REFERENCES

Benjamin, H. (1954). *Amer. J. Psychother.*, **8**, 219.
East, N. (1949). *Society and the Criminal.* H.M.S.O., London.
Ellis, H. (1936). *Studies in the Psychology of Sex.* Random House, New York.
Fenichel, O. (1945). *The Psychoanalytic Theory of Neurosis.* Norton, New York.
Gardien-Jourd'heuil, M. P., and Gardien, P. E. (1948). *Ann. méd.-psychol.*, **106** (i), 52.
Hamburger, C., Stürup, G. K., and Dahl-Iversen, E. (1953). *J. Amer. med. Ass.*, **152**, 391.
Hirschfeld. M. (1910). *Die Transvestiten.* Pulvermacher, Berlin.
Kinsey, A. C., Pomeroy, W. B., and Martin, C. E. (1948). *Sexual Behavior in the Human Male.* Saunders, Philadelphia.
Krafft-Ebing, R. von (1916). *Psychopathia Sexualis.* Philadelphia.
Ostow, M. (1953). *J. Amer. med. Ass.*, **152**, 1553.
Peabody, G. A., Rowe, A. T., and Wall, J. H. (1953). *J. ment. nerv. Dis.*, **118**, 339.
Plichet, A. (1955). *Presse méd.*, **63**, 1245.
Seward, G. H. (1954). *Sex and the Social Order.* Penguin Books.
Vague, J. (1956). *Presse méd.*, **64**, 949.
Wiedeman, G. H. (1953). *J. Amer. med. Ass.*, **152**, 1167.
Worden, F. G., and Marsh, J. T. (1955). Ibid., **157**, 1292.

DISTURBANCE OF MOTOR FUNCTION DURING TREATMENT WITH IMIPRAMINE

BY

A. R. FOSTER, M.B., B.Sc., D.P.M.
Senior Registrar

AND

N. P. LANCASTER, M.D., D.P.M.
Consultant Psychiatrist
Barrow Hospital, Bristol

Imipramine hydrochloride ("tofranil"; N-γ-dimethyl-aminopropyl-iminodibenzyl hydrochloride) has recently been introduced into psychiatric practice. We have been using it for treatment of depressive illnesses and have observed some beneficial results. Some patients, however, have suffered side-effects of such a nature as to preclude further administration of the drug. It has been stated that side-effects are of minor consequence (Kuhn, 1958; Azima, 1959). It is our purpose to draw attention to other side-effects which have led to undesirable consequences even when patients have been under close supervision in hospital.

It would appear that incoordination of motor activity may be produced by the drug when used in therapeutic dosage. In our cases this has presented as falling, dysarthria, and coarse tremor. This may well be a manifestation of the dystonic type of motor disturbance already described by us (Lancaster and Foster, 1959) for imipramine and by Montgomery and Sutherland (1959) for perphenazine.

The following case reports are illustrative of these disturbances. The patients are predominantly female, as we personally deal largely with female patients.

Case Reports

Case 1: Endogenous Depression.—This patient, a woman aged 72, was the one responsible for drawing our attention to this type of symptom. She suffers from recurrent depressive episodes, and had previously been treated by electric convulsion therapy (E.C.T.) with much benefit. In this episode it was decided to give imipramine, and a course was begun, starting with 25 mg. b.d. and increasing by 25 mg. a day to 75 mg. t.d.s. After a few days she was reported to have fallen several times. She said that she "fell backwards" and, indeed, was observed to do just that. She would take several paces backwards and then fall down. One was reminded of the retropulsion of Parkinsonism. No rigidity or other signs to suggest this were found. Fortunately, although she fell down several times, she escaped injury other than bruising. She also complained of the previously described side-effects of dryness of the mouth, sweating, and constipation. She denied that there was any feeling of faintness, giddiness, or dizziness which might have suggested hypotension, and no alteration in the blood-pressure was observed. The drug was stopped in view of this disturbance and E.C.T. was given instead. There were no further episodes of falling, and she made an excellent recovery.

Case 2.—This woman, aged 69, was under treatment for endogenous depression—the fourth occasion since 1951 She also was observed by the nursing staff to "fall backwards." The patient described this as "losing my balance and going down backwards." It happened on several occasions. On one occasion she was staring rather vacantly out of the window, suddenly lost her balance, and fell over backwards. This patient is of special importance in this connexion, since while this paper has been in preparation she has continued to have imipramine 50 mg. t.d.s. Unfortunately, she has fallen again, and this time has suffered a fracture of the neck of the right femur.

Case 3.—A woman aged 55, with involutional depression. She was given imipramine to 50 mg. t.d.s. Two days later she complained bitterly of "pins and needles" in the arms and legs and of a dry mouth. A gross tremor of the hands and feet occurred, without rigidity. She slipped and fell on the fourth day of treatment and has to hold the bannister rail. She feels tottery, but denies any feelings of faintness or giddiness.

Case 4.—A woman aged 72, with endogenous depression. She is a diabetic, and has been a resident in the hospital for two years. She has poor eyesight, with a cataract in the right eye. She tends to become recurrently depressed and has been treated by modified E.C.T. This time imipramine was given in small doses—25 mg. t.d.s. Four days later she fell in the ward and suffered a fracture of the neck of the right femur.

Case 5.—A woman aged 72, with endogenous depression. Previously she had been treated with modified E.C.T. She relapsed within two months of leaving hospital in December, 1958. Treatment with imipramine was carried to quite high dosage and then reduced to 25 mg. t.d.s. She became a little brighter and less depressed, but E.C.T. was given subsequently. She developed a slurring dysarthria and a grossly ataxic gait, so that she had to be constantly attended by the nursing staff. Imipramine was withdrawn and the dysarthria and ataxia cleared up. Modified E.C.T. was continued and a good recovery made. Social factors are solely responsible for her further stay in hospital.

Case 6.—A woman aged 56, with endogenous depression. A long-stay patient living in the same villa for years. Imipramine was given for a depressive episode. She fell twice during treatment—bruises and abrasions only. The first time she slipped and fell while out walking. The second time she described how, while going upstairs, she felt paralysed, felt she had no control over her legs, and fell downstairs; she felt weak and shaky and her face began to sweat. She did not faint, however, and when seen by the nursing staff within a few moments was fully conscious.

Case 7.—A woman aged 47, with endogenous depression. An acute depressive illness. Given imipramine. Describes how she felt "giddy and faint" and fell "sideways on to the grass."

Case 8.—A man aged 49, a case of endogenous depression. He fell while in the "toilet" and suffered a fractured ankle while receiving imipramine in doses of 50, 50, and 75 mg. a day.

Case 9.—A woman aged 54, with involutional depression. Was treated once by modified E.C.T., then relapsed.

Imipramine given, as she refused further E.C.T. At one period she developed a coarse tremor of the limbs so that she dropped objects from her hands. She recovered from this disability when the dose of imipramine was reduced. In her case E.C.T. was also required.

Discussion

During the period covered there were no other fractures in the hospital, and the only other falls recorded in the ward casualty books were during three epileptic attacks. It should be emphasized that falls in a mental hospital may possibly be of considerable legal import and that the records are most carefully kept.

Although the cause of falling in these patients is difficult of proof, a reasonable case can be made for regarding the ones described as due directly to the ingestion of the drug.

Thus:—(1) None of the patients had previously fallen or shown any evidence of motor difficulties or instability. (2) Clinical examination had been uniformly normal. (3) Side-effects, already known to be attributable to the drug, were present. (4) All disturbances disappeared on withdrawal of the drug. (5) There was no unconsciousness, no "black out," and no clinical signs suggesting syncope or epilepsy. (6) One patient (described elsewhere) who ingested 1,500 mg. of imipramine in a "suicidal attempt" suffered from uncontrollable movements of the limbs of a dystonic nature, but not from syncope. (7) Minor falls of blood-pressure have been observed, especially in hypertensive patients. No actual hypotensive syncopal attacks have been seen. (8) The dosage of imipramine did not exceed that recommended by the makers for routine therapeutic administration.

We think that it is therefore possible to say that imipramine may produce disturbance of motor functions, in addition to any hypotensive effect that may be present; also, that from this aspect there are considerable individual differences in tolerance to the drug. In most cases these side-effects are of minor importance, but it should be borne in mind that in some they may lead to serious injury. This would appear to be more probable in the elderly. These observations confirm those made by English (1959), and may represent a serious limitation to the use of the drug.

It should be pointed out that no clinical trials have yet been published in this country and also that early reports can be regarded as no more than encouraging. We would therefore, for the present, advise caution in its use. There is little evidence so far that imipramine can replace E.C.T., which in its modified form has proved extremely safe and effective. Extensive trials will be necessary before the drug can be unreservedly recommended. In the meantime E.C.T. remains the treatment of choice for the severely depressed patient.

REFERENCES

Azima, H. (1959). *Canad. med. Ass. J.*, **80**, 535.
English, H. L. (1959). *Lancet*, **1**, 1231.
Kuhn, R. (1958). *Amer. J. Psychiat.*, **115**, 459.
Lancaster, N. P., and Foster, A. R. (1959). *Brit. med. J.* In press.
Montgomery, R. D., and Sutherland, V. L. (1959). Ibid., **1**, 215.

During the 12 months covered by the Family Planning Association's *Annual Report, 1958-9*, 340,000 people attended F.P.A. clinics, 20 new clinics were set up, making a total of 292, run by 242 branches, and at headquarters, on a conservative estimate, there were over 21,000 requests for advice and F.P.A. services.

C

INFECTIVITY OF THE PRIMARY TUBERCULOUS COMPLEX

SOME COMPLICATIONS IN CHILDHOOD

BY

A. W. DICKIE, M.D., D.C.H.
Senior Hospital Medical Officer, Londonderry

AND

R. D. G. CREERY, M.D., M.R.C.P., D.C.H.
Consultant Paediatrician, South Shields and District
(From the Royal Belfast Hospital for Sick Children)

Recent advances in methods of detection, prevention, and treatment of adult tuberculosis have lowered the incidence of infection and disease in childhood to such an extent that the demand for hospital accommodation for infected children has been greatly reduced. Most paediatric physicians in the British Isles are prepared to treat such children in open children's wards without isolation, but there are those, particularly in the Scandinavian countries, who believe this to be wrong and who regard childhood tuberculosis as potentially infective.

A survey was therefore carried out at the Lissue Branch Hospital of the Royal Belfast Hospital for Sick Children in 1953 and 1954 in an attempt to assess this risk. Out of a total of 374 admissions there were 103 actively tuberculous children. Of these, 72 had simple or complicated hilar adenitis, six had pleural effusions, and one had post-primary pulmonary tuberculosis. There were 13 children with cervical adenitis, five with bone and joint disease, two with mesenteric adenitis, and one each with lupus vulgaris, mastoiditis, chest-wall abscess, and pericarditis. Routine gastric lavages were not carried out on all these children, and only one was given antituberculous chemotherapy (the child with the suspected post-primary disease). The average duration of stay for the whole group was 85 days. Sixty-three children were tuberculin-positive and were presumed to be inactive—48 following natural infection and 15 following B.C.G. vaccination.

Method of Tuberculin-Testing

On admission to the Branch Hospital a diagnostic tuberculin jelly test was applied, irrespective of the tests carried out in the main hospital. This was read as positive or negative in most cases and as doubtful in a few. When the result was doubtful the jelly test was followed by a Mantoux 1/1,000; 10 tuberculin units.

Since the time that this survey was carried out there has been increasing criticism of the efficiency of the tuberculin jelly test. We were aware, even at that time, of the disadvantages of the test, and we therefore took great care in its interpretation. We limited the follow-up tuberculin test to the diagnostic jelly test when we thought the usual criticism of the reading of the test did not apply, as in each case it was clearly negative. This criticism almost always applies to the danger of false-positive results—that is, reaction to the strapping rather than to the tuberculin in the jelly. We feel also that the diagnostic jelly test was sensitive enough for our purpose, because if the individual had developed a primary complex he or she would have reacted quite strongly.

In those cases where the original test was negative, and in all the cases negative to Mantoux 1/1,000, a