A CLINICAL AND PSYCHOMETRIC STUDY OF THE EFFECTS OF PROCAINE AMIDE IN HUNTINGTON'S CHOREA

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INTRODUCTION

BENEFICIAL results with procaine amide in the treatment of Huntington's Chorea were first reported by Goldman (1952). He was led to make an oral trial of the drug after having noticed a patient in the dentist's chair improve following an injection. He found improvement in six cases with the typical syndrome of Huntington's Chorea, of whom four had a positive family history of the disease. The evidence of improvement in these cases was partly based upon clinical observation and partly upon the patient's account of changes in his daily experience, for example, his first case had difficulty in eating, which had led to protests from other customers at a restaurant he had frequented, and this disability is said to have been satisfactorily reduced with the help of the drug.

DeMyer and Dyken (1954) studied nine cases of Huntington's Chorea using procaine amide one gramme four times a day, as employed by Goldman. They found no objective evidence of improvement but remarked that seven patients unequivocally maintained that they were better. Pleydell (1954) treated six cases with oral procaine amide and noted "no beneficial effect which could be attributed to the use of the drug". Lazarte *et al.* (1955a) observed three patients of whom two were co-operative and all had a positive family history. They provided standardized tests of manual ability in addition to taking motion pictures and making clinical observations, and they found much day-to-day variation but no consistent improvement either subjectively, or on clinical observation or in the performance of the objective tests. Their scheme of dosage, however, departed from that of Goldman in significant respects. Most recently, Forrest (1957) using finger-dexterity tests in two cases and scoring the involuntary movements in two others, has been unable to confirm the occurrence of any reduction in hyperkinesis from the administration of procaine amide or any improvement in performance. He believed more benefit to follow from the use of reserpine, as did Lazarte *et al.* (1955b) and Chandler (1955).

Favourable reports on East Indians with the disease have been made by Cohen (1956) and Ganguli (1956). Cohen's case showed objective clinical benefit from as little as 0·25 g. procaine amide, b.d., and this improvement was consistently maintained and extended to the mental state of the patient who was better able to perform mental arithmetic. Ganguli's case showed subjective benefit and some improvement in movement.

Following on these mixed reports, this paper presents an attempt to evaluate the worth of the drug by using both clinical and formal objective tests in an adequate number of patients.

Material and Methods

Six male patients and two female patients, all with mental changes beginning in adult life, were investigated. In five of these cases there is a history of closely similar illness in a parent or sibling. In one more case (J.J.F.) the patient's testimony is inaccurate and unsupported by other evidence but he states that his sister is also affected. Both parents, however, reached the age of sixty-eight and died without showing definite overt signs of the disease when visited in their home by the psychiatric social worker. In a further case (L.M.) the patient's antecedents are unknown and difficult to trace and there are indications that her parents may have been psychologically abnormal. Lastly in the remaining case without a family history of the illness (G.W.G.) the patient's father died at the age of forty-nine in a way which could conceivably be due to the commencement of choreic disturbances, having a fatal fall while working at his trade of steeplejack.

The average age of the patients at the time of study was fifty-four years (to the nearest year), the youngest being forty-three and the oldest sixty-six, and the average known duration of the illness from the date of observed onset was eight years. In no case was there reason to suspect other types of organic illness in the central nervous system and in five cases the constituents of the cerebrospinal fluid, the Wassermann reaction and Lange curves in the cerebrospinal fluid, and the blood Wassermann and Kahn reactions were known to be normal. In the remaining three cases where only the Wassermann and Kahn reactions in the blood were known there was also no serological abnormality.

Observations were made to the same pattern in all cases except L.M., whose clinical course is described separately. The observations were made first before treatment with procaine amide hydrochloride (Pronestyl, Squibb). The remaining seven patients were then given procaine amide orally in increasing doses reaching the level of 1·0 g., q.i.d. in all but one case, J.McA., who became drowsy when receiving 0·5 g., q.i.d. and was then given d-amphetamine 5 mg. morning and noon together with this lesser dose of Pronestyl. The individual top dosage was then maintained in these seven patients for four weeks and the preliminary observations were repeated during the fourth week. The procaine amide was then stopped in the same seven and the final observations were made in the third week after complete cessation of the drug.

Five types of observation were taken into account throughout:

1. Subjective report.
2. Details of nursing needs, physical activity and habits.
3. Examination of the involuntary movements and physical state.
4. Written records of performance.
5. A block-sorting test of manual dexterity.

Special observations were made on the mental state before and during treatment but were subsequently abandoned as showing no difference of note between these two periods.

The observations on the physical state consisted of: (*a*) noting the presence and range and counting the frequency by stop-watch of the involuntary movements; (*b*) noting the performance in the finger-nose co-ordination test; (*c*) examining the gait; and (*d*) making any additional observations which were particularly relevant (e.g. whether there were any changes in the Parkinsonian features in the case of V.F.).

In securing written records the patient was presented with a pencil and a duplicated form on which he was requested to draw a straight line between two marked points and to write—"I see the cat" on a marked line. Each of these actions was requested three times on each occasion before, during and after treatment and the written instructions were supplemented by word of mouth.

The block-sorting test was deliberately chosen for simplicity and ease of comprehension by demented patients. Even so it was beyond the capacity of one case (L.M.) and almost beyond that of another (J.McA.) who required repeated careful instructions. It consisted of a tray with a central grey compartment $10 \times 7 \cdot 5 \times 1 \cdot 4$ inches and one white and one red compartment on either side, each of the latter being $7 \times 7 \cdot 5 \times 1 \cdot 4$ inches. All the compartments were open at the front. Twenty red and twenty white blocks $1 \cdot 4 \times 1 \cdot 4 \times 0 \cdot 8$ inches were mixed together in the central grey compartment and the subject was instructed to sort them out into the compartments of their own colour, red in red and white in white, the process being first demonstrated and the patients being instructed to carry it out as quickly as possible without regard to tidy placing of the pieces so long as they were dropped and remained in the appropriate compartment. The particular piece of apparatus used was specially constructed for this trial and made from wood. Average normal adult subjects complete the sorting in from sixteen to thirty seconds as a rule and after repeating their initial run-through show no appreciable gain in speed due to learning. Mentally defective patients who were chosen to provide some near standard of comparison with the Huntingtonian cases took from fifty to seventy seconds. They were mainly high-grade epileptic imbeciles and showed a tendency to cross their hands in sorting and make uneconomical and clumsy movements. They also showed no significant improvement due to learning after the initial explanation and run-through. Like them the patients in the series were given the opportunity of familiarizing themselves with the test before the first series of observations was begun.

RESULTS

A. Case Histories

Case 1: J.J.F., male, 53 years old. Married. Separated. Parents said to be cousins but both reached old age without showing definite signs of choreic or psychological illness. One sister, not seen but said by patient to have same condition. Illness manifest in 1949 with sudden outbursts of rage and "dirty habits". But he had previously been discharged from the Army on psychiatric grounds as unable to drill and a persistent absentee. In 1951 admitted to hospital in a state of dementia and in 1955 choreiform movements were clearly apparent. Cerebrospinal fluid normal and blood Wassermann and Kahn reactions normal. At the time of this investigation he was slovenly in his person and tended to be doubly incontinent several times a week. His speech was explosive, slurred, incoherent and fragmented; gait unsteady and lurching and he was unable to walk heel-to-toe; subject at rest to more than forty involuntary movements per minute in each upper limb and could hardly touch his nose with his finger when requested. The dementia is evidenced by his idea of the date—24 August, 1939—the actual date being then April, 1957, and by his answer of thirty-four to the request to take seven from one hundred.

During treatment with procaine amide the performance of the finger-nose test improved and his finger-placing was relatively accurate and his incontinence was less (about once a week instead of thrice) but there was no improvement in gait or orientation. After stopping the procaine amide the slight improvement in his habits remained but performance in the finger-nose test deteriorated to its former level. Subjectively he was pleased with the tablets while having them but once they were stopped he was got to say that he was better without them.

Comment: No definite evidence of improvement.

Case 2: V.F., female, 43 years old. Married. Her grandfather died in a mental hospital, her father died of unknown causes, a brother committed suicide and a sister died in Cherry Knowle Hospital with chorea and dementia. Signs of illness appeared in 1947 with a facial

tic and mental changes when she was admitted to Cherry Knowle Hospital during her fifth puerperium. In 1957 immediately before treatment with procaine amide she was dementing steadily and was fatuous, facile, unoccupied and disorientated. Physically she was plump and slow in voluntary movement. Her speech was slurred and limited to single words and she showed one or two irregular movements in one part or another successively, the rate in each arm being about one to two per minute. The pupillary reactions and fundi were normal but the facial musculature was mask-like and spastic despite an occasional grimace. The only other abnormality in the cranial nerves was a bilateral partial nerve-deafness. Her hands were hyperhidrotic yet cold and her arms showed obvious cog-wheel rigidity with pathologically increased tendon-reflexes; performance in the finger-nose test was mildly impaired and her voluntary finger movements were stiff. In the legs there was a lead-pipe mixed spastic and Parkinsonian rigidity and rapid rhythmical sustained fine clonus obtainable at the left patella and both ankles; the tendon-reflexes were much increased but the plantar responses were flexor. Her gait was spastic on a wide base and she was thought to have the widespread changes of the disease referred to by Bell (1934) and which are not infrequent in advanced cases.

Under treatment with procaine amide the mental state and physical signs described altered only in the following respects. Involuntary movements were about five to ten per minute in each upper limb, her gait was stiff but improved and her performance in the finger-nose test was accurate. However, she said the tablets were "awful" and made her feel sick and during the period of treatment with procaine amide she developed an infection of her left fourth finger for which her wedding-ring had to be removed; there was no agranulocytosis however or systemic disturbance and the infection responded satisfactorily to penicillin. After stopping the procaine amide her speech and gait appeared worse and her feeding habits more slovenly. Her conversation was reduced to slurred syllables only. Her performance in the finger-nose test however remained fairly accurate and there was no other change of note. Involuntary movements were at a frequency of five to seven per minute.

Comment: No definite evidence of improvement.

Case 3: G.W.G., male, 58 years old. Married. Separated. His father died aged 49 from a fall whilst working as a steeple-jack. No other family history available to suggest hereditary chorea. Illness manifest in 1955 when he ceased working as an electrician's mate in a transport undertaking. Increasingly worse after admission to hospital and subject to an organic type of dementia with paranoid delusions additionally; thus he was poorly orientated and when asked to take seven from one hundred answered "eighty-nine" and he also asserted that he was in the C.I.D. and in charge of the hospital. Before treatment with procaine amide his speech was rambling, slurred and incoherent. Involuntary movements were present at a rate of some thirty to forty per minute in each upper limb. Performance in the finger-nose test unsteady and inaccurate; gait unsteady and shuffling and unable to walk heel-to-toe. Wassermann and Kahn reactions normal in blood and cerebrospinal fluid.

During treatment with procaine amide involuntary movements were reduced to less than ten per minute in each upper limb; no other signs of improvement or deterioration however. Condition essentially the same on stopping treatment but involuntary movements returned to thirty to forty per minute in each upper limb. Subjectively unchanged maintaining throughout—"There's nothing wrong with me".

Comment: The hyperkinesis did appear to benefit. Otherwise no improvement occurred.

Case 4: G.A.H., male, 43 years old. Married. Mother died in Cherry Knowle Hospital with chorea and dementia. Patient had been deaf for many years (secondary to old otitis media) and prone to temper tantrums all his life. Admitted to hospital in 1954 with a pyrexial illness finally labelled influenza but accompanied by pain in the head, back and legs. His cerebrospinal fluid was normal in all respects. In 1957 he gave a history of generalized pains in the arms and legs, present for ten years, and in January, 1957 he complained of pain in the lower part of the back, radiating to the right leg and ankle and sometimes to the left. At that time the physician who examined him observed that there was a scoliosis and limitation of straight leg raising to 45° on the right side but no muscle spasm and no other abnormality on spinal radiography. It was thought further that the scoliosis was grossly exaggerated by the patient and that the limitation of his spinal movements which was observed was voluntary. He then came under psychiatric care and was observed to show some slurring of speech and choreic movements at rest which were exacerbated during voluntary activity; there was also a typical choreic disorder of muscle control evident in the grasp and worse with excitement or during attempts to co-operate by making particular voluntary movements. His legs were frequently drawn up while he grimaced with pain and his hamstring muscles went into fluctuating spasm and he was tender over his sciatic spines and also over the right ilium in the region of the hip-joint. There was no other abnormality in his motor and sensory systems on objective examination. His emotional state was one of euphoria and mild fatuity except in relation to his pains where his attitude was passably normal.

Further investigations revealed no local cause for these pains although they were thought at first by a consultant physician to be due to local irritation of peripheral nerves by carcinomatous deposits. Radiographs of the pelvis, hips, femora, humeri and both shoulders showed no abnormality; plasma proteins, serum calcium and phosphorus and acid and alkaline phosphatase estimations were within normal limits and there was no protein (including

Bence-Jones protein) in the urine. On 14 March, 1957, his haemoglobin was 16·6 g. per cent., white blood cells 16,500/c.mm., neutrophils 76 per cent., lymphocytes 16 per cent., monocytes 6 per cent., eosinophils 2 per cent. and the E.S.R. 22 mm. at 1 hour (Westergren) and there was some nasal catarrh but no pyrexia. By 27 March, 1957 these figures had altered to W.B.C. 8,700/c.mm., with a normal differential count and the E.S.R. was 4 mm. at one hour. These were the only abnormal laboratory findings at any time and meanwhile the administration of procaine amide was commenced beginning with 0·5 g. q.i.d. on 9 March, 1957 and rising to 1·0 g. q.i.d. on 18 March, 1957 and subsequently for four weeks as with the other cases. The pains did not respond to aspirin or other simple analgesics or even to pethidine 50 mg. by mouth and they continued to cause him immense concern. They were finally regarded as either purely functional or as an unusual manifestation of the central neuropathic process of Huntington's Chorea. Although this has not been previously recorded the latter conclusion is not untenable in the light of subsequent developments.

Before receiving procaine amide, the patient was complaining of numerous pains in the leg and he lay about with his limbs drawn up, quite unoccupied. Involuntary movements were at a frequency of three to four per upper limb per minute and his performance in the finger-nose test was excellent. During treatment with procaine amide less than none to one involuntary movements per upper limb per minute were observable and his pains underwent a steady improvement and were abolished and he could perform straight leg raising to ninety degrees and walk about easily. On ceasing procaine amide pain soon re-appeared in his back although not to the same degree as formerly and he could still walk about although unsteadily. The involuntary movements were at a frequency of 15 per upper limb per minute.

At the end of the trial period he was re-started on procaine amide 1·0 g. q.i.d., and discharged from hospital symptom-free. This state continued for one month when the dose of his procaine amide was reduced to 0·25 g. q.i.d. and he soon re-appeared at the out-patient department with his old pains and hobbling. Since restoring the dose to 1·0 g. q.i.d., he has again improved.

Comment: There was considerable objective and subjective benefit in this case but the exact symptoms that improved most are not ordinarily linked with Huntington's Chorea. The more typical Huntingtonian features showed slight improvement.

Case 5: J.McA., male, 53 years old. Widower. His father died in another mental hospital with some of the physical signs of general paresis at the age of 38 years. No serological evidence was recorded. His sister, C.E., died in Cherry Knowle Hospital with gross chorea and dementia; she had previously contracted G.P.I. which was treated with full doses of penicillin and with malarial therapy but her deterioration continued after this treatment in 1948–49 until her death in 1952, aged 44 years.

The patient himself had no abnormality in the C.S.F. cells, protein, serological reactions and colloidal gold test and his blood Wassermann reaction and Kahn test were negative. He was a joiner and at first was a good workman and husband. In 1939 he fell ill for the first time after joining the Home Guard from which he was speedily released. He had a "nervous breakdown" and was off work for eighteen weeks and his wife regarded him as altered from that time, being irritable and unruly. In 1951 he was admitted to hospital for the first time after having attacked his wife with violence and choreic movements were first recorded in 1955. The movements were very variable in their frequency at different times both before, during and after treatment, ranging from none to forty per minute for all parts of the body taken together so that no effective comparison was possible.

Before treatment his speech was restricted in content and the patient was grossly disorientated; speech slow and intelligible, occasionally explosive but never more than a few syllables uttered at a time. Performance in finger-nose test accurate and gait steady. No evidence of improvement during treatment but subjectively pleased with tablets, saying—"They give you strength".

Comment: No evidence of significant improvement or deterioration.

Case 6: L.M., female, 66 years old. Married. Separated. Family history obscure and indefinite as patient's own father and siblings were unknown to her children, patient's mother died of asthma aged 42 years, and patient was reared by a step-father. Signs of mental illness are said to have appeared in 1940. In 1944 she was treated temporarily in hospital for "nerves and jaundice". In 1950 she was admitted to a London mental hospital suffering from a "paraphrenic psychosis" and in 1952 she was transferred to Cherry Knowle Hospital, at which time choreiform movements were evident.

In this case it was not possible to follow the same plan of investigation as in the others; the reasons for this will be apparent from the account following.

In January, 1957 she was up and about but was very thin and subject to incessant involuntary movements in all parts at a rate well exceeding eighty per minute in each of her upper limbs. She was fatuous and demented, her speech was very limited and slurred and she was extemely greedy, bolting any food within her reach. She was then given procaine amide in doses rising to 0·75 g. b.d. with the apparent effect of slightly lessening her movements. After four weeks, however, she appeared to be still deteriorating generally and the drug was stopped on 24 February, 1957. Within twenty-four hours of stopping the procaine amide however the illness took a dramatic and unexpected turn. Her movements increased in number and

amplitude quite markedly beyond anything previously seen and they were so extensive and she was so agitated that she could hardly be kept within her cot-bed. In fact on the same day she fell over the side and sustained very extensive bruising. For the next two days she was nursed in the protection room and sedated with barbiturates and on 28 February, 1957 procaine amide was recommenced in increasing doses. Before resuming the drug she was fatuous, euphoric and dirty in her habits. She handled faeces indifferently on the floor of the protection room before wiping her face and she did not have one syllable of coherent intelligible speech. Her movements were as described. On 5 March, 1957 after three days' treatment with procaine amide 0·5 g. 6-hourly she had improved and could again be nursed in the open ward. She spoke enough to say—"I'm doing fine now" and to give her Christian name and her movements were less extensive although not apparently diminished in frequency; and she could walk unaided. At this time she looked toxic and this was attributed to the effects of absorption of extravasated blood. Further increases in the dose of procaine amide were made but had no beneficial effect that could be detected and by 12 March, 1957 the movements were again becoming extensive and troublesome; even her tongue protruded irregularly at an uncountable rate. Difficulty in swallowing appeared and the same day she could only take fluids and her 6.00 p.m. dose of procaine amide was only taken in part; steady deterioration continued until she achieved a restless sleep with the help of amylobarbitone sodium, grains iii. Next morning, 14 March, 1957 at 2.30 a.m. she vomited about a pint and a half of brownish fluid and died half an hour later, pale and exhausted.

At autopsy no particular immediate cause of death could be demonstrated and it was supposed that her end was directly due to the Huntington's Chorea, occurring in a fashion observed in others with this illness.

Comment: Symptomatic benefit of moderate degree was considered to have resulted from the use of procaine amide in this case, but without influencing the final outcome or progress thereto. The events immediately after the stopping of the drug raised the question of a "rebound phenomenon" which is further discussed below.

Case 7: N.M., male, 62 years old. Single. Two brothers stated by acquaintance of family to have died of illness similar to Huntington's Chorea and one other sibling said to be affected. Illness known to have been present since 1950 but not admitted by patient who was certified on his admission to hospital in 1956. He had been in receipt of a disability pension for nearly total deafness due to wounds suffered in the 1914-18 War and had not worked for many years. He was cared for by his landlady who finally could manage him no longer and at the time of his admission to hospital showed slurring of speech and generalized choreo-athetoid movements. There was no abnormality in the cerebrospinal fluid and the blood Wassermann reaction was normal. Before receiving procaine amide he was subject to about ten involuntary movements a minute in each upper limb; his speech was repetitive, incoherent and slurred and his performance in the finger-nose test was accurate but jerky. His gait was lurching and he was altogether very much worse when attempting set tasks or when excited.

Under treatment with procaine amide he was subjectively no better, saying—"There's nothing wrong with me. I don't need medicine." Movements were at a frequency of twenty to thirty per minute in each upper limb and there was no definite improvement (or deterioration) in speech, co-ordination or gait. On ceasing procaine amide his movements were at a rate of sixty per minute in each upper limb and appeared somewhat increased in amplitude and his performance in the finger-nose test was inaccurate as well as jerky. He protested how well he was and his gait and speech were unchanged.

Comment: There was no indication of definite improvement but this case (like Case 6—L.M.) also raised the question of whether deterioration had occurred since the start of treatment or whether there was a "rebound phenomenon".

Case 8: J.W.W., male, 57 years old. Divorced. Cause of death of his parents unknown but his daughter was admitted to a hospital in the London region in 1956 with signs of a "rapidly progressive form of Huntington's Chorea". Other members of family of J.W.W. were also believed to have been affected. The patient was known as a conspicuous figure with choreiform movements even before his admission to hospital in 1953 on the death of his father.

Immediately before the administration of procaine amide he was being nursed in a cot-bed. He was deluded that the nursing staff were grossly ill-treating him and he was disorientated and frequently used very foul language. His speech was slurred and incoherent and he was subject to numerous grimaces, head movements and movements of the limbs at a rate of more than eighty per minute in each part. His tongue sometimes protruded and the head and limb movements were of considerable amplitude; following any excitement or an enema they were worse; at meal-times he broke crockery some two or three times a week owing to his lack of control and when he had a bath it was the usual practice to sedate him with amylobarbitone sodium grains iii, as otherwise there was no possibility of his escaping harm owing to the amplitude and vigour of his involuntary movements. He could scarcely do formal tests of co-ordination and his performance in the finger-nose test was wildly inaccurate.

During treatment with procaine amide he was observed to be much less querulous and complaining (without being drowsy). His movements were still more than eighty per minute

in each upper limb but their amplitude was thought to have diminished. There was some improvement in his performance of finger-nose test and his performance in the written tests was distinctly better (he was the only case in which this was so). He spilt less food and rarely broke plates and although he looked thinner and more "peaky" his weight in fact fell by less than three pounds from an original one hundred pounds. During this period of treatment with procaine amide he was also receiving a prophylactic course of sulphaguanidine owing to the occurrence of dysentery in the ward.

On stopping the procaine amide the movements of each part became, if anything, more frequent (although they were already so numerous as to make comparison difficult). They were of greater amplitude however and again necessitated sedation before his bath and it was also necessary to give him a tin basin from which to feed in place of crockery. Further, immediately after stopping the procaine amide his tongue made frequent involuntary protrusions, keeping his lips wet, a phenomenon not previously observed and which disappeared in two to three days. His subjective response was favourable whether he was receiving tablets or not.

Comment: It was considered that some improvement occurred under the drug and this was another case in which the occurrence of a "rebound phenomenon" appeared quite likely.

On these clinical assessments three patients (G.A.H., L.M., and J.W.W.) are regarded as having shown some acceptable improvement from the administration of procaine amide but in one of them the symptoms which seemed most particularly to be benefited are not characteristic of Huntington's Chorea. In these cases the general improvement is partly parallel with some reduction in the frequency of involuntary movements. The figures obtained for the latter are summarized in Table I and it will be observed that two other patients (G.W.G., and J.McA.) also showed this trend but that one patient (V.F.) showed most movements during the period of treatment (which she disliked). The remaining two patients (J.J.F. and N.M.) showed more movements during treatment than previously but more still on ceasing treatment.

TABLE I

Frequency of Involuntary Movements at Rest

Patient	Movements in Each Upper Limb per Minute		
	Before Procaine Amide	During Treatment with Procaine Amide	After Procaine Amide
J.J.F.	40–50	60–80	Over 80
V.F.	1–2	5–10	5–7
G.W.G.	30–40	10	30–40
G.A.H.	3–4	0–1	15
J.McA.	2–3 (Very variable)	0–2	5–7
L.M.	Uncountable	Uncountable	Uncountable
N.M.	10	20–30	60
J.W.W.	Over 80	60–80	Over 80

B. Formal Tests

The written tests before, during and after treatment were given to all cases except L.M. In one instance (J.W.W.) they showed a marked improvement during the treatment period but much of this improvement, although not all, was maintained after treatment. The other cases showed no significant variation.

The results for the block-sorting test are set out in Table II. In four out of seven cases the best mean performance time occurred in the treatment period. In two cases (J.J.F. and J.McA.) the mean times worsen steadily on each occasion and in one case (G.A.H.) they improve steadily on each successive occasion. The overall mean time taken before treatment was 1 minute 21 seconds, during treatment 1 minute 10 seconds and after treatment 1 minute 32 seconds (to the nearest second). These results show a surface trend favouring the treat-

ment. However, the standard deviation of only one of them (the mean figure during treatment of 1 minute 10 seconds) is 40 seconds and without further calculation it is apparent that these figures are not statistically significant.

TABLE II

Performance Times in Block-Sorting Test of Manual Dexterity

Patient	Before Procaine Amide				During Treatment with Procaine Amide				After Procaine Amide			
	Test Times			Mean Times	Test Times			Mean Times	Test Times			Mean Times
J.J.F. ..	133	151	127	137	144	146	158	149	168	142	144	156
V.F.	97	90	97	95	85	72	71	76	124	124	136	128
G.W.G. ..	65	37	46	49	53	46	37	45	59	46	40	48
G.A.H. ..	45	38	41	41	37	39	33	36	30	36	34	33
J.McA. ..	90	97	98	95	111	108	90	103	119	108	123	117
N.M. ..	62	55	55	61	27	27	27	27	34	29	33	32
J.W.W ..	99	83	90	91	49	55	57	54	68	76	74	73
Average of mean scores				81				70				83

The times taken are given in seconds to the nearest second.
Standard deviation of average of mean scores during treatment = 40 seconds.

SIDE EFFECTS

Procaine amide is widely used in the treatment of cardiac arrhythmias and a considerable literature exists on its administration and possible toxic properties. In general it appears to be a fairly safe drug, its commonest side effects being nausea, vomiting and gastric discomfort. In the one case in this series (V.F.) where vomiting occurred, it ceased on the withdrawal of the drug. The same patient, as recorded, had a finger infection while receiving the drug but showed a normal leucocyte response. Agranulocytosis has, however, been recorded (Inouye *et al.*, 1951; Miller *et al.*, 1951) and is an occasional hazard as are severe hypotensive reactions and ventricular fibrillation. These latter phenomena do not appear to occur with the oral form of the drug.

In this series there were no untoward hypotensive reactions and the blood-pressure did not vary excessively in the cases in which a worthwhile reading was obtainable (i.e. all except L.M. and J.W.W.). Likewise there was no granulocytopenia found on routine counts of the white blood cells in all cases during the treatment period and the only additional occurrence to remark is the somnolence which appeared in J.McA.

DISCUSSION

Textbook accounts of Huntington's Chorea (Brain, 1955; Kinnier Wilson, 1940) tend to stress the inexorable, unremitting course of the disease; so also does the major account of the illness given by Bell (1934). Until the studies of Lazarte *et al.* (1955a) no one seems to have thought it worth while to comment on the considerable day-to-day fluctuation which can occur in the frequency and amplitude of the involuntary movements. It is however, well recognized that sleep abolishes the movements in various forms and in hemiballismus and it should not be surprising conversely if excitement exacerbates them. In fact Wilson (1940) did recognize these variations in Sydenham's Chorea, and such changes have often been observed in the patients in this series. Further, although in this study care was taken to count the movements under quiet conditions when the patient was not excited or too much interested in his surroundings it proved very difficult to obtain conditions that could be regarded with satisfaction as "basal". Indeed so long as the immediate presence of the doctor is noticed by the patient it is impossible to assume that such conditions are present

and accordingly only limited weight can be placed upon observations that the movements are decreased unless this effect is consistently maintained. Likewise, the character of the subjective response to the drug is seen to be of little help in determining its value and can only be assessed by a personal appreciation of the patient's attitudes, as will be evident from the reports of several of these cases, particularly V.F. and L.M.

The results of formal test have been inconclusive in other studies (Lazarte *et al.*, 1955a; Forrest, 1957) as in this one. When the wide range of facility in these patients is considered and the many factors capable of affecting the results (including the mental state of the patients) this is not perhaps surprising. It still may be of more value in assessing the worth of procaine amide in this condition if clear examples can be given of facultative improvements with or without the drug. Goldman (1952) does this for procaine amide as do Lazarte *et al.* (1955b) for reserpine, and in the present series where improvement has been accepted as taking place it has been accepted in substantial part on that basis.

The possible occurrence of a "rebound phenomenon" on cessation of the procaine amide was first remarked in the case of L.M. and again in that of J.W.W. In the later cases it seemed of less significance but the case of L.M. discouraged the use of a blind trial of the drug using a placebo. In the light of the other cases this is now a less serious consideration. From the fact that in J.W.W. some of the "rebound phenomena" improved over the course of a week it would appear unlikely that the apparent "rebound" was due to the unmasking of deterioration occurring during the treatment period and concealed by the taking of the drug. And also from the limited evidence so far available it does not seem as if the occurrence of this "rebound phenomenon" need be a contra-indication to giving the drug to patients who might benefit, since it subsides quickly and the patient can be tided over the intervening period with barbiturate sedation if necessary. But like chlorpromazine in excited patients procaine amide in Huntington's Chorea may have the advantage over barbiturates of producing symptomatic benefit without causing undue somnolence.

In this series the majority of patients did not benefit from the drug but some did show what was regarded as valid improvement and it still seems to be the correct policy to give it an adequate trial in all cases of adult chorea unless contra-indicated.

SUMMARY

Procaine amide hydrochloride (Pronestyl, Squibb) was given to eight patients with Huntington's Chorea. Seven of these patients were subjected to tests of manual dexterity and accuracy and all the patients were assessed clinically before, during and after treatment with the drug. There was no significant improvement in test performance during the period of drug treatment but two cases showed symptomatic motor benefit. Of these two, one died, it is believed, from the ordinary progress of the disease. Six patients showed no definite signs of improvement or deterioration. Attention is drawn to the difficulty of assessing alterations in the frequency of the involuntary movements and the occurrence of a possible "rebound phenomenon" on ceasing the drug is noted. It is concluded that procaine amide should be given an adequate trial in all cases of adult chorea unless contra-indicated.

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