neurone paresis, and cutaneous pigmentation led to the examination of the urine for porphyrins. Spectroscopic investigation of a freshly passed specimen showed the typical double band of the zinc-porphyrin complex (Chandler *et al.*, 1939). Ehrlich's benzaldehyde test (Jorgensen and With, 1947) before and after extraction of the urine with acid ether was positive, indicating the presence of porphobilinogen. An amyl alcohol extract of the urine displayed intense pink fluorescence when exposed to Wood's light, as did a specimen of faeces. Urine when first voided was the colour of sherry, and on standing it assumed a dark coffee colour in 24 to 48 hours.

Further investigations resulted as follows: haemoglobin, 94%; R.B.C., 4,500,000; colour index, 1.04; leucocytes, 8,000 per c.mm. (polymorphs 34%, lymphocytes 55%, monocytes 4%, eosinophils 7%); blood urea, 68 mg., fasting blood sugar 94 mg. and blood cholesterol 124 mg. per 100 ml., Kahn, trace; Wassermann ±; Laughlin ±. Total plasma protein, 5.25 g.% (albumin 2.8 g., globulin 2.45 g.), chloride 343 mg., potassium 18.4 mg., and sodium 321 mg. per 100 ml., carbon-dioxide-combining power, 57 vols.%; serum bilirubin, 0.4 mg. per 100 ml. Thymol turbidity test, negative. Alkaline phosphatase, 2.4 Bodanski units. Cerebrospinal fluid: pressure normal; protein, 50 mg. per 100 ml.; Pandey, trace; chlorides, 680 mg. per 100 ml.; lymphocytes 1 per c.mm.; W.R. negative; Benzoin reaction, 00000. The electrocardiogram was normal. Sternal-marrow examination showed normoblastic haemopoiesis with evidence of hypoplasia of erythroblastic elements. The white-cell development was normal. Exposure to bright July sunlight resulted within 45 seconds in an intense irritation of the skin and marked erythema, both of which persisted for an hour. Test exposure to a mercury-vapour ultra-violet lamp for half an erythema dose had no effect.

Family History.—The patient's mother stated that she had never noticed any urinary abnormality in herself or in her children. She had never experienced attacks of colic. The father had died of pneumonia at the age of 29. The maternal grandfather, who had been a painter by occupation, died at 25. It was reported to me that the cause of death was "painter's

colic." One sister, two stepsisters, and a stepbrother were healthy, as was the patient's son, aged 6 years. An attempt to investigate the urine of these individuals met with formidable opposition. Nevertheless specimens were obtained from the patient's son, mother, and sister. No abnormal pigments were detected in the urine of the son and mother, but that of the sister was deeply coloured, darkened slightly on standing, and reacted positively with Ehrlich's benzaldehyde reagent after ether extraction, indicating the presence of porphobilinogen. Schlesinger's test on the same specimen was negative.

Progress.—During the two months that the patient remained at Redhill County Hospital there was a slow but steady improvement in his state of nutrition, and his sleep habit rapidly reverted to normal rhythm. Except for return of contractility, so slight as to be ineffective, in muscles which previously had been quite inert, increase of muscle power did not occur. There was a considerable decrease in the depth of colour of the urine when first passed, and the final depth after standing was less than it had been on admission, but the spectral bands did not indicate that any reduction of porphyrin excretion was occurring. The improvement noted appeared to be independent of the treatment given, which consisted in the seriatim intramuscular administration of liver preparations, folic acid, and calcium gluconate.

Five 24-hour specimens of urine were collected between June 15 and 19 and submitted to Prof. C. Rimington, who confirmed the presence of excess porphyrin and identified it as uroporphyrin III. Coproporphyrin was present in normal amounts. The excretion of uroporphyrin on the five days was 9.7, 9.4, 8.6, 8.3, and 9.5 mg. respectively. The patient was transferred to an E.M.S. hospital near his home on July 14. A progress report from that hospital stated that a relapse had recently occurred, during which power in all muscles, except those innervated by the cranial nerves and those subserving respiration, was quite absent. Colic and nausea were again conspicuous features, as was a marked hypotension, the latter responding to eucortone.

Comment

This case, which presented many of the typical features of acute porphyria, illustrated particularly clearly the nature of the diagnostic problem confronting the clinician when neurological symptoms and signs are pre-eminent. When abdominal symptoms predominate, as they often do, errors in diagnosis have led to injudicious laparotomy. The difficulties in the differential diagnosis of these rare cases presenting a tangle of features referable to many of the bodily systems may be totally resolved by the discovery of abnormal pigments in the urine. Nesbitt (1944) states that "the diagnosis of acute porphyria will be made only if it is borne in mind." The view that acute porphyria is an inborn familial metabolic disorder is supported by the evidence in the above case.

It is thought probable that the grandfather's fatal illness was acute porphyria and not "painter's colic," which it may closely simulate. Porphobilinogen was demonstrated in the urine of the apparently healthy sister, emphasizing that it is important to search for latent porphyria among relatives of the acute case. These individuals should be warned not to take drugs which have been known to precipitate the acute condition. According to Dobriner and Rhoads (1940) the following drugs are suspect: sulphonals, "trional," sulphonamides, barbiturates, arsenicals, alcohol, phosphorus, selenium, and lead. It is noteworthy that, although there is no direct evidence of any causal relationship, mepacrine had been taken by the patient as a malaria prophylactic during the previous three summers. His critical condition prevented investigation of the effect of a provocative dose of this drug.

Although pigmentation and photosensitivity were marked features of this case, both of these effects are rare in acute porphyria (Mason, Courville, and Ziskind, 1933).

Summary

An example of acute porphyria occurring in a young man is described. Abdominal and mental symptoms and neurological signs were present. Pigmentation and photosensitivity were conspicuous features. There was some evidence of a familial distribution of the disease.

I am indebted to Dr. G. H. Jennings for his encouragement and permission to publish this report; to Prof. C. Rimington for his kindness in performing the assays; to the R.A.M.C. officers whose notes furnished the basis of the early part of the case history; and to Miss E. W. M. Johnson for her help with the biochemical investigations.

REFERENCES

- Abrahams, A., Gavey, C. J., and MacLagan, N. F. (1947). *British Medical Journal*, 2, 327.
 Chandler, F. G., Harrison, G. A., and Rimington, C. (1939). *Ibid.*, 2, 1173.
 Dobriner, K., and Rhoads, C. P. (1940). *Physiol. Rev.*, 20, 416.
 Garrod, A. E. (1923). *Inborn Errors of Metabolism*. London.
 Gates, R. R. (1946). *Human Genetics*. New York.
 Günther, H. (1911). *Dtsch. Arch. klin. Med.*, 105, 89.
 Jorgensen, J., and With, T. K. (1947). *Lancet*, 1, 54.
 Mackey, L., and Garrod, A. E. (1926). *Quart. J. Med.*, 19, 357.
 Mason, V. R., Courville, C., and Ziskind, E. (1933). *Medicine*, 12, 355.
 Nesbitt, S. (1944). *J. Amer. med. Ass.*, 124, 286.
 — and Watkins, C. H. (1942). *Amer. J. med. Sci.*, 203, 74.
 Prunty, F. T. G. (1946). *Arch. intern. Med.*, 77, 623.
 Waldenström, J. (1937). *Acta med. scand.*, Suppl. 82.
 Watson, C. J., Schwartz, S., and Hawkinson, V. (1945). *J. biol. Chem.*, 157, 345.

A CASE OF ACUTE MONONITROBENZENE POISONING

BY

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Mononitrobenzene, or oil of mirbane, is a yellow oily liquid which on account of its strong smell is also known as "artificial essence of bitter almonds." Since it was first prepared early in the nineteenth century many cases of poisoning with this substance have been recorded—by absorption through the skin, by inhalation, or when taken by mouth.

Poisoning by skin absorption has followed the use of soap scented with it (Nicholson, 1862), spilling the fluid on the clothes (Loeb, Bock, and Fitz, 1921; Hamilton, 1919–20; Letheby, 1863–4), or application to the hair of anti-louse preparations made with it (Wolpe, 1920; Bohland, 1919; Schultz, 1915). Shoe dyes often contain nitrobenzene as a solvent, and the wearing of recently dyed shoes before they are properly dry has led to many cases of poisoning. Muehlberger (1925) has reviewed the literature on this subject and pointed out that aniline is the solvent most commonly employed, and may give rise to similar symptoms. Levin (1931) has reported a case of orthotoluidine poisoning caused in the same way. Marking-ink also may be prepared with nitrobenzene or aniline, and babies seem to be very easily affected by newly marked napkins: Rayner (1886) first reported a series due to aniline, and Ewer (1920) and Thomsen (1921) have reported cases due to nitrobenzene. In many of these episodes inhalation may have contributed to the intoxication: acute poisoning due to inhalation alone is relatively infrequent, but Stevenson and Forbes (1942) and Stevens (1928) have reported cases following the use of nitrobenzene in bed-bug exterminators.

Poisoning by ingestion has occurred in numerous ways. The majority of cases are accidental, either errors in dispensing (Carter, 1936; Leader, 1932; Thomas, 1926) or mistakes by patients as reported by Chapman and Fox (1945), where furniture polish containing nitrobenzene was taken instead of an alkaline stomach mixture. Hogarth (1912) published a case following the rubbing of nitro-

benzene on the gums as an anodyne for toothache. Other cases have arisen from taking alcoholic drinks which have been contaminated with the substance (Loeb, Bock, and Fitz, 1921; Scott and Hanzlik, 1920) or from drinking a nitrobenzene preparation when intoxicated (Adler, 1934; Wandel, 1919). Food contaminated with the liquid is a rare cause (Hilbert, 1915), though Taylor (1864) reported the case of a woman who tasted the flavouring she was going to use in some pastry and developed nitrobenzene poisoning. Curiosity on the part of children accounts for some cases (Nobécourt and Pichon, 1924); a few are suicidal (Fullerton, 1930; Schild, 1895); and on many occasions the liquid has been taken as an abortifacient, usually without success (Güntz, 1930; Schnopf, 1927; Spinner, 1917; Schild, 1895).

Chronic poisoning is usually industrial. Workers in aniline plants may develop symptoms from nitrobenzene inhalation; it is less common than aniline intoxication, but is more dangerous when it does occur. Engel (1934), Balsac *et al.* (1930), Hamilton (1919–20, 1921), and Letheby (1863–4) have discussed industrial nitrobenzene poisoning, and Adams (1912) has described an unusual case of non-industrial chronic intoxication.

Case Report

The patient, a Polish girl aged 19, was admitted to University College Hospital on July 23, 1947. About three months previously, while she was in Germany as a displaced person, she had married an English soldier, who brought her to London and left her with her mother-in-law while he returned to his unit. She did not get on very well in her new home, and partly out of curiosity and partly, one suspected, hoping to get her husband repatriated she decided to taste the fluid in a bottle labelled "poison." This bottle had been bought by her late father-in-law many years previously and was lying about the house; her husband had warned her that it was poisonous and forbidden her ever to touch it. About 6.30 p.m. on July 22 she poured some of the fluid into a glass and sipped it; she felt nauseated, and vomited several times during the night. The next morning she was seen to be blue, and was therefore sent to hospital.

When seen at 3 p.m. on July 23 she was fully conscious and well orientated. She showed "blue-grey" cyanosis and was vomiting repeatedly, the vomit being bright yellow but without smell. She was afebrile; pulse rate 90; respiration was of normal depth and rate, but the breath smelt strongly of almond essence. Physical examination revealed no other abnormalities. The urine was dark in colour and became darker on standing; it contained a trace of albumin and did not reduce Benedict's reagent.

The stomach was washed out with saline, after which the vomiting ceased. Oxygen inhalations failed to affect the cyanosis, and blood withdrawn from a vein was brownish in colour and shown to contain methaemoglobin. 20 ml. of 0.5% solution of methylene blue was injected intravenously and within 30 minutes the patient's colour was restored to normal.

The next day (July 24) her breath still smelt of almond essence and continued to do so until July 27. The cyanosis was then nearly as deep as before the injection of methylene blue, but it did not seem to be inconveniencing the patient. Oral methylene blue, 2 gr. (130 mg.) four-hourly, was given for two days, and subsequently ascorbic acid, 100 mg. four-hourly, but neither of these seemed to accelerate the disappearance of the cyanosis, which ceased to be detectable on July 29. The urine on July 25 was of normal colour, but still contained a trace of albumin.

On July 29 it was observed that the patient was faintly icteric, and that a severe haemolytic anaemia was developing (see Chart). On July 30 and 31 she passed urine that was almost black, and spectroscopic examination showed that it contained haemoglobin and methylene blue; a sample of plasma on the latter date contained methaemalbumin and haemoglobin. Red cell fragility showed haemolysis starting at 0.48% saline and complete at 0.28%, and a blood film revealed very marked anisocytosis, polychromasia, punctate basophilia, and six