summarizes the results obtained, first using A and B and then K and N. When assessing these results both gastric aspirations and clinical impression were taken into account.

In the investigation a total of 22 cases of gastro-duodenal bleeding were treated—11 with thrombin and 11 with an inert control substance. Our results do not show that thrombin had any influence on the course of the condition in these cases.

It is perhaps of some significance to note that of the seven successes, four were regarded clinically as mild, and would, in our experience, have done well on any treatment. Of the 13 failures, 3 were shown either at operation or at necropsy to have vessels so eroded that an arrest of the haemorrhage was scarcely to have been expected short of major surgery.

Discussion

Thus far the experiences with thrombin in the treatment of acute gastro-duodenal bleeding have been disappointing, and in a short controlled series it has not been possible to establish that it has any convincing value. The series is admittedly a small one, but the cases have all been followed with good care and the trial has been done without knowing what preparation was being used on any individual case.

It may be that our technique was inadequate in various ways, and that greater persistence should have been shown and the doses of thrombin more often repeated. However, a therapeutic agent such as thrombin should be effective after one or two doses, and if evidence of continued bleeding is then still obtainable the treatment has failed to accomplish what was expected of it. Admittedly it was often very difficult to be absolutely certain that bleeding had ceased even when repeated gastric aspirations were being made. Daly *et al.* (1949) emphasize that loose blood clots will be aspirated from the stomach when bleeding is continuing, whereas if bleeding has ceased the material aspirated will contain fine brown granules of different colour and texture. This may sometimes be the case, but we were not always convinced. The techniques that were being followed were rather tedious (especially when performed during the night) and time-consuming if the results were to be of any value, and it was felt that these findings did not justify continuing the investigation. Rather our results confirm the impression that many patients with haemorrhage have no further bleeding after their admission to hospital, and therefore do well on any therapy. Of those who have further episodes of bleeding, some will eventually come to operation or post-mortem examination, when the size of the vessel opened up by the ulcer explains the persistence of the haemorrhage and the failure of all conservative measures, including thrombin.

Avery Jones (1952) has suggested the use of thrombin solution in the treatment of bleeding from oesophageal varices, 10,000 units of thrombin in solution being sipped slowly by the patient over a period of half an hour. It would seem possible that treatment would have more chance of succeeding here, as the bleeding is venous and the thrombin can have direct contact with the affected varices without the diluting effect of acid gastric juice in the stomach. Even in these cases, however, there are, as yet, no figures to substantiate its value.

Summary

An attempt has been made to assess the value of oral thrombin in the treatment of gastro-duodenal bleeding. A controlled series of 22 patients have been treated with thrombin and an inert substance in phosphate buffer. Haemorrhage appeared to be arrested in three of the thrombin group and in four of the control group, while six of the control and seven of the thrombin group showed evidence of continued bleeding.

It is concluded that, with the use of the method described, thrombin has no value in the treatment of gastro-duodenal bleeding. It is possible that it might have some value in the control of oesophageal bleeding.

My thanks are due to Dr. Avery Jones for his encouragement and helpful criticism; to the doctors, sisters, and nurses who co-operated during the investigation; to S. Maw Son and Sons Ltd., and particularly their chief chemist, Dr. Savage, who arranged the supply of the unknown thrombin and control powders.

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THE PROGNOSIS OF ACUTE PORPHYRIA

BY

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Over 300 cases of acute porphyria have been reported, but the previous diagnostic history of many of the recorded cases and the increasing frequency of clinical reports make it probable that the lesser manifestations of the disease have often been overlooked. In consequence, an undue gravity of prognosis has been accepted. In the two cases described below complete symptomatic resolution followed severe episodes of acute porphyria with peripheral neuritis. The striking uniformity of the clinical picture of the disease is emphasized by the close similarity of these cases to previous reported cases.

Case 1

A woman of 23 was admitted to hospital with a history of abdominal pain and vomiting for two weeks. The pain had radiated from the bladder region to the epigastrium. There was no abnormality of the bowel action, but micturition was frequent and difficult. She had been employed in making lead plates and three weeks previously had taken phenobarbitone for one week.

On admission she appeared to be in pain and was over-breathing. The abdomen was soft and not distended. Her blood pressure was 160/130 mm. Hg. She was tender over the bladder. Apart from some quadriceps wasting, full neurological examination was negative. The clinical picture was thought to be partly hysterical. The blood count showed a polymorph leucocytosis; haemoglobin 106%; no punctate basophilia. Urine: no abnormal deposit; porphyrins demonstrated. E.C.G. showed sinus tachycardia with P-T summation. Spasms of severe pain failed to respond to a full range of sedatives and antispasmodics, but the blood pressure returned to normal. One month after the initial onset of the illness the patient complained of tenderness of the upper arms and thighs, but the tendon reflexes and power were normal. She was severely constipated and failed to respond to daily enemata for a week.

Clinical improvement for the next two months was followed by further abdominal pain and vomiting. She was restless, agitated, and distraught. General and neurological examinations were still normal. There was marked increase in the gas shadows seen on abdominal x-ray films. At times she was uncontrollable and was still thought to be hysterical. For two weeks no objective evidence could be found to support her claim of weakness of the wrists. Then bilateral wrist-drop developed, and progressed rapidly. One month later further urgent vomiting occurred and her legs were tender. Her knee-jerks were greatly diminished. The neurological status deteriorated and she developed pareses of the quadriceps femoris muscles and the dorsiflexors of the ankles, with abolition of all tendon reflexes except the ankle-jerks. Sensation was normal. She became emaciated and had episodes of urinary retention.

Eight months after her original admission she failed to attend hospital and was not seen until eight months later, when she was referred to the antenatal clinic in early pregnancy. She had no treatment; her general condition was excellent, and there were no neurological abnormalities. Porphyrins were present in the urine. The pregnancy and puerperium were normal apart from three days of abdominal pain after delivery. When reviewed one and two years later she remained sign- and symptom-free, though the urine remained pigmented. She had a second uneventful pregnancy. Dr. E. E. Rawlings (1950), who supervised this patient through her first pregnancy, has referred to this case.

Case 2

A mechanic aged 29 had developed an abscess which was incised one week before his admission. He had been given sulphadimidine and phenobarbitone. Three days later he had severe upper abdominal pain and was treated with sedatives, antihistamines, and morphine, all with poor response. A surgeon thought that there was no acute abdominal lesion. Two days later the patient was noted to have frequency of micturition, passing small amounts of dark urine. The abdominal pain persisted and was severe, generalized, shooting in character, and associated with absolute constipation. He experienced nausea but no vomiting. There was no personal or family history of similar episodes.

Physical examination on admission was negative, apart from a healing incision of the thigh. In particular, the abdomen, despite severe colicky pain, was soft and no abnormal masses were felt. The blood pressure was 130/80 mm. Hg. Neurological examination was normal. A first specimen of urine, in which porphyrins were demonstrated, was pale in colour. A second specimen was dark. Two days later the patient complained of numbness of the thighs, but no abnormalities were found, and later the same day he complained bitterly of difficulty in micturition. In the next five days he was irrational, disorientated, and deluded. Seven days after admission he developed urinary retention with overflow-incontinence for the first time. The knee-jerks were depressed and the arms were ataxic. He appeared to be mentally normal for two days and then relapsed for a further week into an apparent toxic psychosis.

During the succeeding two weeks a severe and widespread motor weakness developed. There were bilateral wrist-drop, weakness of the shoulder girdle muscles, weakness of the back muscles, which made sitting impossible, and bilateral foot-drop. All tendon reflexes except the biceps-jerks and ankle-jerks were lost. Abdominal pain, which had persisted intermittently, disappeared after two weeks, but constipation, relieved by enema, continued for four weeks. At no time were any sensory abnormalities noted.

Recovery in muscle power began within five weeks of admission, and one week later the patient could sit up and could raise both legs from the bed. After twelve weeks he could walk, stand from a sitting position, dress, and feed himself. He still had marked bilateral wrist-drop, the erector spinae was weak, the quadriceps groups were wasted, and the tendon reflexes were unchanged. In the next month he gained 14 lb. (6.4 kg.) in weight and had minimal disability except that due to some weakness of the abdominal muscles and the extensors of the wrists and fingers. He returned to work—delicate instrument repairing—and has remained in good health for twelve months. No further abdominal pain has occurred and neurological examination was normal.

Discussion

Complete recovery in two cases of acute porphyria with severe neurological damage is an unusually favourable experience when compared with the often-quoted view of Waldenström (1939) that the mortality rate in acute attacks is 50%, rising to 80–90% in cases with neurological damage. However, in a detailed paper Waldenström (1937) gives protocols of 100 cases. Only 4 of the 50 patients who showed neuropathy were alive at the time of writing, but many had repeated episodes. In about a third of all attacks the out-

come was favourable. Other authors who have reported recovery from acute porphyria with neuritis include Mason *et al.* (1933), Hoagland (1942), di Fiori (1946), Michaels (1949), Bonduelle (1950), Gibson *et al.* (1950), and Kiloh and Nevin (1950). Davies (1949) and Denny Brown and Sciarra (1945) reported cases in which second attacks were fatal. The case reported by Petrie (1948) followed a chronic course, and slow recovery was described by Hoagland (1942), Discombe and d'Silva (1945), Halpern and Copsey (1946), Yeager (1947), and Marietta (1949).

The pathogenesis of episodes of acute porphyria is obscure, but barbiturates, aliphatic sedatives, and sulphonamides are known to have an aggravating effect. The attacks are incidents in a chronic inborn metabolic disorder, and Waldenström (1939) thought the role of porphyrin excretion to be the equivalent of that of uric acid to gout, there being no specific variation in relation to acute attacks. Waldenström has witnessed retinal angiospasm causing amblyopia in a patient undergoing an acute attack. Nesbitt (1944) held the opinion that the smooth muscle spasm occurs in the attacks, and Berg (1945) demonstrated extreme contraction of the skin capillaries in his case. Denny Brown and Sciarra (1945), on the basis of histological examination of nervous tissue, expressed the view that acute attacks might be due to locally acting vasoconstrictor substances.

In view of the potentially reversible nature of the damage resulting from an acute attack of porphyria, these views offer the prospect of rational therapy. Grubbschmidt (1950) and Wehrmacher (1952) claim alleviation of severe episodes by the use of various drugs with direct or indirect vasorelaxant effects—intravenous procaine, tetraethylammonium chloride, tolazoline hydrochloride, splanchnic block, and tubocurarine. These unconfirmed reports suggest further important lines of study.

Early diagnosis in acute porphyria is made difficult by the nature of the presenting symptoms, which are, however, consistent enough to constitute a precise syndrome. Hoagland (1942) estimated that a third of all cases are operated on as acute abdominal conditions; and Calvy (1950), with an experience of 16 cases, stressed the adverse effects of operation and of the attendant sedation. Associated hypertension and electrocardiographic changes are not rare, and neurological abnormalities are common. Halpern and Copsey (1946) reported a case which was transferred to their care, after a highly unsuccessful laparotomy, with a diagnosis of "acute posterior myocardial infarction; paralytic ileus; caecal fistula; infective polyneuritis"—virtually a diagnostic mnemonic.

Important features in the neurological diagnosis of acute porphyria are that sensory change is very uncommon, so that poliomyelitis may be mimicked, and the frequency of psychological manifestations, which were present in both cases reported. A Scandinavian practitioner, quoted by Waldenström, asserted, "In this parish, a typical hysteric who dies from respiratory paralysis always means acute porphyria."

Summary and Conclusions

Two cases of acute porphyria with severe neuritis are reported in which complete functional recovery occurred.

The available evidence suggests that an unduly grave prognosis is not entirely justified and that persistence in supportive treatment is well justified.

There is some evidence that angiospastic changes may bring about the acute episodes, and claims have been made for the therapeutic value of angiorelaxant drugs. Such measures, if confirmed, would have their greatest value early in the attacks.

The importance of the surgical, neurological, and psychiatric forms of presentation of the disease is emphasized.

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INCIDENCE OF NEONATAL INFECTION IN HOSPITAL AND DOMICILIARY MIDWIFERY

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A great deal has been written about the risk of infection to which the infant born in hospital is exposed. It is usually assumed that the hazard in this respect is less in domiciliary midwifery. It was felt that it would be of interest to study a series of infants from this point of view, some of whom were born in hospital and some in their own homes.

The Investigation

Records were kept of all infants born in Sorrento Maternity Hospital over a period of 12 months (Group A) and of all infants born over the same period in the practices of 22 domiciliary midwives in Birmingham, these midwives being recognized as district teachers by the Central Midwives Board (Group B). In Group A all attendants were masked, and visitors saw the infants only through glass. Mothers were not masked. Reasonable precautions were taken to prevent infection by contact or dust. In Group B the midwives were masked, but the mothers, relatives, etc., were not. Here, too, reasonable precautions were taken to prevent infection by contact or dust. The comparison was possible for only the first 10 days of life, as the majority of hospital patients were discharged on the tenth day. All babies under observation in both groups were seen daily for that period.

In Group A there were 1,459 births, of which 41 were stillborn. In Group B there were 1,846 births, 21 of them being stillborn. In Group A, 61 premature infants under

TABLE I

	Group A	Group B
Total births	1,459	1,846
Babies removed from observation:		
Stillbirths	41	21
Transfers within 48 hours:		
Prematures	61	21
Mature domiciliary births to hospital	—	9
Mature hospital births to home	13	—
Deaths under 48 hours among remaining births	8	7
Total removals	123	58
Babies exposed to risk of infection	1,336	1,788

4½ lb. (2 kg.) were transferred to the premature baby unit and 13 infants over 5½ lb. (2.5 kg.) were discharged for home nursing within 48 hours of birth. In Group B, 21 premature babies were transferred to premature baby units within 48 hours of birth and 9 babies over 5½ lb. (2.5 kg.) were transferred to hospital for various reasons. For the purpose of this investigation only babies in Group A who were nursed in the ordinary nurseries and those in Group B who were nursed at home were considered. Table I gives the numbers involved in each group.

The following definitions of infection were used. Discharging eyes: discharge from the eye, either watery (lasting for 24 hours) or purulent. Skin infection: sore buttocks or one single spot or blister. Umbilical infection, however slight. Otitis media or otorrhoea: in Group B this could be diagnosed only by discharge from the ear.

If a baby had more than one type of infection each was counted. On this basis it was found that there were 140 infections in Group A and 259 infections in Group B, giving a rate of 10.48 infections per 100 babies in Group A and 14.48 infections per 100 babies in Group B.

Table II shows the incidence and time of onset of each type of infection in each group.

TABLE II

Type of Infection	Day of Onset										Total
	1	2	3	4	5	6	7	8	9	10	
Group A:											
Discharging eyes ..	8	23	13	11	2	9	7	9	8	5	95
Skin infection ..	3	2	2	3	10	4	3	3	1	3	34
Paronychia ..	—	—	—	—	—	—	—	2	1	—	3
Nasal discharge ..	—	—	—	—	—	—	—	—	—	—	—
Respiratory infection ..	—	—	—	—	—	—	—	—	—	—	—
Otitis media ..	—	—	—	—	—	—	—	—	—	—	—
Thrush ..	—	—	—	—	1	—	—	2	1	1	5
Infected umbilicus ..	—	—	—	—	—	—	—	—	1	—	1
Abscess ..	—	—	—	—	—	—	—	—	1	—	2
Total ..	11	25	15	14	13	13	10	17	12	10	140
Group B:											
Discharging eyes ..	5	29	36	26	25	22	19	14	10	10	196
Skin infection ..	—	1	1	4	1	2	2	3	1	—	15
Paronychia ..	—	—	—	—	—	—	2	—	—	4	7
Nasal discharge ..	—	1	6	—	3	—	5	2	1	1	19
Respiratory infection ..	—	2	1	—	1	—	1	1	1	—	7
Otitis media ..	1	—	—	—	—	—	4	—	—	—	2
Thrush ..	—	—	—	1	—	—	1	—	—	4	10
Infected umbilicus ..	—	—	—	—	—	—	—	—	1	1	2
Abscess ..	—	—	—	—	—	—	—	—	—	1	1
Total ..	6	33	44	31	31	24	34	21	14	21	259

Table III compares the risk from various types of infection in the two groups.

TABLE III

Type of Infection	Group A (1,336 Babies)		Group B (1,788 Babies)	
	No. of Infections	Incidence per 100 Babies at Risk	No. of Infections	Incidence per 100 Babies at Risk
Discharging eyes ..	95	7.12	196	10.97
Skin infection ..	34	2.54	15	0.84
Paronychia ..	3	0.22	7	0.39
Nasal discharge ..	—	—	19	1.06
Respiratory infection ..	—	—	7	0.39
Otitis media ..	—	—	2	0.11
Thrush ..	5	0.37	10	0.56
Infected umbilicus ..	1	0.08	2	0.11
Abscess ..	2	0.15	1	0.05
Total ..	140	10.48	259	14.48

The most prevalent type of infection in both groups was discharging eyes, the majority of which were very slight. None resulted in permanent damage. In Group A there was a greater preponderance of skin infections owing to the increased risk of contact infection. In Group B there were more nasal discharges, discharging ears, and pulmonary infections, all of which might easily be explained by the greater hazards to which the infant born at home is exposed by visitors, small children, and others who are not masked.