

A CASE OF RECURRENT SYMPATHETIC EXCITEMENT :
ITS TREATMENT AND SOME OBSERVATIONS ON
PARASYMPATHETIC STIMULANTS.

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THIS case has shown so great an improvement by symptomatic treatment with parasympathetic stimulants and a sympathetic depressant that it seems worthy of record for its own value, apart from the interesting investigations to which it leads.

HISTORY AND PREVIOUS TREATMENT.

The patient is *æt.* 25, well built, athletic and in excellent physical health ; undescended testicles are his only evidence of deformity or degeneration. There is no family history of insanity. His school days were not very happy ; he came down from the University without taking a degree, and was working in an office until his first period of excitement five years ago, which was followed by a succession of similar disturbances with some intervening confusion. The following year he was admitted to this hospital in an acutely maniacal condition. For a month he had daily continuous baths, and by this time had become quiet, amenable, and able to occupy himself in many different ways. A full pathological investigation failed to reveal any focus of infection or metabolic disorder. He had a series of thirty weekly injections of testicular extract (·5 grm. of dried gland in each), followed by another course of six injections alternating with a calcium and vitamin D preparation. Dried testis was given in 5-gr. doses three times daily by mouth, and sun-baths during the summer months. Blood iodine estimations were made (1) at the Courtauld Institute of Biochemistry with the following results :

In a normal period (July 31, 1933)	insoluble iodine	3γ/100	c.c.	soluble.
		6γ/100	„	„
In an excited period (August 22, 1933)	„	3·5γ/100	„	„
	„	7γ/100	„	„

For the next year he was on a low protein diet with large quantities of milk and two tablets of tyranormone three times daily. Tyranormone is a German preparation which antagonizes the action of the thyroid, and has been used with success in the treatment of hyperthyroidism. The estimations were then repeated :

When normal (July 2, 1934)	insoluble iodine	9 γ /100	c.c.	soluble iodine.
		6 γ /100	„	
When excited (December 4, 1934)	„	5 γ /100	„	„
		28 γ /100	„	

(This specimen of blood was slightly hæmolysed.)

Since his admission he had been at various times either excited, confused or normal, and it was noticeable that his confused periods were growing relatively longer.

CORRELATION OF MENTAL AND PHYSICAL SYMPTOMS.

Since August, 1934, a daily record has been kept of his mental condition, and several physical factors. Each morning whilst lying down his blood-pressure has been measured with a baumanometer; his left arm has always been used (2), and the readings taken at the same hour from day to day. Gillespie (3) found considerable variations in this reading with no change in the mental state, but in this case the values reflected so accurately his condition that there seems no doubt of their inter-dependence. Unlike the results usually obtained in these series the diastolic pressure varied with the systolic pressure, though to a less degree.

The pulse-rate was taken, the knee-jerks tested and the pupils examined during excitement as well as being observed periodically at other times. The morning urine volume was measured; that for the whole day could not be collected. The chloride percentage was estimated by the Volhard method, and also sugar when present. The specimens were collected as soon as he awoke.

The complete curve strikingly illustrates the cyclical nature of his mental condition and the accompanying variations in the physical factors, in particular the blood-pressure, the morning chloride percentage and the reducing substance in his urine.

For about ten days he was apparently normal; he would read, write, play games, go out to matches and to the cinema. His blood-pressure was 110 to 120 mm. Hg., his pulse-rate below 60 per minute, his urine gave no reduction with Fehling's solution, and the morning chlorides were below .6%.

Irregularities in his dress and conduct could then be seen. Euphoria was followed by increasing confusion, and after two or three sleepless nights he grew so hallucinated, impulsive, dirty, noisy and destructive that he was unfit to be with the other patients or to sleep in his own bedroom. His blood-pressure had risen to 140 mm. Hg. or higher, his urine chlorides to more than 1.4%, the pulse-rate to over 100 per minute, his reflexes had become very brisk, his pupils dilated, and his urine contained between .2 and .5% of sugar (Fig. A).

After about a week he became quieter and could be moved back to his own

room, but he remained confused and hallucinated for perhaps another three weeks, seeking to isolate himself and taking no interest in the things about him. His blood-pressure had fallen to its normal level or perhaps lower, the chloride values showed considerable variations, his pulse-rate was between 70 and 80 per minute, and his urine gave no reduction.

Another excited phase followed, resembling the first, then suddenly his condition returned to normal. In two or three days his blood-pressure fell by some 30 mm. Hg., the urine chlorides by 1%, and the pulse-rate by about 40 per minute (Fig. B).

TREATMENT.

After three similar cycles had been observed, successive attacks of excitement were treated as follows :

(1) With a parasympathetic stimulant : Further experience showed that the amount used was not sufficient ; $\frac{1}{100}$ gr. eserine was given one day and $\frac{1}{30}$ gr. two days later, producing a fall in pulse-rate of 8% and 12% respectively in two hours. There was no apparent sedative action.

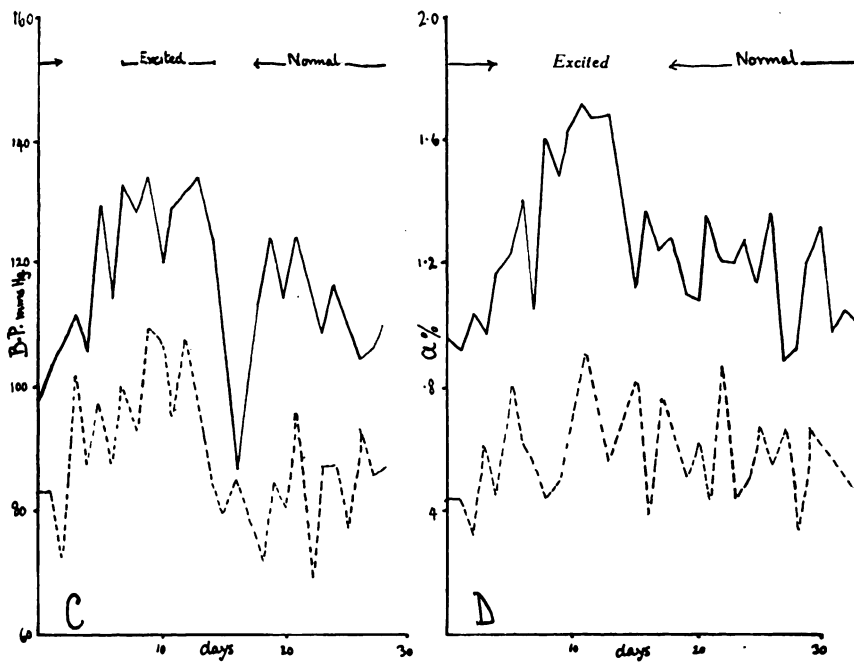
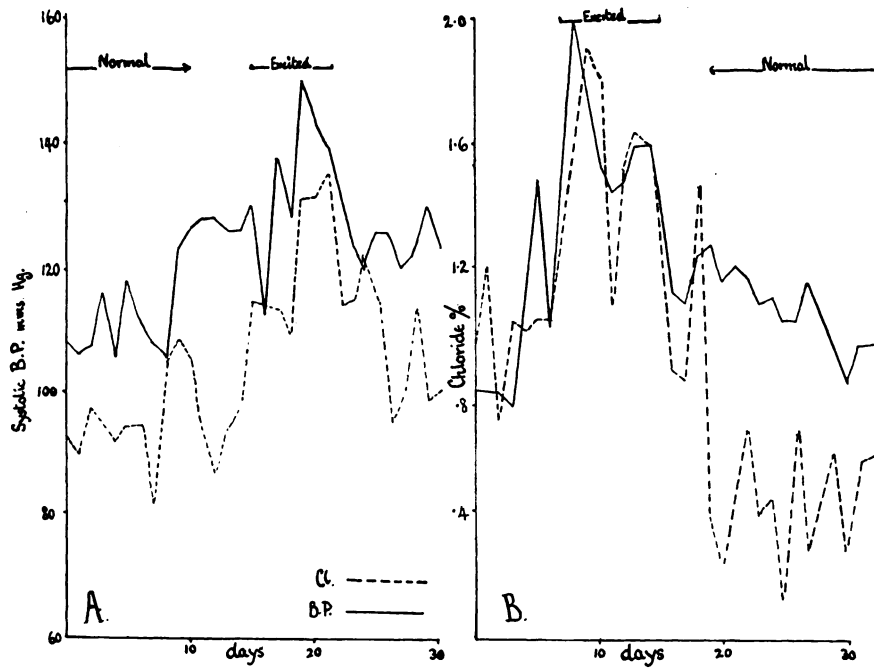
(2) With a diaphoretic mixture : The raised chloride percentage might, it was thought, indicate a general increase in chloride elimination as a compensatory mechanism, and the drugs were given to aid this excretion. The perspiration was never evident and no mental change occurred.

(3) With a sympathetic depressant : Quinine hydrobromide, gr. v, and hydrobromic acid, ℥xx, were given three times daily for this purpose (4). The attack was less acute than usual, and the low chloride level throughout was evident ; on the seventh day an intra-muscular injection of .2 gm. acetyl choline was followed by a rapid return to normal, though by this time recovery might have been expected (Fig. c). Instead of the anticipated confusional period following, for the next eighteen days he was normal.

(4) With a combination of various parasympathetic stimulants and the sympathetic depressant : In addition to the quinine hydrobromide, injections on successive days of .1, .1, .2, .2, .2 gm. of acetyl choline, $\frac{1}{30}$ gr. eserine and on the next $\frac{1}{3}$ gr. and $\frac{1}{3}$ gr. of pilocarpine were given, after which he returned to normal (Fig. D). Every time before this when his blood-pressure had been over 130 mm. Hg. he had been unfit to remain in his own room, but on this occasion he was quiet enough to stay in bed, slept better, was not obviously hallucinated and denied hearing voices.

Since then the excitement has not been so acute and he can mix with other patients during the day. Less heroic measures have been employed ; the dose of quinine is doubled without cinchonism, and one or two injections are given after several days' confusion and restlessness.

On one occasion $\frac{1}{4}$ gr. of pilocarpine was injected too early in an attack, and



though the subsequent recovery was rapid, signs of violent parasympathetic stimulation resulted, relieved by atropine ; this is the only time he has suffered discomfort or any ill-effect.

DIAGNOSIS.

The obvious physical cause to exclude was a suprarenal tumour in view of the periodicity of the sympathetic stimulation, though the small change in pulse pressure in the attacks and the duration differ from the reported cases of paroxysmal hypertension (5).

A plain X-ray showed well-defined normal renal shadows. After an injection of uroselectan B no distortion of either renal pelvis was found and the substance was rapidly excreted.

The case would appear to be a schizophrenic reaction, his excitement being more like that of katatonia than acute mania. He has some insight into his condition and will mention events which took place whilst he was excited and apparently dissociated ; but he says that he tries not to think of the times " when he is ill ", and wants to forget about them. He dislikes being questioned about himself and attempts to evade the replies. He has shown little deterioration in the past five years ; he can do his shopping, go to football and cricket matches and to the cinema without his behaviour appearing irregular.

The excitement is fairly abrupt in onset and termination ; he is not markedly elated or exalted, though he shows increasing euphoria and insomnia before the commencement. His actions at this time are impulsive and apparently unreasonable. He makes unprovoked attacks on fellow patients and attendants and will suddenly run a few yards kneel and pray aloud. Sometimes he walks up and down a passage for hours, always turning at the same points, continually talking to himself, violently resisting interference and ignoring those about him. He has marked auditory hallucinations, and talks continually though often incoherently. He exhibits various attitudes suggesting homosexuality, but does not show negativism or automatic obedience. He is somewhat anæsthetic. Neither his speech nor actions are influenced by the things happening around him unless he is interfered with or opposed.

DISCUSSION.

It is particularly to be emphasized that the blood-pressures observed in the excited phases were not due to the exercise ; the very great majority of readings were taken after a period of quiescence. Of three other cases, one of recurrent mania showed somewhat similar changes in an attack, but since the exercise factor was predominant it is not worth recording. In one of the other cases 19% (8/42) of the readings differed by more than 15 mm. Hg. from the lowest reading (this was an excited case of secondary dementia), and in the other, a schizophrenic, all thirty readings were within that limit.

There is no relationship between any of the values recorded and the occasional purges administered. When he is restless his careless habits are counteracted by enemata.

Since the morning chlorides would vary with the blood chlorides (Mazza found these to be normal except in epilepsy (6)), the pH of the blood, the CO₂ content, sleep, the plasma proteins, exercise, emotional unrest and pituitary activity, in addition to the blood-pressure, no certain significance can be allotted to the values observed on a fairly constant diet. Very roughly, the percentage varies directly with the volume of the morning urine. In this case the volumes fluctuated between 100 and 800 c.c., for he was often unwilling completely to empty his bladder; thus those readings under 400 c.c. were discarded, for in the past he had tended to pass a large quantity of morning urine when excited. For two normal people, one showed this relationship to the same degree of accuracy, and the other gave a fairly definite linear relationship, but the ratio of the morning to the day's total chlorides varied from 1/2.5 to 1/5.

Six controls (two normal, a schizophrenic, a secondary dementia, a recurrent mania and an involuntal melancholic) have been observed for about a month each. In 85% of the readings (143/169) there was no greater difference from the lowest morning chloride percentage than .6%. For the patient before treatment with quinine hydrobromide only 48% (80/168) were within these limits, but following its use more than 90% of the readings (94/103) fell within this range. After the first week it was used (Fig. c) the readings practically without exception corresponded to the level in Fig. d. Had Armstrong's paper (7) been consulted before treatment began, the urine chloride estimations could have been made at similar times for comparison.

An opportunity arose to compare the relative potency of acetyl choline, pilocarpine and physostigmine used in maximum doses, though from the results of treatment it appears that the quinine hydrobromide facilitates their action. Pulse-rates were taken half-hourly after injection throughout the day. The results are best shown in tabular form :

	Pilocarpine nitrate ($\frac{1}{2}$ gr. sub- cutaneously).	Acetyl-choline (.2 grm. intra- muscularly).	Eserine salicylate ($\frac{1}{2}$ gr. sub- cutaneously).
Sedative action	Remained quiet and sleep induced .	Fairly quiet, with restless periods .	Fairly quiet, with restless periods .
Time of greatest fall in pulse-rate	5 hours .	3 hours .	2 hours .
Percentage fall of initial rate in 2 hours	14 .	13.5 .	16 .
Maximum percentage fall of initial rate	20 .	16 .	16 .
Time to rise again to initial value	9 hours .	8 hours .	7 hours .
Maximum percentage fall of initial blood- pressure	17 (4 hours) .	15 (2 $\frac{1}{2}$ hours) .	8 (3 hours) .

(These blood-pressure results were more indefinite since only four complete observations were made.)

Pilocarpine was the only drug which produced sweating. This began half an hour after injection, and lasted from one and a half to two hours ; sleep usually followed.

In no case was salivation marked.

The pupils only contracted slightly.

There was a slight temporary rise in pulse-rate after injection (8) in only two out of the fourteen sets of readings.

No muscular twitchings were observed with eserine, nor was there any rise in blood-pressure (8).

The time of action is about twice that usually observed in other cases.

SUMMARY.

A schizophrenic reaction type of case with recurrent attacks of intense sympathetic excitement showed a regular periodicity in his mental condition : Normal—excitement—confusion—excitement—normal. A number of factors, the blood-pressure and morning urine chloride concentration in particular, showed dependent variations.

By the use of full doses of parasympathetic stimulants and quinine hydrobromide (as a sympathetic depressant) the anticipated excitement has been reduced to confusion with normal periods intervening. The blood-pressure under this treatment shows the same variations as before, but the chlorides remain at a constant level.

A number of control cases have been observed and the results analysed.

Some observations on the relative strengths, for this case, of pilocarpine, eserine and acetyl choline have been made.

I should like to thank Dr. A. A. D. Townsend, the Medical Superintendent, for allowing me to publish this case, and for his kind help ; and Sir Walter Langdon-Brown, at whose suggestion the quinine hydrobromide was first used.

References.—(1) Dodds, E. C., Lawson, W., and Robertson, J. D., *Lancet*, 1932, ii, p. 608.—(2) *Amer. Journ. Med. Sci.*, 1932, p. 335.—(3) Gillespie, R. D., *Journ. Ment. Sci.*, 1926, p. 325.—(4) *Boston Med. and Surg. Journ.*, September 15, 1910, per *Prescr.*, December, 1910.—(5) *Lancet*, 1932, ii, p. 1287 ; 1933, ii, p. 1382 ; 1934, i, p. 665, ii, pp. 630, 714, 1130.—(6) Mazza, A., per *Journ. Ment. Sci.*, 1933, p. 797.—(7) Armstrong, R. W., *ibid.*, 1929, p. 644.—(8) Hale White, *Materia Medica*, 14th ed., p. 417.