then synthesized by the organized enzymes present into a fluorocitric acid which cannot during life easily leave the mitochondria. Put dogmatically, it is a case of lethal synthesis, in which the effect of the toxic agent is magnified by the structural biochemistry of the cell. It is a protective synthesis in reverse, and must be distinguished from toxic conversions, of which several examples could be quoted. From the proved reversal of arsenical poisoning by British anti-lewisite, there is no theoretical reason why an antidote should not be able to cope with the double permeability barrier, because this must happen when dimercaptopropanol removes arsenic from the cells. Unfortunately, the latter still remains the only example of a therapeutic agent developed on logical lines from biochemical principles; because, in fluoroacetate poisoning, though we now know more definitely what must be done for reversal, this knowledge has only intensified the puzzle and difficulty of reversing the biochemical lesion.

On the other hand, if we can catch it in time, we now have good biochemical reasons for the therapeutic use of substances which can prevent the entry of fluoroacetate into the tri-cycle. In so far also as citric acid accumulation is induced in the poisoning, it is a medico-legal point that we have some means of detecting the criminal use of such a substance of this type, though the estimation should be done soon after death; thus biochemistry has aided forensic medicine.

In a way, in so far as the virus grows inside the cell, it much resembles the large cell granule; hence in the case of this obscure poison attacking the mitochondria we have a somewhat close analogy to what we should like to do with the intracellular virus. In one case, indeed, low concentrations of fluoroacetate have been used to inhibit the production of influenza virus in the lungs of mice. At any rate, we know that there are agents, like chloramphenicol, which are toxic to the virus and must be able to penetrate to it. There is a valuable thought here for cancer research, which has been exploited in part by the attempt to synthesize radioactive substances which will specifically attack the cancer. It may be noted that 5-fluoronicotinic acid has been found by Hughes (1952) to stop bacterial growth by inhibiting cozymase synthesis; this may well turn out to be a case of a lethal synthesis.

No longer need therapeutic medicine be the slave of empiricism. Though the failure of the logical approach has so often in the past led to total discouragement, there must come the time when the biochemical complexities in living matter are sufficiently understood and related to the physiology to enable a start to be made. From work in the last 25 years it can be claimed that there are signs of a change based upon improved knowledge of the intracellular enzymes and their collective functioning.

I know that much of medicine must remain an art, and that it would be indeed somewhat dull if it all became a science. These biochemical analyses take a long time, I fear, and are only too apt to give the impression that the biochemist fiddles while the disease does its work. Yet I believe that each case thoroughly studied teaches us much and will accelerate our advance to the goal of logical therapy.

I wish to express my thanks to the President and Council for the great privilege of delivering this lecture. I am also grateful to the Chief Scientist, Ministry of Supply, for permission to quote work by Dr. Rivett, and to the Editor of the *Journal of Ecology* for permission to publish; and to the Editor of the *Proceedings of the Royal Society* for permission to reproduce Fig. 2.

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SUBCONVULSIVE ELECTRICAL STIMULATION IN TREATMENT OF CHRONIC NEUROSIS

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A certain proportion of patients seen at a psychiatric out-patient department are ill enough to require more intensive treatment than superficial psychotherapy and advice. This group includes patients with severe anxiety and psychosomatic symptoms such as tachycardia, epigastric pain, asthma, stammer, etc. Others are unable to free themselves from some antisocial habit, such as exhibitionism, while others have become ill through some frightening experience. It is often impracticable to send such cases to a mental hospital, and so some more radical form of treatment such as intense abreactive therapy may be employed. This development is largely due to the work of British psychiatrists, particularly Horsley (1943), and its use has widely spread in different countries. Sargant (1949) has described in detail the emotional outbursts which can characterize the changeover from the neurotic reaction pattern to a more normal adjustment. Many of the drugs used for this purpose, however, have certain disadvantages. Barbiturates, for instance, may merely make the patient sleepy, while amphetamine is apt to be too lasting in its excitatory effects. Treatment with carbon dioxide is often refused by the patient, as it is so unpleasant.

One of us (A. S. P.) was therefore interested to observe in the Veterans Hospital, Lyons, New Jersey, in 1950 the use of an electric current of low intensity applied to the heads of patients after light anaesthesia. In about 80% of cases the patient showed a marked emotional response, which was generally in the nature of weeping and sobbing, and only occasionally of rage (Alexander, 1950; Hirschfeld, 1950). The Reiter B machine was used by these workers, and one of these instruments was brought back to this country. This is therefore a preliminary paper reporting our findings with this treatment, which could also, however, be administered by any electronarcosis apparatus.

Technique of Treatment

No description of the mechanism of the Reiter machine has been published. An examination of the wave-form on a cathode-ray oscilloscope, however, showed that it delivered a unidirectional interrupted current, the wave being very variable in shape, with many spikes which were half a millisecond in duration—that is, below the chronaxie for the larger cortical neurones. The frequency was variable, but was equivalent to about 40 effective pulses a second. The B3 current which we used had an intensity three times greater than that of B1. We also used a machine which provided alternating current similar to that used for electronarcosis, but with an ammeter which reads accurately between 1 and 50 mA. (A serviceable machine is obtainable from the Malven Electro-Medical Laboratories, Ltd., 423a, Hertford Road, Enfield, Middlesex.) In what follows reference is made to the strength of current as read on the Reiter ammeter, and also to the equivalent reading on an A.C. machine.

About 0.5 g. of thiopentone is given to a 10-stone (63.5 kg.) man, and the electrodes are placed just above and in front of the ears; if necessary a little hair can be cut. Nickel-plated electrodes are used, with lint well saturated with normal saline or sodium bicarbonate solution after the skin has been cleansed with "ether-meth," and after electrode jelly has been applied. Atropine, 1/100 gr. (0.65 mg.) is advisable either subcutaneously or intravenously. An airway should be used.

With the electrodes in position, 50 to 60 mA A.C. (10 mA Reiter B3 current) are passed through the patient's skull. This causes a flexion of the arms at the elbows and of the legs at the knees. At the same time respiration is inhibited. If this current is maintained respiration will start again after a period of between 30 and 45 seconds. If cyanosis is marked the current can be lowered at the end of about 30 seconds and then gently raised again. In some cases respiration recommences after about 10 seconds with 60 mA A.C. The flexion of the elbows and knees during the passage of this higher current is caused by stimulation of the motor tracts at the level of the internal capsule.

It may be remarked here that, if the current is raised to about 140 mA A.C., in nearly every case this has an anaesthetic effect, and in some cases if this current is given for 20 to 30 seconds a convulsion will be caused by a spread of the excitation to the motor cortex.

After 60 to 120 seconds, if the current is about 60 mA A.C. (10 mA Reiter B current), the patient may raise a hand towards his head as if to remove an unpleasant stimulus. When this is done the current is gradually lowered. The patient may again raise his hand as the effect of the thiopentone wears off, when the current is again lowered. During this part of the treatment the strength of current is not sufficient to stimulate the diencephalon. The current, however, is tending to make the patient wake up, and it is also stimulating certain autonomic structures outside the brain. The stimulation of the skin on both sides is also tending to cause some pain to the patient, who is just below or at the threshold of full consciousness. It is possible that this pain is a factor in causing the patient to show excessive emotion when he awakes; nevertheless, we do not obtain as good therapeutic effects if we do not initially give a current sufficient to stimulate the diencephalon itself. As the patient appears to be waking up he is asked to squeeze the physician's hand, and when he responds in this way the electrodes are removed. The whole treatment may last 3 to 15 minutes.

In a typical case the patient then remains in repose for up to about half a minute, but soon begins to shiver and tremble, and there may be marked sweating. Then he begins to weep or even becomes affected by convulsive sobbing. This may last as long as 20 minutes. During this time he may discuss at great length some emotional conflict related to his maladjustment. In other cases the patient, though weeping, is unable to relate the affect to any particular subject. In still other cases the emotional release is not one of sobbing but of great excitement, during which the subject relives some terrifying experience in the war. The patient may have described the event previously in an unemotional manner, but during the abreaction he may be unaware of his surroundings and relive the experience emotionally. In one case the patient, a British soldier, had been recaptured after escaping from a prisoner-of-war camp and had been thrown into a concentration camp. During his treatment eight years later he became wildly excited and threshed about with his arms in a fierce struggle with his supposed gaolers. We made some sound records of these events.

Other patients are in a euphoric state after the application of the current. They often express relief at being free from their haunting fears and discuss their symptoms and emotional problems fully. At this stage the patient often expresses gratitude that he can do this. He is in a highly suggestible state, a fact that can be exploited therapeutically.

The number of treatments varies according to the gravity of the symptoms and also to the nature of the abreaction. In some cases it may be carried out once only as an incident in the psychotherapeutic management of the case, while in others treatment is given every other day for ten times. With each treatment the violence of the abreaction tends to decrease.

If the subject is an out-patient he can go home after an hour or so. The treatment is less disturbing than E.C.T. It appears to be without danger. The chief risk is that of electric burns, especially if a relatively high unidirectional current is used. These can, however, be avoided if care is taken that the electrodes are non-polarizable. There should be plenty of conducting jelly. The use of sodium bicarbonate, suggested by some workers, does not seem to be superior to normal saline. The chief causes of burns are sparks, which can pass only if there is much resistance at the electrodes. This is apt to occur if the apparatus employs a specially high voltage and if rust causes some resistance at the electrodes.

In this treatment, if an intravenous anaesthetic is used it is advisable to have a closed oxygen circuit with a rebreathing-bag, so that if there were any prolonged inhibition of respiration before or after the application of the electrodes artificial respiration could be applied.

Physiological Considerations

When the patient has been anaesthetized with thiopentone the current is raised to about 50 to 60 mA A.C. (about 10 mA on the Reiter ammeter, B3 current). This appears to be about the threshold for stimulating the brain itself, for if electrodes are placed on the motor area, then there is a movement of a limb on the side contralateral to the negative electrode. With rather higher currents (about 80 mA, or 12 mA Reiter B3) both arms and legs may be contracted by stimulation of the pyramidal tracts probably about the level of the internal capsule. If the current has a low frequency—for example, 10 effective beats per second—then the muscles are seen to jerk synchronously with the current pulse. If this stimulation is prolonged and the current spreads to the motor area of the cortex, then a fit may occur. With the level about 50 to 60 mA, however, the optimum results are obtained. When the current is lowered below the threshold for brain stimulation some motor phenomena persist, such as a rhythmic contracture of the facial muscles, the platysma, and the trapezius muscles. This is caused by stimulation of the seventh and eleventh cranial nerves as they leave the skull. When the muscles contract through stimulation of the motor cortex, however, the movements are smoother, as in a voluntary contraction.

There is also stimulation of the autonomic nervous system, which in some cases is very pronounced. Further work may indicate that this is the essential factor in producing the therapeutic effect. If atropine is injected before treatment, overaction of the vagus, which is stimulated on both sides as it leaves the skull, is diminished. Sometimes a sympathetic effect like dilatation of the pupils and quick-

ening of the pulse is followed by vagal effects. More often, however, flushing and sweating of the skin are seen, as also are slight dilatation of the pupils and a rise followed by a slow fall of blood pressure, often reaching in time a subnormal level. A current of 60 mA will for a time inhibit respiration by approximation of the vocal cords from stimulation of the vagus. This effect is also lessened if atropine is given beforehand.

Although shivering and weeping occasionally occur when thiopentone is given alone without a current, these effects are brought out more frequently and more markedly by the addition of electrical stimulation.

Occasionally, after the early treatments a patient complains of a certain degree of nausea, or of an increase of mental depression, or of a feeling of malaise lasting a day or so, although the last is very rare. As a rule, however, the relief of tension easily outweighs any transitory feeling of malaise.

Electroencephalographic Studies

Thirteen patients had an E.E.G. taken before treatment and in only two cases was it normal. Two of the 11 abnormal cases showed tracings suggestive of epilepsy. In each of the other nine the E.E.G. was characteristic of tense unstable individuals.

Roth (1951) has described changes in the E.E.G. which occur in a high proportion of cases of depression just at the stage in E.C.T. treatment when the patient is conscious of subjective improvement. We were therefore interested to see whether similar results would appear with subconvulsive electrical stimulation. Five patients were tested at intervals during this type of treatment. The only case, however, in which the E.E.G. changes described by Roth occurred was that of a married woman aged 29 who had suffered for many years from severe anxiety with obsessional fears of impending disaster, so that she would repeatedly go back to see if she had left the gas on or a door open. She was in a perpetually tense state. However, during treatment she described herself as becoming more relaxed and as being in better health than for four years. Coincident with her improvement she showed the changes in the E.E.G. described by Roth.

Further study, then, is required to ascertain whether the Roth phenomenon occurs in a high proportion of patients treated with subconvulsive electrical stimulation, as only one in five of our cases showed the change.

Clinical Material

Our clinical material consisted of 50 (27 male and 23 female) relatively young subjects, 21 aged 20–29, 18 30–39, 7 40–49, 2 in the fifties, and 1 each in the subsequent two decades. In some cases only one treatment was given, but the most usual number was five. Two patients had 17 and a few 10 or over. The total number of treatments was 252.

Although on the whole relatively young, most patients had been ill for a long time: 43 (86%) had been ill for over four years, 6 (12%) for one to four years, and 1 for less than a year.

Special attention was paid to the question whether a terrifying experience had been a factor in the onset of the neurosis: 11 (22%) had been subjected to one or more terrifying experiences in wartime, while 10 (20%) had suffered a severe emotional trauma in civilian life. Attention was paid to whether the patient re-enacted the event with a release of emotion and whether the incident was in any way related to his current conflicts and symptoms.

The series included 15 patients (30%) who had acquired abnormal sexual or other antisocial habits, some of a criminal character. In the ordinary way it is difficult for a psychiatrist to induce such patients to talk freely about their problems. If, however, at a comparatively early stage in treatment the patient could be induced to discuss his problems freely, there would be considerable saving of time.

On the whole the patients were emotionally tense individuals who complained of various psychosomatic symptoms, the commonest of which was the feeling of a weight on the top of the head, or as if the head was held in a vice. Other symptoms in order of frequency were trembling feelings or "wobbly legs," over-sensitivity of sound, generalized weakness, indigestion, faintness and giddiness, ejaculatio praecox, and backache. More serious conversion symptoms were attacks of asthma or of severe epigastric pain without an ulcer, severe tachycardia, eczema, Raynaud's disease, writer's cramp, and severe stutter. The actual clinical groupings were:

Psychopathic behaviour disorders	10
Neurasthenics	4
Hysteria	17
Anxiety states	7
Obsessionals	7
Schizophrenics	4
Agitated melancholic	1

Three of those diagnosed as obsessionals had severe washing mania. Ten psychoneurotics with other diagnoses also complained of obsessional symptoms. Five psychotics were also included, four being schizophrenic and one an agitated melancholic.

Results of Treatment

The characteristic effect of the treatment was to produce a highly emotional state of mind, most often weeping, so that the patient eventually became less tense and lost his psychosomatic symptoms. The most remarkable phenomenon was the manner in which patients talked freely about their personal conflicts. One patient who was shy and awkward with women spoke of his fears that his genitals were so small in size that he would be ashamed to marry. Case 2 (see below) lost his urge to interfere with young girls. Another man whose personality had greatly suffered from war strain had developed an urge to exhibit himself at a window, and this also cleared up.

Some patients used exaggerated language to express the relief experienced on the day following this treatment. One described it as "bliss," and another as "the happiest day of his life." It must be emphasized, however, that the treatment was not necessarily curative in itself, but it permitted the psychiatrist to establish good rapport with the patient and to utilize this for subsequent therapy.

Thirty-eight patients (76%) said that they felt at once a certain relief from the treatment. Only 25, however (50%) have shown a marked improvement since the treatment, lasting up to the date of writing—that is, from six months to two years. In some cases severe physical symptoms such as asthma, tachycardia, and severe epigastric pain cleared up.

Attention was paid to the problem of whether patients who had incurred a severe mental trauma either in wartime or in civilian life eventually did better than the others. There were, in fact, 11 cases in which terrifying war experiences had been an important aetiological factor. Nine of these re-enacted their traumatic experience, some of them in a trance-like state, as described above. In the whole group the abreaction took the form of weeping more often in women than in men (16 out of 23 women, and 11 out of 27 men). Another reaction was euphoria, sometimes with laughter, while others showed rage. The reaction depended partly on temperament and partly on the original experience. The mode of reaction could be suggested to the patient. Thus a man who was weeping could be made to show aggression if appropriate noises were "heard off." Similarly, a man in a state of rage could sometimes be quieted by a gentle voice. There were 10 cases in which the trauma occurred in civilian life, such as sexual assault or a sudden bereavement. The abreactions in these cases were not on the whole so violent.

All these patients were found to have current problems which were instrumental in causing them to prolong an anxiety state which had started in the war or to revert to an anxiety state which brought their war experiences back to their minds again. The treatment facilitated the subsequent resolution of these problems.

It was found that those cases which showed a strong abreaction had a better end-result than those who failed to react, although there were some notable exceptions to this rule. The following figures seem to indicate that a good abreaction to an emotional trauma was of good prognostic significance : the 21 best results in the whole group included 7 out of 11 cases that had abreacted a wartime trauma ; the 13 worst results were on the whole characterized by a poor emotional response and poor rapport.

Even in the cases of two schizophrenics who had failed with insulin-coma therapy this treatment was useful. One of these became much less tense and for a time at least almost lost a severe stutter. In another case the diagnosis of a doubtful schizophrenia was confirmed only when the patient during this treatment expressed grandiose ideas that he was one of the great intellectuals of the age and fit to associate only with them.

Cases which failed to respond included schizophrenics, a mentally retarded patient, and an alcoholic dement.

With regard to obsessional illness, there were three compulsive hand-washers. On one of these the treatment had no effect and he subsequently had a leucotomy. The second, who had a depressive background, reacted better to electronarcosis. In the third case, however, the patient, who had been ill for some years, gave up a practice of spending half an hour washing himself after urinating. He returned to work after an absence of many months. He had intensive psychotherapy as well. There were 15 others who had obsessional symptoms of less pronounced degree in a setting of anxiety with psychosomatic symptoms.

Of the nine patients who did best, four were classified as hysterics, four as psychopaths (two being homosexuals), and one as a chronic anxiety case. Four of these had obsessional symptoms—one being the washer mentioned above, one had a "going-back" mania, one was ruminative, and one was a claustrophobic with fears of being shot in the street.

Illustrative Cases

The following two case histories indicate what results can follow the treatment : Case 1 illustrates how a patient may relive horrific experiences during the treatment, and Case 2 shows the successful treatment of an aggressive egocentric psychopath who was a parasite on society and who could not give up the practice of interfering sexually with young girls.

Case 1.—A male clerk aged 30 was first seen on July 7, 1947. He had developed an anxiety state two years previously, with recurrent feelings of pressure on the head, giddiness, tremors, and inability to concentrate. He could give no account of why the illness should have started at that time. No progress was made with the usual psychotherapy, and on January 6, 1948, he was given narcoanalysis, when he relived a terrifying experience in an air raid at Canterbury during the war. On this treatment he improved for a time, but a year later he appeared to be depressed and was given some treatments with electro-shock, with only transitory improvement. On July 7, 1951, he was given electrical stimulation, when the abreaction was more intense than that previously experienced. This time he expressed intense feelings of guilt for the death of three young soldiers in the raid, as they had been carrying out his orders at the time. On four subsequent occasions the same scene was relived and the incidents were discussed, until finally he stated that he had lost his feelings of tension, pressure on the head, giddiness, etc. He was later able to carry out his work efficiently.

Case 2.—A man aged 36 had suffered from severe mental tension for some years, complaining of giddiness and inability to go out alone. He had no intention of undertaking steady work. He had hitherto been teaching pupils to play the piano, but attempted to behave indecently to one young girl. He had decided to become a photographer, with vague ideas that he might photograph girls in the nude. He stated that he had been rejected for military service. He was first seen on February 21, 1951, as fits of depression had caused him to consider suicide. His wife stated that he was aggressive at home, and on one occasion had put his hands round her neck threatening to strangle her. She stated, however, that she was quite prepared to remain longer with him to give him a chance to have treatment. She stated that the patient's father had been killed in 1916 as a soldier, and that the patient had been brought up to be completely self-centred. During the treatments with electro-stimulation he was able to show great emotion and achieve a close rapport with the psychiatrist. He was able to describe how between the ages of 14 and 16 he had regularly had coitus with his young sister, who was 10 at the beginning. Since then he had been obsessed with the idea of sexual intimacy with young girls. He also related how in the second world war, with his mother's co-operation, he had run away and lived in hiding to avoid conscription. In the course of treatment he was able to discuss how his emotional development had gone wrong. He was able to lose his narcissistic attitude and develop as a member of the community. By the end of six lengthy treatments at weekly intervals he was on good terms with his wife and had lost his severe feelings of tension. He has since obtained a promising position.

Discussion

From our experience with this treatment we would agree with American workers (Alexander, 1950; Wilcox, 1951) that it is of value in treating tense anxious psychoneurotics. It is necessary, however, to draw a distinction between the effect of passing a very low current (for example, 3 mA Reiter B1 or 10 mA A.C.) and the effects of passing a higher current which is strong enough to penetrate to the diencephalon (for example, 12 mA Reiter B3 current or 60 to 100 mA A.C.). In the former case, as the current is not strong enough to excite the brain there is merely stimulation of cranial nerves as they leave the skull. For instance, excitation of the seventh nerve causes twitching of the face, of the ninth salivation, of the tenth slowing of the heart and inhibition of respiration, and of the eleventh twitching of the shoulder. On the other hand, the stronger current actually passes through the diencephalon, as judged by the fact that this current excites the motor tracts at the level of the internal capsule, so that the arms and knees are flexed.

If a low current of only 10 mA A.C. is used the patient may show excessive emotion as he wakes, but this effect may result only from the painful stimulus on the forehead at the site of the electrodes. This effect, however, has not, in our experience, the same therapeutic value as when one gives a current which is strong enough initially to stimulate centres in the diencephalon. We obtained the best results only when we raised the current to this level. This matter is of some importance, because one American worker (Bennett, 1952) has stated that the low-current therapy is not superior to simple psychotherapy. This subject is fully discussed by Spencer Paterson (1952).

Summary

A series of 50 patients, mostly young adults who had suffered from chronic neurosis and in whom the usual forms of treatment had failed, were subjected to a new form of electric abreactive therapy. Nearly all were emotionally tense and anxious. In all, 252 treatments were given.

The machine first employed was the American Reiter machine, but any electronarcosis machine would appear to be equally effective.

The technique of the treatment is described. It is safe and not unpleasant for the patient. The current was intense enough to stimulate the diencephalon, and it is thought likely that excitation of emotional centres was related to the therapeutic effect. Side-effects, such as stimulation of certain cranial nerves and of subcortical motor tracts, are described.

In six cases E.E.G. studies were carried out to ascertain if the phenomena described by Roth as occurring in the electric shock treatment of depression would occur. The change was seen in one case out of six, and at the point when a striking clinical improvement occurred in a woman suffering from obsessional illness.

With this unpromising material it was possible to obtain a much closer emotional rapport than by using other forms of abreaction. The patients would show great emotion, and discuss previously repressed material relating to their conflicts in the frankest manner and with great emotion. In some cases the patients were able to free themselves from antisocial sexual habits of a criminal character.

In cases in which horrific war experiences had been a causal factor the patient relived the incident with marked emotional expression of fear and rage. A strong abreaction was of favourable prognostic significance.

Thirty-eight (76%) patients stated that they had received immediate emotional relief from the treatment. Twenty-five (50%) have shown an improvement lasting from six months to two years. Illustrative cases are given.

The treatment has been found valuable in conjunction with psychotherapy in treating chronic cases of neurosis and behaviour disorder, and may be superior to other methods of abreactive therapy.

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ACUTE PORPHYRIA

EXPERIMENTAL TREATMENT WITH A.C.T.H.

BY

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In the past two decades the clinical study of the porphyrias has received growing attention. The aetiology of these diseases, however, remains obscure and their treatment symptomatic. It was perhaps inevitable that a new therapeutic agent, such as A.C.T.H., would be tried in the treatment of this puzzling group of diseases, particularly as it has been suggested that there may be some connexion with hypofunction of the adrenals. Myerson (1951) and Oltman and Friedman (1951) did not find A.C.T.H. of value in this condition. This paper reviews the clinical features of two cases of acute idiopathic porphyria, in one of which a course of A.C.T.H. was given.

Case 1

A man aged 28 was admitted to the Western Infirmary, Glasgow, on February 21, 1946, suffering from severe abdominal pain; he gave a history of four previous attacks of abdominal and limb pain. His first bout was in September, 1944, when he was serving in the Royal Air Force, and his condition was diagnosed in an R.A.F. hospital as idiopathic porphyria. He had been a coal-miner before joining the R.A.F., and had had no previous ill-health. There was no family history suggestive of porphyria.

Since February 21, 1946, six further attacks were observed in the Western Infirmary, and he was admitted on numerous occasions to Ayr County Hospital. Dr. R. Hill is publishing observations made on this case while under his care in the latter hospital. Some episodes of porphyria were characterized by abdominal pain only, but several showed both colicky pain and polyneuritis. They varied in duration from a few days to a month.

A typical bout observed in the Western Infirmary and beginning on September 22, 1946, had the following features. While in apparently good health, the patient noticed that his urine became darker in colour. Within a few hours generalized abdominal pain developed; the pain was continuous and was punctuated by frequent bouts of colic of great severity. At this stage the abdomen was as rigid as in a case of perforated peptic ulcer. He was constipated and his urine became scanty and reddish black in colour. A persistent tachycardia up to 150 a minute was present, and the blood pressure rose to 170/130 (his normal blood pressure was 120/90). Within one week the abdominal pain subsided and was succeeded by pain in the thighs, with marked spasm of the abductors and hamstrings. The pain spread to involve the muscles of all four limbs, which showed hypotonicity, pronounced wasting, and diminished tendon reflexes. No loss of vibration or tactile sense was noted, but the muscles were very tender. This polyneuritic phase lasted three weeks. The pain gradually lessened during the final week, and this was accompanied by reduction in the intensity of the urinary coloration. Convalescence was rapid when the pain subsided.

During the acute stages of a few attacks mental confusion and hallucinations were noted. Staphylococcal skin infections were common, and in one episode bronchopneumonia developed (September 10, 1948). The patient stated that during his attacks he tended to become "blue in the face." Body weight fell by about 30 lb. (13.6 kg.) during each attack, but weekly records failed to demonstrate any weight loss before the onset of pain.

Investigations.—Repeated clinical and laboratory investigations were carried out during the attacks, and the following abnormalities were found: (1) The patient continuously excreted uroporphyrins, almost entirely the Series III isomer, with a marked rise in excretion during acute attacks. The isomer type was established by partial decarboxylation and separation of the resulting mixture of coproporphyrins. (2) The plasma chlorides fell to levels around 0.52 g.% (as NaCl) during attacks. (3) Liver-function tests showed some impairment of hippuric acid synthesis.

Treatment of the acute attacks by intravenous calcium gluconate, by saline and glucose–saline, or by the injection of whole adrenal extracts ("eucortone"), of D.C.A., and of B-group vitamins produced no significant improvement. The symptomatic treatment of pain required large doses of morphine-type drugs over long periods.

At the time of writing the patient's condition is satisfactory, though his urinary porphyrin excretion is still above normal and includes uroporphyrin. Recently the episodes have consisted of mild attacks of abdominal discomfort of a few hours' duration, occurring every three to four months. The attacks are adequately controlled by minor analgesics, and he is able to work as a storeman.