PSYCHOSES DUE TO AMPHETAMINE CONSUMPTION

By

P. BEAMISH, M.B., Ch.B.

Registrar
Department of Psychological Medicine, Newcastle General Hospital

and

L. G. KILOH, M.D., M.R.C.P., D.P.M.

Senior Lecturer
Department of Psychological Medicine, University of Durham

INTRODUCTION

IN spite of the publication of Connell's monograph on amphetamine psychoses in 1958, the frequency of such states does not yet seem to be widely recognized even among psychiatrists. Nor is it fully appreciated in what unexpected settings such psychoses can occur, so that many cases must still be overlooked, masquerading for the most part as examples of paranoid schizophrenia.

Before Connell began collecting the material on which his monograph is based, only three cases of psychosis due to amphetamine had been published in this country and during the progress of his work only three further cases were described. Yet Connell was able to add 42 cases to this scanty literature. The frequency of the condition is again emphasized by the fact that in the past sixteen months, seven cases of amphetamine addiction, each of which has been seen in the Department of Psychological Medicine of the University of Durham, has at some period suffered a psychotic breakdown.

The first examples of psychosis associated with the taking of amphetamine were described by Young and Scoville (1938). Of three cases described, in one only was the psychotic episode definitely attributable to amphetamine. This was a man of thirty-four years taking 40–60 mg. of amphetamine daily for narcolepsy. He believed that he was being poisoned and expressed intense ideas of reference. He improved quickly once the drug was withdrawn. Increasing attention was paid to the condition on the Continent and eleven cases were described in 1954 by Bonhoff and Lewrenz. Many more cases have been reported from the United States of America, notably among prison inmates (Munroe and Drell, 1947).

The pattern of the psychiatric disturbances reported in the literature varies considerably. Cases of delirium are described by Brown (1945) and Delay (1950), acute mania by O'Flanagan and Taylor (1950) and catatonic states by Micheaux (1950) and Abely (1950). The greater number of the reports mention the existence of paranoid features, and in many the illness is described as taking the form of a paranoid psychosis (Herman and Naylor, 1954; Askevöld, 1959). Amongst Connell's cases the pre-eminent features of the psychoses were ideas of reference, paranoid delusions and hallucinatory experiences. Only three patients were disorientated and in two of these other factors existed which may have been responsible for this phenomenon.

https://doi.org/10.1192/bjp.106.442.337 Published online by Cambridge University Press

Case 1. A male patient aged 35 years whose parents belong to Social Class 1. During adolescence he developed a fetish associated with tension symptoms. In 1941 as a student he began to take "benzedrine", partly to stay awake at night and because he found that it increased his erotic sensations. In 1947 he suffered an attack of gastro-enteritis which persisted for about five weeks and was followed by an acute psychotic episode. He became paranoid and convinced that he had committed a murder which he had seen reported in the newspapers. He heard voices discussing and criticizing him and saw faces which peered at him from behind pillars. He was depressed and agitated and made a suicidal attempt. A diagnosis of paranoid schizophrenia was made and he was given a course of modified insulin. Within a year the same state recurred and he was treated with E.C.T. followed by a course of deep insulin. He continued to obtain amphetamine whilst in hospital and showed wide mood swings and fluctuating psychotic features. He was eventually discharged and remained out of mental hospitals for the next eight years, during which time he drifted from job to job. He then became acutely paranoid, thought he was the victim of an international gang and in 1956 sought mental hospital admission. His condition settled on chlorpromazine. Six months later his paranoid state returned and during the next year he was readmitted to hospital three times. The last of these admissions was prompted by a suicidal attempt with barbiturates. He continued to be aggressively paranoid and early in 1958 a prefrontal leucotomy was performed. On his discharge from hospital he began to take "persomnia"—as well as dexamphetamine—and was readmitted after taking an overdose. He was transferred to another hospital but absconded and was eventually admitted to this Department in August, 1958 after taking an overdose of chlorodyne.

He was quiet and withdrawn with flattened affect and showed a number of paranoid ideas relating to the details of hospital routine. There were no florid psychotic features. Whilst out one afternoon he took an overdose of chlorodyne and "persomnia" and in a subsequent search of his possessions many empty tubes of preludin were found. He admitted that he had taken it persistently for the previous six weeks whilst in hospital. A close watch was kept and during the next few weeks the patient lost his paranoid ideas and his insomnia. He became morose and more solitary and eventually took his own discharge. He has since been admitted to another mental hospital.

Case 2. A male patient aged 39 years belonging to Social Class 3. He was illegitimate and for many years had practised as a passive homosexual. He was invalided from the Army in 1943 on the grounds of psychoneurosis and subsequently took up nursing but failed to qualify. He vacillated between various nursing jobs and spent occasional periods in a Dominican Order. In February, 1953 he began to take methylamphetamine. During 1954 he increased the dosage to 100 mg. a day because of loss of confidence and towards the end of that year began to hear many distant, indistinct voices and felt that he was being followed about by the police. The voices became nearer and more distinct and people started to laugh at him. He was admitted to a mental hospital in April, 1955 where a diagnosis of paranoid schizophrenia was made. He was given a full course of deep insulin therapy. His symptoms ceased within a week of admission, before his first coma. He continued to take methylamphetamine after his discharge and towards the end of 1956 developed ideas of reference concerning his homosexuality. He was admitted to another mental hospital for four months where his symptoms rapidly improved. During 1957 he began taking mist. pot. brom. et chloral in quantities up to 5 ounces daily and by April he was again auditorily hallucinated and was once more admitted to a mental hospital. He heard voices which he recognized, accusing him of various delinquencies and the night after admission he saw "a full coloured film" on the walls of his room and through the window. in which a tremendous conspiracy against him was played out, culminating in the arrival of police cars. He continued to take mist. pot. brom. et chloral after his discharge and soon felt that people were talking about him and spying on him with glasses which could see through walls. His sleep became disturbed by hallucinatory voices which commanded him to go to various places and others which threatened police action. He was readmitted to a mental hospital in November, 1957 for a period of eight weeks. The diagnosis was regarded as schizophrenia and he was treated with E.C.T. and "frenquel". Following his discharge he began to take sodium amytal up to g. 18 daily with a small amount of "drinamyl". He felt tense, with strong feelings of insecurity and was admitted to another hospital where he was given lysergic acid with little effect.

Coming north, he obtained supplies of "drinamyl" from two doctors and was taking about ten tablets daily together with 250 mg. of preludin. He was admitted at the request of a general practitioner, who was alarmed at the quantities of "drinamyl" he was taking in view of his previous history. At this time he showed no psychotic features though he was very tense and anxious.

Case 3. A female patient aged 32 years belonging to Social Class 1. In 1953 for a period of several weeks she took large doses of pethidine following a miscarriage. When the pethidine was discontinued she began to take variable quantities of dexamphetamine and preludin. She had always been quick tempered, easily offended and an inefficient housewife and these character traits became accentuated at this time. In 1954 she showed a variable depression and made a number of threats to attempt suicide. Following the birth of a child she became very excited, restless and sleepless and was mildly disorientated and confused. She felt that her

https://doi.org/10.1192/bjp.106.442.337 Published online by Cambridge University Press

husband was trying to harm her and attempted to shoot him. She was admitted to a mental hospital but her transfer took several days and by the time she arrived her mental state was normal. Several weeks later it was realized for the first time that she was taking large quantities of drugs, including preludin—up to 50 tablets (1,250 mg.) daily. Her supply remained controlled until July, 1958, when she discovered it was freely available without requiring a prescription. During this period of over three years she was quarrelsome and subject to periods of depression but showed no psychotic features. She increased her intake of preludin and latterly was taking up to 75 tablets (1,875 mg.) daily. She became restless, clumsy and "appeared to do things too quickly"; she was mildly confused and seemed to have "a false idea of time". She felt that her husband and children were behaving in such a way as to get her into trouble and believed that her husband was trying to get rid of her. She felt that people outside were laughing at her and as a result became unwilling to leave the house. In the dark she saw ill-defined moving shapes "like a mirage" but retained insight into this phenomenon. She lost one stone in weight.

At various times in the past five years she has taken pethidine up to 300 mg. daily when available, alcohol episodically, small quantities of morphine, sodium amytal, which she found to be of no value, and promethazine hydrochloride, which she has taken in doses of 150 mg. as a sedative. Her paranoid features disappeared within a few days of admission to hospital.

Case 4. A male patient of 35 years belonging to Social Class 1. His previous history revealed evidence of psychopathic traits. For three years he had become increasingly aggressive and solitary and was retrospectively jealous of his wife, constantly questioning her about possible infidelities. Latterly he began to indulge in a lot of religious and metaphysical discussion. He admitted to taking dexamphetamine for a period of two years, latterly as much as 250–300 mg. daily.

On admission he appeared very tense. Much of his conversation centred around his search for perfection of a religious nature which he believed could be attained by a spiritual union of man and woman by a process he described variously as "binary fission" and "binary fusion". He believed that the world was going to end the following day and was convinced that a bearded fellow-patient was John the Baptist. In the presence of this patient his conversation on religious topics became rambling and almost incoherent. There was no clouding of consciousness.

His condition settled and he was allowed out. Once again he developed psychotic symptoms, insisting that people had given him drugs with some evil intent and that the nursing staff was putting "knock-out" drops in his tea. This state settled within 36 hours but for the following five days he was very depressed, lying in bed weeping. Both on admission and during this relapse his urine gave a positive methyl orange test for amphetamine.

This patient was still well a year after his discharge from hospital. The diagnosis of paranoid schizophrenia was considered very seriously in view of the form of his illness, but the clear relation of the psychotic episodes to dexamphetamine consumption left no doubt as to the true nature of the illness.

Case 5. A male patient aged 30 belonging to Social Class 1. During 1955 he began to take dexamphetamine to help him with his studies and shortly afterwards had to take quinalbarbitone for insomnia. During 1956 his work became erratic, he was unpunctual and he would often remain awake all night doing odd things about the house. After some months his behaviour improved and he remained fairly well until June, 1958 when various difficulties led him to increase his intake of drugs. His behaviour became increasingly disturbed. He accused his wife of inefficiency, of hiding his personal possessions, of lying and of stealing from him. During the next five nights he scarcely slept; instead he would wander restlessly about the house, abusing his wife's relatives and crying at times. Occasionally he would destroy books and small articles of furniture or throw them out of a window. He was aggressive to his wife on several occasions. During the day his behaviour was more controlled.

He was seen on the morning of the 5th day. He was restless, unable to sit still and his speech was slurred. At times he talked incoherently and he was unable to give a consecutive account of his illness. He was querulous and insisted that it was his wife who was mentally ill, not himself. There was evident clouding of consciousness. He was admitted to hospital where his mental state returned to normal in two or three days. In his possession were found large quantities of various barbiturate preparations, dexamphetamine and "drinamyl". He would not admit to taking more than therapeutic doses of these drugs.

Case 6. A female patient aged 19 years belonging to Social Class 4. The general behaviour and work record of this patient were characteristically psychopathic. She was associating with a married man and when her sister, with whom she lived, discovered this fact she was given the choice of breaking the association or leaving home. She had been attending her general practitioner because of tension symptoms with periods of variable depression and had been given a supply of "drinamyl". Following the squabble with her sister, impulsively she swallowed her entire supply of 50 tablets. Three hours later, on admission to hospital where her stomach was washed out, she was drowsy but there were no abnormal physical signs. Her pupils were normal, her pulse 76 per minute and her blood pressure 130/75 mm. Hg. Two

https://doi.org/10.1192/bjp.106.442.337 Published online by Cambridge University Press

hours after this she became restless, excited and appeared fearful. For 24 hours she was hyperkinetic, showed some clouding of consciousness with disturbed orientation and was both visually and auditorily hallucinated. The following morning her mental state was normal and she was able to give a clear account of herself.

Case 7. A male patient aged 36 years belonging to Social Class 1. This patient is unique in the series in so far as his psychosis was a withdrawal phenomenon. His addiction was to "desbutal", each capsule of which contains dexamphetamine 5 mg. and pentobarbitone sodium 30 mg., and it may be therefore that it was withdrawal of the barbiturate rather than of the amphetamine which played the major part in provoking his symptoms. He began taking "desbutal" in 1952 and latterly was taking up to 25 capsules daily. He was noted to have become bad tempered and to show mood swings and since 1956 his work had become very erratic. He would sleep at odd times during the day and for periods seemed dazed and would stagger. He decided to stop taking his capsules and three days after became mildly confused, wandered restlessly through the house at night and insisted that there was a stranger in the room with him. He was admitted to hospital after a further three days following a single grand mal convulsion. He was confused, showing disturbed orientation with a degree of confabulation. He was hallucinated, stating that he saw blue fish behind the curtains and in the ward syringes and that there were mice under his bed. This state continued for 48 hours and recurred in diminishing degree during the following six nights. Subsequently his mental state became normal and he has remained well for the past year.

Discussion

It might be expected that the consumption of large quantities of the amphetamine series of drugs would give rise to clouding of consciousness with delirious features, excitement and evidence of overactivity of the sympathetic nervous system. In fact such states do occur, as in Cases 5 and 6, but this is not the common picture. In the majority, the picture resembles more closely that of paranoid schizophrenia and if there is any clouding of consciousness it is of such subtle degree as to remain undisclosed by clinical examination and the use of ancillary methods of investigation. Without knowledge of the drug intake and an accurate picture of the development of the psychosis, it is all too easy to misdiagnose the condition as schizophrenia. This is well exemplified by Case 1, who had been regarded as a schizophrenic for a number of years and who had received courses of E.C.T. and of deep insulin therapy in various hospitals, culminating in a prefrontal leucotomy carried out largely because of disturbed behaviour associated with his auditory hallucinations. We, too, were content at first to accept this diagnosis, though he showed no florid psychotic features, until his large intake of amphetamine and preludin came to light. Another of the series (Case 2) had received a course of deep insulin treatment after a firm diagnosis of schizophrenia had been made, but the correct diagnosis was made during his second episode when he was admitted to another hospital. In other cases, the diagnosis of schizophrenia was strongly suspected or considered, only to be abandoned when the aetiological agent was discovered.

As a rule, once suspected, the diagnosis of amphetamine psychosis is easily confirmed by ensuring that the drug intake ceases. Amphetamine addicts are at least as resourceful as chronic alcoholics and tablets are particularly easy to conceal. Nevertheless, an experienced nursing staff should have no great difficulty in eliminating the possibility of amphetamine consumption once this has been considered. The psychotic symptoms can be expected to disappear within a few days of drug withdrawal, though it is likely that as in other symptomatic psychoses an occasional patient may continue to have symptoms for weeks or even months after the causal agent has been removed. In five of Connell's cases, symptoms persisted for 2–4 weeks and in two for more than 4 weeks after withdrawal of the drug. Persistence of symptoms for many weeks was a feature of two cases described by Chapman (1954).

https://doi.org/10.1192/bjp.106.442.337 Published online by Cambridge University Press

In the great majority of cases, withdrawal of amphetamine can be carried out without danger. Depression or sleepiness may occur and it is possible that occasionally a psychosis may result. Askevold (1959) describes four cases in which acute delirious reactions occurred 3–10 days after the withdrawal of amphetamine. Three of these cases were also taking barbiturates and in one, the psychosis was preceded by convulsions. Nevertheless, the author believes that the effective agent was amphetamine. In Case 7 described in this paper, a withdrawal psychosis occurred after a latency of three days, but in view of the coexisting heavy barbiturate consumption, it is difficult to attribute this entirely to amphetamine.

Clinically, the first psychotic episode associated with amphetamine may be difficult to distinguish from a process disorder, but in a long-standing case there are a number of points which suggest the true diagnosis even though the drug intake be denied. Behavioural disturbances of a psychopathic kind are frequently present long before the onset of the illness; the history is often remarkably episodic, the psychotic symptoms generally responding quickly to hospitalization, whatever form of treatment is given. Once the episode has been terminated by withdrawal of the drug, however long the total duration of the illness, it is apparent that there is little or no evidence of personality deterioration. The patient's powers of abstraction are unimpaired, there is no particular paucity of ideas, no limitation of interests, no withdrawal and no autistic features.

The methyl-orange test as modified by Connell (1958), though time consuming, is of value in detecting the presence of amphetamines in the urine and in estimating their amount. It has the disadvantage that other amines also give a positive result. Paper partition chromatography can be used when it is felt necessary to use a test of absolute specificity.

Before the commencement of their drug addiction, evidence of an abnormal personality is common in these patients. In some, the personality disorder appears to be emphasized and aggravated by the amphetamine and grosser disturbances of behaviour may be displayed. This was seen in Cases 3, 4 and 6. A case not described above, as at no time did he show psychotic features, may also be relevant in this context. This was a man of twenty-five years who both as a child and an adult had found great difficulty in making satisfactory interpersonal adjustments. Whilst in the R.A.F. he suffered periods of amnesia and was eventually discharged following a suicidal gesture when arrested for being absent without leave. He began to take up to 24 tablets of dexamphetamine and "drinamyl" daily at the age of 19½ years and shortly afterwards claimed that he felt he was really a woman and occasionally dressed up in female clothing. He persisted in these views for two years and was regarded and treated as a transvestist. When his intake of amphetamine was discovered and curtailed, he proclaimed that the views he had expressed were "a load of rubbish" and since this time his behaviour has been more stable. This patient is so psychopathic and unreliable a witness that too much importance should not be attached to his history. However, the suggestion remains that not only was his psychopathic behaviour aggravated whilst he was taking dexamphetamine but transvestist tendencies were brought to light, fading when the drug intake ceased.

All the cases described in this paper, in fact, showed evidence of a psychopathic personality as defined by Schneider (1950) before they became addicted to amphetamine. This is a common observation in published cases (Herman and Nagler, 1954; Monroe and Drell, 1947), though in two of the cases described by Nandelstadh (1957) it is claimed that there was no evidence of

https://doi.org/10.1192/bjp.106.442.337 Published online by Cambridge University Press

any previous psychopathic traits. The added disability of recurrent psychotic episodes renders the achievement of such social adaptation of which the patients might be capable much more difficult and is reflected in their work records. This was particularly evident in Cases 1 and 2, whilst in others, Cases 4 and 5, the full realization of their potentialities appears to have been prevented by the drug intake and its consequences. As with other drugs, it seems that amphetamine addiction is likely to arise only in patients of abnormal personality. The factor of opportunity is also evident in this series, five of the patients described having access to the drug through their nursing or medical duties.

Another striking feature is that in many of the cases, excessive quantities of other drugs were also taken from time to time. Varying amounts of barbiturates, preludin, alcohol, potassium bromide, "persomnia", chloral, pethidine, chlorodyne and morphia were taken by different patients and sometimes it appeared almost immaterial what was taken providing the quantity was large enough. In Case 2 a psychotic episode indistinguishable from those occurring earlier as the result of amphetamine, followed the consumption of large quantities of bromide and chloral. Levin (1947) has described thirteen cases of bromide intoxication in which a schizophrenic-like illness resulted. Three patients who encountered difficulties in acquiring sufficient supplies of amphetamine, found a satisfactory substitute in preludin. These three patients have taken large quantities of this drug and in one of them the psychotic episode which occurred appeared to be largely attributable to this agent. The recent literature confirms the increasing frequency of psychotic illnesses due to preludin and in the last two years a number of such cases have been reported in this country (Bethell, 1957; Clein, 1957; Glatt, 1957; Kahan and Mullins, 1958; Silverman, 1959). The psychosis may take the form of a schizophrenic-like illness, or may be accompanied by clouding of consciousness and disorientation. Preludin can still be purchased freely from chemists' shops and it would appear highly desirable that it should be placed on Schedule IV of the Poisons Rules at an early date.

The series of cases described in this paper shows two trends which appear to be typical of amphetamine psychosis. The frequency of the condition is greater in males than in females and, as emphasized by Askevold (1959), the social status of these patients—at any rate before the commencement of the period of addiction—tends to be high. Five of the seven patients described belonged, at least for a period, to the Registrar General's Social Class I.

It is of considerable interest that a euphoriant drug should give rise to a clinical picture so similar to that of schizophrenia. The simplest explanation of this fact would be that an incipient or latent schizophrenia had been brought to light by the amphetamine. The cases described in this and other papers provide little or no support for this view. The course of the illness differs sharply from that of schizophrenia, as has already been emphasized. Furthermore, in the seven cases described, in none could a history be obtained of any schizophrenic relatives. As already noted, in one of our patients a psychotic episode of the same kind was associated with a high dosage of bromide and chloral. Langfeldt (1957) points out that the majority of drugs of addiction may give rise to paranoid reactions, though in this respect amphetamine appears to be particularly potent. In no way can such paranoid states be regarded as specific effects of amphetamine, for, apart from the fact that so many other agents give rise to a similar picture, amphetamine itself may on occasion give rise to other forms of psychosis. Similar schizophrenic-like illnesses may be associated with aetiological agents other than drugs. That an epileptic psychosis

https://doi.org/10.1192/bjp.106.442.337 Published online by Cambridge University Press

can take a form clinically indistinguishable from schizophrenia is a matter of common observation. Both myxoedema and pernicious anaemia may give rise to paranoid psychoses and the picture of alcoholic hallucinosis (Benedetti, 1952) has many similarities. Some cases of post-operative subacute delirium, in which such clouding of consciousness as may be present has to be inferred, bear a very close resemblance to amphetamine psychosis, and their distinction from schizophrenia is made more on the obvious relationship to the operation and on their favourable outcome than from differences in the clinical picture. Particularly in the case of amphetamine psychosis, it is tempting to view the condition in the light of some of the theories concerning the aetiology of schizophrenia, notably the view of Hoffer and Osmond (1959) that the symptoms result from the products of abnormal adrenaline metabolism. That the same clinical picture results from so many processes suggests that the immediate aetiologies may be related. The paranoid psychosis may be regarded as the expression of a final common path. In the case of schizophrenia, this is activated by a metabolic abnormality dependent in part on genetic structure. It is also capable of activation by many other metabolic disturbances, including the excessive consumption of amphetamine.

Summary

Seven cases are described in which psychotic illnesses occurred in association with amphetamine consumption.

In four of these the diagnosis of schizophrenia had been made or was seriously considered.

In two cases, the psychosis took the form of a delirium and in one a delirium occurred as a withdrawal phenomenon. In this latter case, barbiturates may have played a more important aetiological role than amphetamine.

The differential diagnosis of paranoid psychoses due to amphetamine consumption from schizophrenia is considered.

Acknowledgments

We are most grateful to Professor Martin Roth and to Dr. P. H. Connell for their advice and co-operation.

References

Abely, P., *Ann. méd.-psychol.*, 1950, **108**, 354.
Askevöld, F., *Acta Psychiat. et Neurol. Scand.*, 1959, **34**, 145.
Bendetti, G., *Die Alkoholhalluzinosen*, 1952. Stuttgart: Thieme.
Bethell, M. F., *Brit. med. J.*, 1957, *i*, 30.
Bonhoff, G., and Lewrenz, H., *Über Weckamine*, 1954. cit. Askevöld, F. (q.v.). Berlin, Göttingen, Heidelberg.
Brown, C. T., *Milit. Surg.*, 1949, **104**, 365.
Clein, L., *Brit. med. J.*, 1957, *i*, 282.
Connell, P. H., *Amphetamine psychosis*, 1958. London: Chapman and Hall.
Delay, J., *Methods biologiques en clinique psychiatrique*, 1950, pps. 394 and 446. cit. Connell, P. H. (q.v.). Paris: Masson et Cie.
Glatt, M. M., *Brit. med. J.*, 1957, *i*, 460.
Herman, M., and Nagler, S. H., *J. nerv. ment. Dis.*, 1954, **120**, 268.
Hoffer, A., and Osmond, H., *J. nerv. ment. Dis.*, 1959, **128**, 18.
Kahan, A., and Mullins, A. G., *Brit. med. J.*, 1958, *i*, 1355.
Langfeldt, G., *Laerebok i klinisk psykiatri.*, 1951. cit. Askevöld, F. (q.v.). Oslo.
Levin, M., *Amer. J. Psychiat.*, 1947, **103**, 229.
Micheaux, L., *Ann. méd.-psychol.*, 1950, **108**, 354.
Monroe, R. R., and Drell, H. J., *J. Amer. med. Ass.*, 1947, **135**, 909.
von Nandelstadh, O. W., *Acta. psychiat.*, 1951. Kbh. Suppl. **60**, 164.
O'Flanagan, P. M., and Taylor, R. B., *J. Ment. Sci.*, 1950, **96**, 1033.
Schneider, K., *Die Psychopathischen Persönlichkeiten*, 1950. Vienna.
Silverman, M., *Brit. med. J.*, 1959, *i*, 69.
Young, D., and Scoville, W. B., *Med. Clin. N. America*, 1938, **22**, 637. Boston Number.

https://doi.org/10.1192/bjp.106.442.337 Published online by Cambridge University Press