immunization? This one cannot answer finally, but it is an eventuality to be feared, with its great risk for the young un inoculated child.

Comparing methods of prophylaxis, the present dosage of 0.2 ml. and 0.5 ml. of A.P.T. emerges as the best procedure, followed closely by the use of three 1-ml. doses of T.A.F. The smaller doses of 0.1 ml. and 0.3 ml., and latterly 0.1 ml. and 0.5 ml., of A.P.T. seem somewhat inadequate, and the fatal fully inoculated Gateshead case actually received 0.1 ml. and 0.3 ml. of A.P.T. It is possible to establish active immunity by injection of toxoid while the subject is protected with the passive immunity of a small dose of antitoxin.

The duration of immunity apparently depends on the factor of individual variation, which can never be accurately assessed. Nevertheless once antitoxin has been established it may easily be stimulated anew, and the practical application of this is the recommendation to administer 0.5 ml. of A.P.T. to the previously immunized entrant school-child. As mortality from diphtheria really begins in the third year of life, prophylaxis should always be sought in the second year of life, preferably at the beginning.

Contacts and Carriers

Contact carriers present a problem of disposal. In Gateshead we have been content to exclude them from school and work and keep them under observation. Most are carriers for very short periods, but occasionally one encounters the more chronic type. For these individuals hospital treatment is a waste of beds. In some areas swabbing of contacts has been abandoned and the emphasis placed on prophylaxis, but there is one justification for the routine swabbing of contacts in the discovery of a number of early cases of the disease. It is difficult to keep people under observation for the carrier condition without doing something for them, and some local antiseptic treatment has been adopted, such as throat paints in tonsillar cases and nasal insufflations. Lately the Kromayer lamp has been used to irradiate tonsils. In the chronic carrier it is always wise to assess the organisms for virulence before proceeding to surgical measures, such as tonsillectomy, and it looks also as if penicillin should be tried when it becomes available.

Does immunization increase the carrier percentage? The answer is "No," although the immunized person tends to become a carrier if the bacilli gain a lodgment in his tissues.

Conclusion

It must be obvious that we have not yet succeeded in our warfare against diphtheria, although we have made remarkable progress. Our future attack must be along two lines. We have to make our immunization against diphtheria more effective, either by exploring and stimulating the antibacterial defences of the tissues or by perfecting the means of evoking full antitoxic immunity in the body. Our second line demands a more intimate knowledge of the tissue combination with diphtheria toxin, especially in relation to the heart muscle and the nervous system. It also demands a reassessment of the role of the specific antitoxin in relation to this interaction of tissue and toxin. Such an inquiry must keep in view possible differences between the natural disease in humans and that induced in laboratory animals.

With a fuller understanding of the problem than we now possess it may be possible to improve our serotherapy so as to abort the cardiotoxic and paralytic syndromes and perhaps even to treat them along specific lines. The fact that diphtheria very seldom leaves any permanent disability in those who survive, no matter how ill the patient, shows that the tissue damage inflicted by the diphtheria toxin is not necessarily final and irremediable.

The solution of our present difficulties must come from clinicians, pathologists, serologists, and bacteriologists working in the close liaison of the team.

REFERENCES

- Banks, H. S. (1934). *Publ. Hlth.*, **47**, 132.
 Deicher, H., and Agulnik, F. (1927). *Dtsch. med. Wschr.*, **53**, 825.
 Dudley, S. F., May, P. M., and O'Flynn, J. A. (1934). *Med. Res. Cncl. Sp. Rep. Ser. No. 195*, p. 90, London.
 Goodall, E. W. (1928). *Inf. Dis.*, p. 197, London.
 McLeod, J. W., et al. (1933). *J. Path. Bact.*, **36**, 170.
 McSweeney, C. J. (1941). *Lancet*, **i**, 208.
 Neubauer, C. (1943). *Ibid.*, **2**, 192.
 Registrar-General's *Stat. Rev.*, 1940, Pt. 1, p. 170, London.
 Von Bie (1922). *Acta med. scand.*, **66**, 337.

PREFRONTAL LEUCOTOMY IN TREATMENT OF POST-ENCEPHALITIC CONDUCT DISORDER

BY

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There can be few more difficult or tragic cases of juvenile delinquency than those conduct disorders arising from the ravages of epidemic encephalitis, and, although it is 20 years since the last major epidemic, many of the more severe cases continue to spend years of turbulent isolation in our mental hospitals, defying all attempts at re-education. The mental sequelae of encephalitis seem to have transformed these patients into veritable "little devils" with *apache* propensities characterized by uncontrollable and vicious impulses uninfluenced by ordinary disciplinary measures, and their abnormal conduct ranges from excessive naughtiness to gross criminal acts.

In a study of a group of 144 severe cases Gibbs (1930) found that, over a period of eight years of special training, only 8 cases could be discharged recovered, and he considered that the outcome for the majority of the remainder was very gloomy. He concluded that the fundamental cause of much of their abnormal behaviour was an emotional dysfunction, a state of tension or irritability of affect, driving them to periodic outbursts of impulsive conduct of characteristic simplicity, unpremeditated and unplanned. Such a state of affairs would appear to afford the clearest indication for prefrontal leucotomy, which has alleviated many emotional psychotic states by the surgical division of the fibre connexions between the thalamus and the prefrontal area of the brain, thereby reducing the emotional tension. In the words of Freeman and Watts (1944), "Once the emotional nucleus has been successfully abolished, the sting drawn, the reconstruction of the personality can be attempted."

The present paper records two adult cases of post-encephalitic Parkinsonism in which severe behaviour disturbances present from childhood have been removed by prefrontal leucotomy, leaving immature but socially acceptable personalities.

Case I

This patient, a man aged 28, had an insomnic type of encephalitis in 1924, when 7 years old. Previously a normal healthy boy, he became restless and hyperactive, turning somersaults, whistling, noisy at night, and disturbing the neighbours. After a period of 26 weeks in hospital he returned home with little change in his conduct, and he became a constant source of trouble to his parents during the next seven years. He was mischievous and impulsively violent, and he would suddenly hit out without warning. He stole from shops and school, and was on probation for two years. School attendance was spasmodic, and at 14 he started work but was too erratic to continue. Nothing could be done with him, and in 1931 he was certified and sent into the mental hospital.

For the next thirteen years his conduct was similar to that at home. He was irritable, impulsive, and violent, stating that he couldn't stop himself. If he happened to be near a window he would suddenly put his fist through it. He once pushed his head through a window. On another occasion he threw a knife at a patient. He would become angry at the least provocation.

A slight degree of Parkinsonism was apparent on admission, and has shown little change during the years in hospital. He has the typical facies and gait, and a slight degree of generalized rigidity, but is very active and otherwise healthy. His intelligence grading was dull and backward, with a mental age of 8 or 9 years on the progressive matrices test. He was the firstborn of four children in a working-class family, and no factor other than the encephalitis could account for his change of conduct.

Operation.—Bilateral prefrontal leucotomy was performed by Mr. J. Hardman, neurosurgeon, Sheffield Infirmary and Hospital, in January, 1944. Under local analgesia after omnopon and scopolamine, a burr-hole was placed 3 cm. behind the orbital margin and 6 cm. above the zygoma. A brain needle was introduced and carried through an arc upwards and downwards to section the subcortical fibres in the plane of the coronal suture just anterior to the tip of the lateral ventricle (McKissock, 1943).

The patient was quiet throughout the operation, and afterwards remained in a dull and stuporous state for two weeks, lying in bed with his eyes closed but easily roused for feeding and attention. He was incontinent of urine. During the next three months he made

rapid progress,*and soon regained his former alertness. He is now cheerful and contented, eager to co-operate in the rehabilitation programme. Incontinence gradually lessened, but it has never disappeared entirely. His impulsive and violent conduct has been entirely abolished, and during the two years following the operation he has not once attacked anyone or broken a window. He is now of equable and cheerful temperament, and appreciates that he can sit by a window without fear of pushing his fist through it (only the scars on his hands serve to remind him of his former misdeeds). He has been on leave many times, and returns to hospital without protest. His parents report that, although he no longer has violent outbursts, he is impetuous and not easily diverted from a course of action. He is selfish, and is indifferent to conventional good manners. He is careless in his attire, and will no doubt require a much longer period of habit-training before he can take a place in the home environment.

He is handicapped by an intellectual as well as an educational defect due to retardation by the encephalitic process in childhood. A recent psychometric report by Mr. E. V. G. Bradford gives him a mental age of 11 years, scored as follows: Shipley vocabulary, 12; Shipley abstraction test, 10; problems, 11; mechanical reading (Burt), 13; verbal repetition, 10; Kohs' blocks, 10; cube construction, 10. This shows a fairly even performance on a variety of tests, but there was a noticeable lack of sustained attention, and he was too easily satisfied with the results. Nevertheless, it is doubtful if he could have done as well before the operation, although his interest in reading has fallen off considerably since.

His Parkinsonism has remained unchanged, but he has had three epileptic attacks since the operation, and it is noted in the case records that a fit occurred in 1932. This suggests that he has an epileptoid disposition which has been activated by the operation. Unfortunately, electro-encephalography was not available.

Case II

This patient, a woman aged 31, had an attack of encephalitis lethargica in 1924 at the age of 10. The main feature of this attack was sleepiness during the daytime, and she remained in hospital for four weeks. The parents state that on the day of her return home she began fighting with other children, which was unusual for her, as she was formerly of even temper. From then onwards she developed temper tantrums, screaming attacks, and destructive impulses. She smashed windows and broke crockery, and her parents were continually embarrassed by complaints from neighbours regarding her assaultive tendencies. She said the other girls tormented her. She told lies, but did not steal or show any sexual tendencies. School attendance was intermittent, and from 14 years onwards she remained at home until 21, when she became unmanageable, and was admitted to the mental hospital under certificate in 1936. She was the elder of two children, and no social-environmental factors could be found likely to influence the development of her conduct disorder.

In the first eight years of her stay in hospital she had frequent emotional outbursts often lasting a week or more. She was then violent, aggressive, and destructive. Quiet periods became less frequent, and she was always irritable, excusing herself by saying that other people got her "ratty." She would not concentrate on intelligence tests, and her score on the progressive matrices, sets A, B, and C, was only 15. Slight Parkinsonism was shown by the facial expression and the posture of the fingers of the left hand with occasional slight tremor. The pupils were irregular and failed to react to light. There was no noticeable muscular rigidity. This degree of Parkinsonism has not progressed much since admission. Menstruation was normal, but did not start until the age of 18. Electric convulsion therapy was attempted in 1944 with little effect, and she refused to complete a course of treatment.

Operation.—Bilateral prefrontal leucotomy was carried out by Mr. J. Hardman in November, 1944, using the same technique as before, under local analgesia. She was a trifle apprehensive and emotional during the operation, but afterwards was noticeably calm and placid. On return to the ward there was little disturbance of consciousness, her attitude being one of watchfulness and expectancy. There was no incontinence of urine, and in a week she was up and about, somewhat irritable at first; but after a month she settled down calmly to the hospital routine, showing none of her former angry outbursts.

During the past 14 months she has remained in an even temper, willing and co-operative in simple daily tasks, contented, and apparently quite satisfied with life. Whereas before the operation she was never stable for long enough to permit even a day's leave from hospital, she has now been home on many occasions, and returns quite willingly. Her mother reports that when at home she is somewhat impetuous and self-willed, keen to have her own way, and seems unable to concentrate for any length of time. She will, however, read a book for long periods.

A psychometric examination by Mr. Bradford resulted in a mental age of 12 years, scored on the various tests as follows: Shipley

vocabulary, 14; Shipley abstraction test, 10; problems, 10; mechanical reading (Burt), 13; verbal repetition, 12; Kohs' blocks, 13; cube construction, 11. As with the first case, the patient showed undue hastiness and a lack of sustained attention. Her score on the progressive matrices had increased from 15 to 20.

Comment

There can be no doubt that both patients have benefited by the operation, and enough time has now elapsed to justify an optimistic view of the stability of the results. Both are contented and happy; they had willingly consented to the operation, realizing that it was an attempt to help them to control their temper and violent outbursts. They have both made satisfactory adjustments within the sheltered life of the hospital, yet enjoy frequent visits to their families. Their parents are grateful, and the work of the nursing staff in regard to their supervision is now a pleasure. They are still irresponsible, however, as judged by normal social standards, but this is only to be expected, since leucotomy cannot give them personality attainments they never possessed. They have never been responsible citizens, and their personalities were still undeveloped when they were stricken with epidemic encephalitis. Although not mentally defective, they are below the average in intelligence and education, and it is doubtful if they will ever achieve full responsibility. Their capacity to learn may always be limited, but after 20 years of gross maladaptation we are satisfied with a reasonable degree of mental stability and a possible chance of continued development of their personalities.

It is recognized that the best results from leucotomy are to be obtained in individuals who have had well-integrated personalities. These subjects are often able to resume their former occupations, and ordinary tests of intelligence have, in uncomplicated cases, failed to reveal any special defect which could be attributed to the operation. This is borne out by our two patients, who show no appreciable degree of intellectual deterioration on the tests given, and their present social defects are more likely to be due to the virus than to the surgeon.

Ten years have elapsed since Moniz (1936) conceived of brain surgery for the relief of abnormal mental states, and considerable success has been achieved in the alleviation of many distressing symptoms in otherwise incurable psychotic states; much evidence has accumulated to suggest that the essential part of the operation consists in the interruption of fibre connexions between the hypothalamus, the thalamus, and the orbital areas of the prefrontal lobes, which, in effect, brings about a diminution in the emotional tension or irritability responsible for these symptoms. In this respect it is of interest to recall that William James (1901) maintained that the best proof of his theory of the emotions (that the immediate cause of the emotion is the physical effect on the nerves) lay in those pathological cases, found in every asylum, in which objectless emotion leads to unmotivated fear, anger, melancholy, or conceit. He might have welcomed leucotomy in support of his theory, for it may well be that, by the surgical interruption of affective-conative pathways, autonomic reactions are so modified that coarser emotions like anger and fear lose much of their intensity. Evidence of this is suggested by the finding of Reitman (1945) that the leucotomized patient shows a diminished response to autonomic stimuli.

Prefrontal leucotomy has already proved beneficial in the epileptic conduct disorders (Ström-Olsen *et al.*, 1943), and it is well known that emotional irritability is a characteristic feature of most of the psychopathic behaviour symptomatic of organic brain disease. It is questionable, however, whether the operation would be of equal benefit in the aggressive constitutional psychopath, since the morbid disposition in these cases is due to an innate or developmental imbalance of instinctive trends. Emotional tension is unusual, and many cases respond to psychotherapy and re-education.

Summary

Bilateral prefrontal leucotomy has been performed on two cases of post-encephalitic conduct disorder of 20 years' duration and present since childhood.

Complete alleviation of the aggressive and impulsive trends was produced in both cases, and has been well maintained over a period of two years and fourteen months respectively.

I am indebted to Sir Arthur Hall for much encouragement and advice.

REFERENCES

- Freeman, W., and Watts, J. W. (1944). *J. ment. Sci.*, **90**, 532.
 Gibbs, C. E. (1930). *Amer. J. Psychiat.*, **9**, 619.
 James, W. (1901). *Principles of Psychology*, **2**, 459.
 McKissock, W. (1943). *J. ment. Sci.*, **89**, 194.
 Moniz, E. (1936). *Lisboa med.*, **13**, 141.
 Reitman, F. (1945). *J. ment. Sci.*, **91**, 318.
 Ström-Olsen, R., Last, S. L., and Brody, M. B. (1943). *Ibid.*, **89**, 165.

PENICILLIN IN GONORRHOEA THE SINGLE-INJECTION METHOD

BY

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One of my main problems in the treatment of venereal disease in the Port of the Clyde was to cure, or at least render non-infectious, merchant seamen as speedily as possible. Many of those men by necessity of war conditions were able to attend only on one visit or two at most. Continuation of treatment was therefore very problematical. Some men were permitted to stay ashore the requisite length of time, but most seamen were reluctant to take advantage of this. It therefore became necessary to find a rapid method of curing men with gonorrhoea, or rendering them non-infectious, and with this in view a routine treatment of one single intramuscular injection of 200,000 units of penicillin was given. Very acute infections received 300,000 units. Concurrent urethral irrigations were also given if the seaman could attend; if not, their use on board ship was advised.

The supply of penicillin for this purpose was made available to me only in the last few months of the war, and in only 30 cases has enough time elapsed after treatment for a reasoned opinion to be formed of the efficacy of the method. Nevertheless I venture to put forward this small series for two reasons. (1) With the hope that, in some clinic dealing with larger numbers and where patients can be under more continuous supervision, the single-injection method will be tried out on enough cases to provide accurate statistics. (2) The present method of estimating the potent concentration of penicillin in the blood is too coarse—at least, so far as the gonococcus is concerned. The quantity of penicillin required to inhibit growth on artificial media can only roughly approximate to that required to inhibit growth *in vivo*.

Most of the early work on the penicillin treatment of gonorrhoea has been done by American workers. Uniformly good results are claimed in new and old cases, failed sulphonamide cases, and in articular gonococcal infections. All writers stress the importance of maintaining an adequate level of penicillin in the blood. Schemes for repeated injections vary in detail but are identical in principle—intramuscular or intravenous injections repeated at intervals of two or three hours. This undoubtedly maintains a definitely demonstrable level of penicillin in the blood. The same result can, of course, be reached by continuous intramuscular or intravenous drip, but this is hardly justified in gonorrhoea, for which out-patient treatment is a major consideration.

The Literature Reviewed

References to the use of penicillin in gonorrhoea are already voluminous, especially in American literature, but I here refer mainly to recent British medical literature.

McLachlan (1945) recommends 150,000 Oxford units administered in 5 doses of 30,000 units three-hourly, and reports it curative in "nearly all" cases; the gonococci disappear in two to four hours, and the discharge rapidly becomes mucoid and is often absent after 12 to 24 hours. Any cases failing to respond clear up with 100,000 or 150,000 units on the following day.

Harrison (1945) says penicillin is now the first line of attack in gonorrhoeal infections. He recommends 5 doses of 30,000 units two-hourly. Lloyd Jones and Maitland (1945) believe that the serum concentration must be such that a serum dilution of one in eight gives "serum inhibition," and recommend 5 doses of 30,000 units two-hourly. Lloyd Jones, Maitland, and

Allen (*Lancet*, 1945), in a masterly report on penicillin for early syphilis, give very interesting figures of penicillin levels in blood and urine. After a single intravenous dose of 300,000 units, penicillin is demonstrable in the blood for 6 to 7 hours after and in the urine up to 17 hours. Given intramuscularly, the same dose is detectable in the blood 7 to 11½ hours after and in the urine 17 to 23 hours.

Recently an element of doubt has been creeping in as to the absolute necessity for this maintenance of demonstrable serum levels. Lloyd Jones and Maitland observe that penicillin must be present in the blood for more than eight hours, though the amount is presumably too minute to be detected by our present laboratory methods.

Suchet (1945) quotes American observers who have shown that blood penicillin levels undetectable by bacteriological examination can still be clinically efficient. Dyar, Scholtz, and Hammond (1945) conclude that a total dose of 50,000 to 70,000 units given in 5 doses yields a cure rate of 83% and 100,000 units give 91%.

Discussion

It may now be reasonably assumed that first choice of medication in the treatment of gonorrhoea should be penicillin. It is also reasonable to assume that a patient suffering from gonorrhoea would prefer to be an out-patient than abed. That at once excludes the use of penicillin by continuous-drip methods. To continue the argument to its logical conclusion, the patient would prefer to attend as an out-patient once daily instead of two- or three-hourly for the injections. If this method can be proved to be equally efficient the medical profession also would undoubtedly prefer it. It would effect a great saving in time and trouble, and probably encourage patients to attend much earlier and more readily.

The cure of gonorrhoea by a single injection has been claimed by the American workers Romansky, Murphy, and Rittman, who use penicillin suspended in a beeswax-peanut-oil mixture; the rationale is that absorption is delayed, with consequently a more prolonged effect. Experiment showed this to be the case. The preparation of the beeswax-peanut-oil mixture is a troublesome procedure, but the results are good, and the method appears to offer the most promising line of study. Purely from a medical point of view, the overwhelming advantage of being able to cure gonorrhoea with one injection is obvious. From the social aspect its great advantages are rapid and complete cure with no prolonged and frequent clinic attendances to interfere with work or to invite publicity. No local ill effects from the injection of the beeswax-peanut-oil mixture are demonstrable clinically; histologically, in rabbits and hamsters minimum residual findings after several months were the only signs.

Urethral Irrigation

All writers are agreed that penicillin will cure gonorrhoea without concurrent urethral irrigation, and I can confirm this. Penicillin will readily lead to the death of the gonococcus, but it will probably have no direct effect on the inflamed mucosa. It is logical, in my view, to remove any products of inflammation by urethral irrigation with any bland fluid; saline would do, but time-honoured potassium permanganate is even better. It is quite conceivable that stricture would be much more prone to develop in a urethra which had not been mechanically cleansed of the products of inflammation.

The Single-injection Method Described

In this series the duration of symptoms before penicillin treatment was instituted varied from one day to six weeks. Ten of the cases had received sulphapyridine or sulphathiazole, but had failed to respond. On admission all the cases were clinically acute, with a copious purulent urethral discharge. In every instance the diagnosis was confirmed by microscopical examination. No cultures were made; and may I forestall any criticism on this point by saying that the number of non-gonococcal cases of urethritis whose smear shows Gram-negative diplococci morphologically indistinguishable from the gonococcus is very small indeed. Muir and Ritchie (1932) say the diagnosis on microscopical grounds alone is "practically conclusive."

The preparation used was sodium penicillin in powder form dissolved in 5 ml. of pyrogen-free sterile water, but ordinary