and these patients tend to be more excitable than normal. They may be made worse by the excitement of attending a clinic or being admitted to a ward, while some are made worse even by a visit from a friend. From hospital records it is apparent that many patients have deteriorated on arrival in a ward and gradually improved spontaneously over two to three days.

Neglected nutrition and personal tidiness are often found in affected patients, who will improve greatly after these are corrected in hospital or when the patient is induced to live with relatives. Incidental febrile illness such as influenza has often been found to accentuate the choreic symptoms in our patients. The influence of alcohol and the improvement following abstinence has frequently been demonstrated in this series.

Religious tendencies were noted in some patients but assumed serious proportions only in the cases of K, IV 32 and N, III 27. Superstition and religion are commonly intertwined with the life of any fishing community and are well in evidence here.

Features of persecution, aggression, and grandiose behaviour are occasionally found in the hospital records.

"That form of insanity which leads to suicide" is part of Dr. George Huntington's original description of the disease. Bickford and Ellison (1953) have observed a high incidence of suicide in their series in Cornwall and give this as a reason for some of their cases receiving awards for gallantry during the war. The fishermen of North-East Scotland have long had a reputation for skill, endurance, and courage. This is probably a feature of the breed, whether affected or not, and as the patients here reviewed have a complete lack of insight it is unlikely that self-destruction need be feared here. Suicide has been suggested for only one patient (L, III 5), but of course cannot be verified.

Sexual forms of mental disturbance have been observed by American writers, who claim that it is commonly part of Huntington's chorea. This tendency does not occupy a prominent place in the accounts in this country and was encountered only once (P, IV 8) in this series.

Neurology.—Accurate information about the neurological changes is available for a very few of the cases in this series. The majority appear to have presented the typical picture, and the spread of the disease has followed the usual pattern, with individual variation covering a wide range. One case (K, IV 26) showed an increase in muscle tone suggesting an extension of the disease process to neighbouring areas. The involvement of the respiratory muscles by chorea is reported by Julia Bell (1934) as a great rarity. An example of this complication has been noted in R, III 2.

Summary

Huntington's chorea appears to have been first recognized in the Moray Firth area in 1893.

The disease is not found in the families of Highland stock, and some of the reasons for this are given. The affected patients can all claim their origins from one small fishing village in Ross-shire which was probably settled about 300 years ago. The place whence those peoples came is uncertain.

The earliest case of Huntington's chorea diagnosed by implication is S, II 1, who was probably born about 1810.

The pedigrees of seven affected families have for the first time been disentangled and are presented with some suggested links between them.

Some psychiatric aspects are discussed and mention is made of the clinical features employed locally for early diagnosis.

For the great interest and encouragement shown in this work I thank Dr. J. Ronald. Both he and Dr. Martin Whittet have kindly made all their hospital records available. Without the very willing help of the physicians, psychiatrists, local practitioners, and the district registrars, this survey could never have been completed.

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NON-HEREDITARY CHRONIC ADULT CHOREA AS A CLINICAL ENTITY

BY

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When Dr. George Huntington (1872) first described the form of chronic adult chorea which now bears his name he emphasized "its hereditary nature," stating that "it is confined to certain and fortunately a few families, and has been transmitted to them, an heirloom from generations away back in the dim past."

The appearance of Huntington's chorea in patients whose parents have been free from the disease has long been the subject of debate, and family circumstances are seldom clear enough to be acceptable as proof. In the Moray Firth area we find a sufficiently regular pattern of spread to permit conclusions being drawn from the breeding habits of patients' ancestors in assessing the likelihood of hereditary disorders.

During a recent survey of the disease in this area it has been shown that all the choreic patients can trace the family origin to a small fishing village in Ross-shire. These fishermen appear to have settled here about 300 years ago and to have kept themselves quite apart, marrying within their own community or occasionally bringing brides from other ports. In contrast to this nest of Huntington's chorea, two patients were discovered who appear to resemble true cases of Huntington's chorea so closely that they were in fact given this diagnosis, but on scrutiny they lack the necessary hereditary background.

Family A

This clan's name is mainly associated with Inverness-shire. A small branch has for many years been settled in Sutherland, and this family can be described as small farmers who lived and worked about five miles from Bonar Bridge.

A, I 4.—No details of this man's parents could be verified though he is known to be of Highland stock. He died of tuberculosis about the age of 40, four years after his wife (*A, I 5*), who had the same complaint and is also considered to be a Highlander.

A, II 5.—This woman was born in 1900, was brought up by a maternal grandmother, and married a farm servant in 1922. About 1945 she found a nervousness starting, particularly when she was excited. Three years later a "fidgeting" of the right hand began and has slowly progressed to involve all the limbs. Hospital assessment was undertaken in 1950. She was noted to be emotional and to have constant coarse jerking movements of the arms, face, and head. The right leg was spastic. In the ensuing years the family moved several times and regular medical supervision was lost until traced for the present review. Both her person and the house showed signs of moderate neglect. The chorea was more obvious in the arms than in the legs. Her head often jerked and the tongue and mouth muscles were also involved. The limbs showed a slight increase in tone; reflexes were slightly increased but the plantars were flexor. Electroencephalograms did not suggest cortical degeneration. The patient has become a little

depressed from time to time but is generally well composed mentally and has a good memory. There had been no obvious deterioration of function nor increase in chorea over the past 10 years. No suggestion of Huntington's chorea is noted in the children, the eldest of whom is 37 years old. The evidence which was taken as supporting a hereditary disorder was that the following two relatives had a "shake" and this was further examined.

A, I 2.—This man died some years ago, but those who remember him describe the typical picture of Parkinson's disease.

A, II 1.—The eldest sister of the patient has a tic of the right hand. This was present at the time of her wedding over 40 years ago, and although it varies a little there has been no progression. This sister is mentally normal. Her daughter has some hesitation of speech and her son has a spastic torticollis.

Family B

The clinical details of *B, III 3* were obtained from the local mental hospital, where she was admitted on October 31, 1943, and where she died six years later. This patient grew up in a farming family. Her parents had been farm servant and housemaid at an estate in Easter Ross-shire at the time of their wedding in 1881. The paternal grandfather was a farm worker and the maternal grandfather a saddler. The family fortunes rose and the patient's father became first a small-holder, then moved to a farm a few miles east of Inverness.

The patient moved about, taking housekeeper's jobs, and it is perhaps significant that she was on the point of becoming engaged to be married but had to return home urgently to nurse (for 12 years) her mother, who had suffered a shock. Thereafter the patient looked after her father, who was a "fine old man" and who died at the age of 84.

For the next few years she continued housekeeping and is described as being "old-maidish" and given to affectations.

At the beginning of October, 1943 (aged 47), she became nervous and excitable, with frequent grimacing and wild claims that she was going to be married. She had delusions of supposed associations with the man.

As the excitement and confusion became worse she was admitted to hospital with the diagnosis of an acute confusional state. Physical examination showed a fine tremor and erratic co-ordination. In hospital she became gradually calmer, but about two months later jerking choreiform movements were observed. A diagnosis of Huntington's chorea was made.

FAMILY B **Discussion**

It has already been shown that Huntington's chorea is not uncommon in the Moray Firth area but that it is confined to those connected with a fishing community.

The ancestry of the two patients described here has been traced back about 100 years without finding any relatives with chorea. There has been no association with the fishing families, and any connexion is most unlikely in earlier times because of the almost complete lack of mixing among the fisher folk, the clansmen, or the farm servants. Nobody can disprove that the affected gene may have been implanted illicitly into this otherwise healthy stock. Such an explanation is, however, extremely unlikely in view of the complete lack of promiscuity among the fishermen that was demonstrated during the survey.

Spontaneous mutation must be considered as a cause for these isolated cases, but insufficient information is available on which to base useful comment.

It will have to be left to the future to decide whether *A, II 5* has a hereditary disorder. She has four living children, the eldest of whom is 37, but none shows a tendency to chorea. *B, III 3* has no offspring, and her sister's children, aged 35 and 40 years, are unaffected.

On the present evidence, therefore, we can fairly claim that these two patients do not have a hereditary disorder. The second case might well correspond to Paracelsus's classification of chorea lasciva, but a diagnosis of chronic adult chorea is preferred.

As suggested by Julia Bell (1934), the appearance of athetosis in adults depends more on the site of the histological changes than the pathological process involved, and a chronic adult form other than the hereditary chorea of Huntington must be clearly recognized. The importance of this lies not so much in obtaining a purity of diagnosis as being able to advise the relatives with conviction. If extra work is required to clarify the aetiology of a patient's chorea the ability to remove the shadow from the oncoming generations is the reward.

Summary

The cases of two patients who bear a superficial resemblance to Huntington's chorea are described. The reasons against the condition being hereditary are explained and the importance of a diagnosis of non-hereditary chronic adult chorea is stressed.

I am indebted to those medical colleagues and the district registrars of births and deaths who made the ancestry of these patients so clear.

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DRUG TREATMENT OF HUNTINGTON'S CHOREA

A TRIAL WITH THIOPROPAZATE

BY

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In Huntington's chorea the main features requiring treatment are dementia and a psychosis, in addition to the chronic choreic movements from which the title derives.

In ancient times some patients were said to have had their heads opened to allow the escape of devils, and Vessie (1932) has described how many were burned as witches in Connecticut. When these remedies fell into disfavour it was not, however, because any more effective therapy became available.

With the first description of the condition, Dr. George Huntington was able to draw on experience of many years with the affected families, but he recognized that "treatment seems to be of no avail." In more recent times Russell Brain (1951) states that no form of treatment is known to arrest progress of the dementia or to control the involuntary movements, and Kinnier Wilson (1954) can only offer institutional care for the choreic.

Drug treatment has often been sought, and up to about 10 years ago sedatives must have formed the basis of most schemes of treatment, phenobarbitone being the one most widely used. More recently various different substances have been claimed as cures but have not shown up well in practice. A suggestion by Tomlinson (1947) that an extract of Bulgarian belladonna was helpful has been denied by De Meyer and Dyken (1954). Goldman (1952) conducted a trial with procainamide after the chance observation that a patient relaxed well after an injection for a dental extraction. De Meyer and Dyken (1954) did confirm a subjective response to this but showed no improvement in any of their patients' chorea. Reserpine was advocated by Chandler (1955) and Lazarte *et al.* (1955). Nielsen and Butt (1955) reported from Los Angeles a poor result with the use of dimercaprol.

Over the years some of the patients described in our local survey have been tried on these drugs but rather spasmodically and by many different observers (see Table). In tabulating these results for convenience it should be noted that dosage has varied and is not mentioned, the stage of the patients' disease has varied, many patients had died before the newer drugs were available, and the observations are so lacking in standardization that any slight improvement has been noted. Where no sign appears there is no record of that drug being given. The patients' numbers refer to the classification in the preceding articles.

The variables already mentioned make impossible the assessment of these results in concrete terms. The table does bear out the impression of several local practi-

tioners that the advent of the phenothiazine derivatives has for the first time brought some measure of relief to their patients. Compared with the hopelessness of previous experience these results have been an encouragement to continue the search for a substance

Response to Various Drugs by Patients with Huntington's Chorea

Patient	Phenobarbitone	Belladonna	Tolazoline	Amlylo-barbitone	Procainamide	Diethazine	Ethiopropazine	Benztropine	Benzhexol	Reserpine	Mephensin	Propantheline	Chlorpromazine	Prochlorperazine	Acetyl-promazine
A, II 5	+														
C, IV 13	++					+									
K, V 2	++			+											
P, IV 5	++														
P, IV 8	++														
P, IV 9	++			+				+							
R, III 2	++			+											
R, III 4	++														
T, IV 8	++					+									
T, IV 11	++														
T, V 9	++			++									+		
N, III 27	++			++									++		
C, IV 9	++														
K, IV 32	+														

+ = Some improvement. — = No response.

which will be effective. To this end a controlled trial has been carried out with thiopropazate dihydrochloride (1 - (2 - acetoxyethyl) - 4[3 - (2 - chloro-10-phenothiazinyl) - propyl] - piperazine dihydrochloride; "dartialan"; SC-7105).

Method

Many local peculiarities made it possible to collect together only five cases of proved Huntington's chorea, and to these was added a case of non-hereditary chronic adult chorea. Patients whose condition had advanced beyond hope of improvements were not included, nor were any who were suspected but unproved.

In order to achieve a standard environment for the trials the patients were all treated at home, as previous experience had shown that hospitalization could help or worsen the chorea over short periods. Fortunately none of the patients suffered any serious infections which might have affected their condition adversely.

Though the patients were specially examined before, during, and after the trial, the regular visits were paid by their own practitioners, men with local knowledge and much experience of this disorder.

In view of the small number of patients concerned it was not practicable to follow the double-blind technique. Instead the patients formed their own controls