

HEAD INJURIES : A NEW TREATMENT FOR THE POST-CONCUSSIVE SYNDROME.

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GUNSHOT and shrapnel wounds of the head during the war have produced various disabilities not commonly seen in the injuries of peace-time.

The symptom complex which usually appears subsequent to head trauma has become very familiar during the past few years. The resemblance from case to case of certain sequelae to head injuries has been grouped together in syndromes, variously labelled post-concussive syndrome, post-traumatic personality change, post-traumatic neurosis and post-contusional state, all indicating an oft-recurring persistent disability following concussion of the brain.

Many different types of investigation have been carried out, and in each instance some light has been shed on some particular phase of the symptom complex.

PATHOLOGY.

Definite pathologic changes in this syndrome have not been fully established. While various investigators believe the disorder is primarily of an organic nature, other observers have advanced evidence of its being a pathophysiologic derangement. Neustatter (1) has demonstrated the difficulty in deciding whether the syndrome is physiogenic or psychogenic.

The definition of concussion as presented by Strauss and Savitsky (2) is broad enough to allow for many of the theories of its pathophysiology—"a series of events resulting from a blow to the head severe enough to cause disruption of intracranial equilibrium."

It has been suggested by several investigators that the effects of cerebral trauma may be cumulative. As far back as 1874 Koch and Filene (3) proved that animals could be killed by repeated small blows on the head without showing evidence of any structural damage to the brain.

Martland (4), in 1928, recognized a condition occurring among prize-fighters which he named "punch drunk," and which was attributed to the repeated head punishments they had suffered while in the ring. Later, Shaller, Tarnaki and Newman (5) showed the apparent increase of vulnerability of the cerebral vessels induced by the application of repeated blows.

More recently Denny Brown and Russell (6) demonstrated that paralysis of respiration of increasing duration and rise of blood pressure occurred with successive blows, and that concussion could be obtained readily by repetition of moderately severe blows.

Penfield (7) has advanced the theory that the development of dural adhesions is the basic cause of the symptoms, and has demonstrated in a number of cases thin adhesions in the subdural hemisphere. Histologically these lesions are composed of a thin layer of blood undergoing the process of organization and adherent to the arachnoid as well as the dura. On pressure being applied, by means of a curved instrument on the under-surface of the dura during the course of an operation under local anaesthesia, the patient complained of a head pain of the same character as the chronic headache of a post-concussive syndrome. In such cases, apparently, the exciting agent may be either constant traction or pressure on a sensitive area in the under-surface of the dura. Penfield also believes that during the actual trauma the brain is temporarily "knocked out" of position by the blow, and when the normal relationship is restored, traction adhesions are formed. These findings induced him to adopt lumbar air insufflation as treatment.

Zacks (8) has given adequate proof of degenerative changes in the cells themselves, which bring about an altered physiologic state. He believes it probable that there is a change in the irritability of the vasodilators and vasoconstrictors, with resultant areas of localized altered circulation.

Glaser (9) agrees with this theory, and adds that these changes are transient and may be actively reversible.

Courville (10) suggests that the mental changes often seen as part of this condition are primarily vaso-motor phenomena.

A striking liability of headache, localized to the site of previous scalp injury, to provocation by posture or physical effort, provides evidence that such provocation in the more diffuse types of headaches indicates underlying structural damage. Provocation by histamine, particularly when the headache has been unilateral, suggests that intracranial localized vascular or perivascular changes may occur (Brenner, Fieldman, Merritt and Denny Brown, 11).

Ruesch and Bowman (12) state that in head injuries the organism seems to respond more slowly and less extensively to stimulations requiring metabolic and circulatory adjustments. They consider it might be worth while to investigate further biochemical and circulatory aspects in post-traumatic conditions, thus reducing the number of cases whose symptoms have been explained on a "psychogenic basis."

Kozol (13) found little or no correlation between pre-traumatic personality and liability to development of post-traumatic mental symptoms.

A post-traumatic condition cannot be regarded as a definite purposive reaction to trauma of a very varying nature. "The change that has escaped notice is that the psychogenic stimuli which now produce symptoms would not have been effective before the injury" (Sargant and Slater, 14).

We are presenting additional proof in support of Malone's (15) evidence that such vascular pathophysiologic changes play an important if not dominant role in this symptom complex.

DIAGNOSIS.

Psychiatric symptoms are common among the sequelae of head injuries. These symptoms vary in intensity and duration from case to case. At one extreme may be increased irritability and occasional headache. At the other extreme may be a fully developed syndrome. The post-concussive syndrome usually presents a triad of symptoms—headaches, dizziness and various emotional disturbances.

A series of 88 soldiers who had suffered head injuries with unconsciousness was investigated at Sutton Emergency Hospital. As some months, and in some cases years, had elapsed before the admission of such cases, in all instances defects were of such severity and duration as to render the patient incapable of existing satisfactorily in his previous environment, and the fact that in 44.3 per cent. of cases symptoms had existed for a year or more seemed to indicate a poor prognosis.

This group of individuals showed a superficial uniformity of symptoms. Headaches, dizziness, disturbances of feeling and behaviour with vasomotor and emotional instability, impaired efficiency and fatigue were the commonest complaints related to the disability, particularly to prolonged disability. Many were handicapped through memory defects, defects in intellectual capacity and ability to concentrate, or through personality changes, such as moodiness and irritability (Table I).

Of the total number examined, 6 had suffered two head injuries, 4 cases had had three, and 1 case four.

The time which had elapsed between the accident and the date of admission to hospital is shown in Table I. Twenty-five patients were admitted within six months of the accident, 27 from six to twelve months after, and 20 from one to two years after. In addition, 16 patients were admitted at periods of from two to seven years following trauma.

Fifty patients developed symptoms immediately following the accident, 17 from one to two months after, 4 within three months, 4 after an interval of from three to four months, and 2 within six months. In the remainder the onset was gradual.

Forty-eight patients had had previous hospital treatment for varying periods with little or no benefit.

Patterson, Raynall and Kremer (16) recently discussed various aspects of the development of post-traumatic personality disorders, and made it clear that disturbances of even mild degree may have serious consequences, therefore early hospital treatment is advocated.

THERAPY.

The rehabilitation of such men who had undergone combined organic and psychic injury has provided a serious problem during the war, an organic injury rarely occurring without concomitant psychologic effects. Because of the fact that psychogenic factors frequently complicated the clinical picture, many of these patients were unfortunately labelled neurotic.

Treatment so far has been carried out on no approved lines, and there has

Case.	Age.	Date since injury.	Fracture.	Unconscious.	Post-traumatic amnesia.	Symptoms.			
						Headaches.	Dizziness.	Emotional instability, lack of concentration, memory impairment, irritability.	
1	40	3 yrs.	+	15 mins.	1 day	+	+	+++	
2	23	4 mths.	+	4 hrs.	Days	+	+	++++	
3	27	18 wks.	+	10 mins.	..	+	+	+++	
4	38	4 yrs.	..	15 mins.	..	+	+	++	
5	31	6 yrs.	..	30 mins.	3 days	+	+	+++	
6	25	6 mths.	..	20 mins.	..	+	+	++	
7	34	11 mths.	..	7 hrs.	..	+	+	++	
8	35	1 yr.	+	1 hr.	1 day	+	+	+++	
9	44	4 yrs. 6 mths.	+	2 days	..	+	+	+++	
10	52	1 yr. 10 mths.	+	5 hrs.	Days	+	+	++++	
11	34	10 wks.	..	45 mins.	Hours	+	+	++	
12	22	9 mths.	..	5 hrs.	3 days	+	+	+++	
13	27	8 mths.	..	7 hrs.	..	+	+	+++	
14	25	8 mths.	..	15 mins.	Dazed	+	+	+++	
15	20	10 wks.	..	2 hrs.	Hours	+	+	+++	
16	38	6 mths.	+	2 hrs.	24 hours	+	+	+++	
17	35	2 yrs. 6 mths.	..	12 hrs.	..	+	+	+++	
18	27	21 wks.	..	5 mins.	Dazed	+	+	+++	
19	24	1 yr.	..	10 mins.	..	+	+	++	
20	22	3 mths.	..	20 mins.	2 weeks	+	+	++++	
21	31	21 wks.	+	10 mins.	3 days	+	+	++	
22	31	4 wks.	..	5 mins.	48 hours	+	+	++	
23	24	1 yr. 7 mths.	+	1 hr.	Hazy for days	+	+	++	
24	39	2 yrs.	..	10 mins.	..	+	+	++	
25	25	2 yrs.	..	35 mins.	..	+	+	+++	
26	23	1 yr.	..	30 mins.	..	+	+	++	
27	21	6 mths.	+	2 hrs.	Dazed for time	+	+	+++	
28	25	61 wks.	..	10 mins.	..	+	+	++	
29	23	7 yrs.	+	3 hrs.	Hazy for days	+	+	+++	
30	26	10 wks.	+	5 mins.	..	+	+	++	
31	26	4 yrs.	+	15 mins.	2 days	+	+	++++	

Examination.				Number of injections	Result.
Ocular fundus.	Tinnitus.	Nystagmus.	Vision.		
Normal	No	None	Normal	17	Gradual relief of symptoms with complete recovery. No recurrence 6 months after.
"	Yes	Spontaneous rotary	"	20	Rapid recovery with relief of all symptoms. Had 3 head injuries. No recurrence 3 months after.
"	No	None	"	16	Complete relief of all symptoms.
"	"	"	"	20	Rapid recovery with relief of all symptoms.
"	"	"	"	19	Gradual relief of all symptoms. No recurrence 8 months after.
"	"	"	"	14	Gradual improvement with complete recovery.
"	"	"	"	12	Complete relief of symptoms. No recurrence 3 months after.
"	"	Spontaneous lateral	Presbyopia	16	Rapid recovery with relief of all symptoms.
"	"	None	Normal	20	Gradual relief of all symptoms.
"	Yes	Bilateral rotary spontaneous	"	21	Gradual improvement with ultimate complete recovery.
"	No	None	Hypermetropia	16	Relief of all symptoms except emotional instability.
"	"	"	Normal	20	Gradual relief of all symptoms. No recurrence 4 months later.
"	"	"	"	18	Complete relief of all symptoms.
"	Yes	"	"	15	Rapid recovery with relief of all symptoms.
"	"	"	Refractive error	20	Relief of all symptoms except emotional instability.
"	No	Lateral	Normal	17	Gradual relief of all symptoms, with complete recovery.
"	"	None	Presbyopia	14	Complete relief of all symptoms. No recurrence 7 months after.
"	"	"	Normal	18	Gradual relief of all symptoms, with complete recovery.
"	"	"	"	14	Gradual improvement with ultimate complete recovery.
"	"	Bilateral rotary spontaneous	"	16	Gradual relief of all symptoms, with complete recovery. No recurrence 6 months after.
"	"	None	"	14	Rapid recovery with relief of all symptoms.
"	Yes	"	Refractive error	16	Complete relief of all symptoms.
"	No	"	Normal	18	Gradual improvement with eventual complete recovery.
"	"	"	"	14	Complete relief of symptoms. No recurrence 6 months after.
"	Yes	Lateral	"	17	Rapid recovery with relief of all symptoms.
"	No	None	"	17	Complete relief of symptoms. No recurrence 5 months later.
"	"	"	"	15	Gradual relief of symptoms, with complete recovery.
"	"	"	Presbyopia	18	Rapid recovery with relief of all symptoms.
"	Yes	Bilateral rotary spontaneous	Refractive error	20	Gradual improvement with eventual complete recovery. No recurrence 6 months after.
"	No	None	Normal	16	Rapid recovery with relief of all symptoms.
"	Yes	Spontaneous rotary	"	18	Relief of all symptoms except emotional instability.

Case.	Age.	Date since injury.	Fracture.	Unconscious.	Post-traumatic amnesia.	Symptoms.		
						Headaches.	Dizziness.	Emotional instability, lack of concentration, memory impairment, irritability.
32	33	4 mths.	..	10 mins.	Dazed for time	+	+	++
33	32	11 mths.	+	1 hr.	Hours	+	+	+++
34	40	3 mths.	..	3 hrs.	1 day	+	+	++
35	27	3 yrs. 10 mths.	+	5 days	Dazed for time	+	+	++
36	24	7 mths.	..	30 mins.	..	+	+	++
37	31	4 yrs.	..	15 mins.	..	+	+	++++
38	25	1 yr. 4 mths.	..	1 hr.	Dazed for time	+	+	++
39	28	1 yr. 5 mths.	..	35 mins.	Hours	+	+	++
40	26	5 mths.	+	10 mins.	1 week	+	+	+++
41	21	10 wks.	..	45 mins.	..	+	+	+
42	27	14 wks.	..	2 hrs.	Dazed for time	+	+	+++
43	20	19 wks.	..	4 hrs.	Ditto	+	+	++
44	23	7 mths.	..	10 mins.	..	+	+	+++
45	27	4 mths.	..	15 mins.	..	+	+	+++
46	21	9 mths.	..	20 mins.	..	+	+	+++
47	29	18 mths.	..	10 mins.	..	+	+	++
48	28	18 mths.	..	7 hrs.	..	+	+	+++
49	21	13 mths.	+	30 mins.	4 days	+	+	+++
50	26	11 mths.	+	20 mins.	24 hours	+	+	++++
51	32	7 mths.	+	6 hrs.	1 week	+	+	++++
52	27	9 mths.	+	8 mins.	24 hours	+	+	+++
53	26	54 wks.	+	3 days	..	+	+	++
54	31	7 mths.	+	30 mins.	10 days	+	+	+++
55	35	5 mths.	..	10 mins.	Dazed for time	+	+	++
56	38	4 yrs.	+	17 hrs.	..	+	+	+++
57	29	4 mths.	..	6 hrs.	6 weeks	+	+	++++
58	39	3 yrs. 4 mths.	+	1 day	..	+	+	++++
59	25	3 yrs. 1 mth.	..	20 mins.	Dazed for time	+	+	+++
60	23	6 yrs.	+	1 day	3 days	+	+	+++

Ocular fundus.	Examination.			Number of injections.	Result.
	Tinnitus.	Nystagmus.	Vision.		
Normal	No	None	"	10	Rapid recovery with relief of all symptoms.
"	"	"	Refractive error	15	Rapid recovery with relief of all symptoms.
"	Yes	"	Normal	15	Complete relief of all symptoms.
"	No	Spontaneous rotary	"	21	Gradual improvement with ultimate complete recovery. No recurrence 6 months after.
"	"	None	"	16	Complete relief of all symptoms.
"	"	Bilateral rotary spontaneous	"	44	Gradual improvement with ultimate recovery except emotional instability.
"	"	None	"	14	Rapid recovery with relief of all symptoms. No recurrence 3 months after.
"	Yes	Lateral	"	18	Gradual relief of symptoms with complete recovery. No recurrence 4 months after.
"	"	Spontaneous rotary	Presbyopia	15	Complete relief of all symptoms.
"	No	None	Normal	15	Complete relief of all symptoms.
"	Yes	Bilateral spontaneous rotary	Refractive error	14	Relief of all symptoms except emotional instability. Improvement maintained 6 months after.
"	No	None	Normal	16	Rapid recovery with relief of all symptoms.
"	"	"	"	15	Gradual improvement with ultimate complete recovery.
"	"	None	Normal	14	Rapid recovery with relief of all symptoms.
"	"	"	"	14	Rapid recovery with relief of all symptoms.
"	"	Lateral	"	12	Complete relief of all symptoms. No recurrence 7 months after.
"	Yes	Spontaneous rotary	Refractive error	16	Gradual improvement with ultimate complete recovery. No recurrence of symptoms 4 months later.
"	"	Bilateral spontaneous rotary	Normal	18	Gradual relief of all symptoms with complete recovery.
"	No	None	"	20	Gradual relief of all symptoms except emotional instability.
"	Yes	Spontaneous rotary	"	19	Gradual relief of all symptoms except emotional instability.
"	"	Lateral	Hypermetropia	19	Gradual improvement with ultimate complete recovery. No recurrence of symptoms 7 months later.
"	No	None	Normal	17	Gradual relief of all symptoms with complete recovery.
"	Yes	"	"	19	Gradual relief of all symptoms with complete recovery. No recurrence of symptoms 4 months after.
"	No	"	"	14	Rapid recovery with relief of all symptoms.
"	"	Spontaneous rotary	"	20	Gradual relief of all symptoms with complete recovery. No recurrence 8 months after.
"	Yes	Lateral	Refractive error	18	Gradual improvement with relief of all symptoms except emotional instability.
"	No	Bilateral spontaneous rotary	Normal	20	Gradual improvement with ultimate complete recovery. No recurrence of symptoms 6 months after.
"	"	None	Presbyopia	21	Gradual relief of symptoms with ultimate complete recovery.
"	Yes	"	Refractive error	23	Gradual relief of all symptoms. No recurrence 6 months after.

Case.	Age.	Date since Fracture-injury.	Unconscious.	Post-traumatic amnesia.	Symptoms.			
					Headaches.	Dizziness.	Emotional instability, lack of concentration, memory impairment, irritability.	
61	21	2 mths.	..	30 mins.	..	+	+	+++
62	26	3 yrs.	..	8 hrs.	2 days	+	+	++++
63	24	1 yr. 9 mths.	..	2½ hrs.	1 day	+	+	+++
64	27	4 mths.	..	40 mins.	..	+	+	++
65	29	1 yr. 3 mths.	..	1½ hrs.	..	+	+	+++
66	30	5 yrs.	..	1 hr.	..	+	+	++++
67	39	1 yr. 1 mth.	..	2 hrs.	..	+	+	+++
68	25	1 yr. 6 mths.	+	8 hrs.	1 week	+	+	+++
69	29	9 mths.	..	20 mins.	..	+	+	++
70	32	7 mths.	+	3 days	3 months	+	+	++++
71	27	1 yr. 5 mths.	-	30 mins.	..	+	+	++
72	26	47 wks.	-	10 mins.	Dazed for time	+	+	++
73	31	19 wks.	-	1 hr.	..	+	+	++
74	37	14 wks.	+	7 hrs.	1 day	+	+	+++
75	22	7 mths.	-	10 mins.	..	+	+	++
76	42	2 yrs.	+	3 hrs.	Dazed for time	+	+	+++
77	35	3 yrs.	+	6 hrs.	1 week	+	+	+++
78	45	1 yr. 3 mths.	+	30 mins.	Hours	+	+	+++
79	27	9 mths.	..	2 hrs.	..	+	+	++
80	29	7 mths.	..	1½ hrs.	..	+	+	+++
81	25	1 yr. 2 mths.	..	25 mins.	Dazed for time	+	+	++
82	31	11 mths.	..	30 mins.	..	+	+	++
83	28	1 yr. 4 mths.	..	2½ hrs.	Dazed for time	+	+	+++
84	23	5 mths.	..	1½ hrs.	..	+	+	++
85	29	31 wks.	..	45 mins.	..	+	+	++
86	30	11 mths.	+	3 hrs.	Dazed for time	+	+	+++
87	32	23 wks.	..	30 mins.	..	+	+	++
88	35	27 wks.	..	1½ hrs.	..	+	+	+++

Ocular fundus.	Examination.			Number of injections.	Result.
	Tinnitus.	Nystagmus.	Vision.		
"	No	"	Normal	19	Gradual improvement with ultimate complete recovery.
"	Yes	Spontaneous rotary	Myopia	24	Gradual relief of all symptoms except emotional instability. No recurrence of symptoms 5 months after.
"	No	Lateral	Normal	15	Complete relief of all symptoms. No recurrence 7 months after.
"	"	None	"	15	Rapid recovery with relief of all symptoms.
"	"	"	"	15	Rapid recovery with relief of all symptoms. No recurrence 6 months after.
"	Yes	Spontaneous rotary	"	22	Gradual relief of all symptoms except emotional instability. No recurrence of symptoms 6 months after.
"	"	Lateral	"	18	Gradual improvement with ultimate complete recovery.
"	No	Bilateral spontaneous rotary	Myopia	20	Gradual relief of all symptoms with ultimate complete recovery. No recurrence of symptoms 6 months after.
"	"	None	Normal	16	Rapid recovery with relief of all symptoms.
"	Yes	"	"	24	Gradual relief of all symptoms except emotional instability. No recurrence 4 months after.
"	No	"	"	18	Gradual improvement with ultimate complete recovery.
"	"	"	"	15	Rapid recovery with relief of all symptoms.
"	"	Spontaneous rotary	"	18	Rapid recovery with relief of all symptoms.
"	Yes	Bilateral spontaneous rotary	Refractive error	20	Gradual relief of all symptoms with ultimate complete recovery.
"	No	None	Normal	19	Rapid recovery with relief of all symptoms. No recurrence of symptoms 6 months after.
"	Yes	"	"	25	Gradual improvement with eventual complete recovery. No recurrence of symptoms 6 months after.
"	"	Spontaneous rotary	Refractive error	24	Gradual improvement with ultimate complete recovery. No recurrence of symptoms 4 months after.
"	"	Lateral	Normal	16	Complete relief of all symptoms. No recurrence of symptoms 3 months after.
"	No	None	Presbyopia	15	Rapid recovery with relief of all symptoms.
"	Yes	"	Normal	14	Rapid recovery with relief of all symptoms. No recurrence of symptoms 4 months after.
"	"	Spontaneous rotary	"	16	Gradual relief of all symptoms with ultimate complete recovery. No recurrence of symptoms 3 months after.
"	No	Lateral	Myopia	16	Rapid recovery with relief of all symptoms.
"	Yes	Bilateral spontaneous rotary	Refractive error	20	Gradual improvement with ultimate complete recovery. No recurrence of symptoms 3 months after.
"	"	None	Normal	15	Rapid recovery with relief of all symptoms.
"	No	"	"	18	Gradual improvement with ultimate complete recovery. No recurrence of symptoms 3 months after.
"	Yes	Spontaneous rotary	"	20	Gradual improvement with relief of all symptoms. No recurrence 4 months after.
"	No	None	"	14	Rapid recovery with relief of all symptoms.
"	"	"	"	15	Rapid recovery with relief of all symptoms.

been uncertainty as to choice of therapeutic procedures. Penfield (17) in 1927 introduced the procedure of lumbar air insufflation, which was, and still is, employed by some clinicians. The purpose is to have the air break up the subdural adhesions. In cases which proved particularly obstinate, Penfield advised bilateral trephination with mechanical rupture of the offending membranes.

In a series of 9 controls the effectiveness of barbiturates on the syndrome could not be proved—narcosis with sodium amytal proving unsatisfactory. Many patients had been receiving daily doses of luminal for various periods prior to admission with no improvement.

Brahdy (18) tried the effect of ergotamine tartrate on a series of 6 cases without improvement.

One of the effects of injecting hypertonic saline into the circulation is a diminution in the volume of the brain—hence it has been advocated for the relief of headache in post-contusional and post-concussional states. Feiling (19) found that even 100 ml. of 30 per cent. solution could be given, but usually 50 ml. of 15 per cent. was effective. Twelve controls in the present series showed no satisfactory response to this form of treatment.

At the General Hospital, Johannesburg, oral administration of prostigmine hydrobromide, 15 mg. *t.d.s.*, was given for 6–8 weeks, together with intramuscular injection of 1 c.c. of a solution of prostigmine methyl-sulphate, 1 in 2,000 twice weekly for 6–8 weeks, combined with a restricted fluid intake. Prostigmin helps the action of acetylcholine, which is a powerful vaso-dilator, and thus abolishes vaso-constriction of meningeal and labyrinthine arteries, which vaso-constriction is presumably the cause of persistent post-traumatic headaches (Malone, 15).

In view of the long duration of symptoms in the majority of cases it was felt that an expedient was necessary which would promote quick readjustment and reduce stay in Hospital to a minimum. Believing that in the majority of cases the disorder was on the basis of a disturbed vascular physiologic change, we decided to use the preparation Afenil, with which we had previously obtained very encouraging results in the treatment of the catatonic form of schizophrenia (20).

Afenil, or calcium chloride urea, is a preparation of calcium for intravenous administration. It is a double combination of one molecule of chloride of calcium (31.6 per cent.) and four molecules of carbamide (68.4 per cent.), prepared in ampoules, each containing 10 c.c. of a 10 per cent. solution = 0.11 gm. calcium. Given intravenously, if the technique be scrupulously attended to it is free from pain and risk, but special warning must be given of the risk of necrosis if there is any leakage into the intramuscular or subcutaneous tissues. Intravenous injection is performed in the customary manner with the aid of a compressor bandage; location of the needle in the lumen of the vein should be carefully ensured in order to prevent any of the injection fluid entering the perivascular tissue.

An instantaneous vaso-dilatation is produced, with access of heat to the head, accompanied by flushing, sensations of heat in the mouth and stomach, and slight cerebral pressure, the injection being carried out slowly. Variations

in blood pressure are of the slightest. Alterations in the urine were not seen, nor was there any noteworthy acceleration of the pulse beat during the injections. Given every second day the injections were always well tolerated. After each injection the patients lay down and relaxed completely for two to three hours.

All cases received a complete neurologic survey, including intelligence tests and psychiatric studies before and after treatment.

The following objective signs were taken in evaluating the amount of labyrinthine vertigo present: (1) Nystagmus after quick movements of the head; (2) spontaneous nystagmus with patient's head extended backward to the right and to the left; (3) ophthalmic examination.

RESULTS OF TREATMENT.

There was a subjective sensation of a lack of muscular tension with attendant relaxation shortly after the first injection. As a consequence of this lessened tension irritability decreased, fatigue disappeared and sleep became more normal. Conduct disturbances became much more modified, and, after a week or two of treatment, disappeared. By the fourth injection improvement was obvious and was maintained in all cases; the onset of headaches and giddiness had considerably diminished, and in many cases were reduced to rudiments, concentration improved and the patient's outlook altered appreciably. It was a noteworthy fact that patients who were at first distrustful or even antagonistic to the injections asked directly for a repetition because they said they found their effect quietening, beneficial and only pleasant.

By using this preparation a syndrome which had been established for varying lengths of time could be greatly diminished at an early stage of the treatment. On completion, this improvement was fully maintained in all cases; symptoms had disappeared, the outlook was bright and optimistic, morale and confidence were restored. Average duration of stay in hospital was 60.2 days, which is satisfactory in view of the severity of symptoms presented and the time which had elapsed in the majority of cases before treatment was started.

Appended are details of three typical cases. Each patient kept his own notes on progress:

CASE I.—Admitted 14.xi.44; discharged 19.i.45. Glider crash D day, 6.vi.44, with head injury and slight crash injury to spine.

Was unconscious for about eight hours. M.O. who first saw him saw C.S.F. coming from wound in L. temporo-parietal region. Had a faint recollection of being in a R.A.F. Station Hospital, and of afterwards being taken to Oxford. Complained of severe headaches, almost constant, L. temporal passing to occiput. Was very light-headed at times. Had frequent dizzy spells, everything swimming round him. Loss of concentration and loss of confidence. Head went "all queer if he went to a cinema or to a dance." Memory impaired. Was very irritable, moody and bad tempered.

Notes.

2nd injection: "The injections seem to make me restful and steady."

3rd injection: "Sleep good. Head clearer. Feel better."

5th injection: "Can enjoy things better. Feel much more easy with people and can now mix with the others and talk to them. Can concentrate a lot better."

7th injection : " Feeling 100 per cent. better. Finding much more pleasure in life. Can enjoy myself and feel I am going to recover. Temper much better."

12th injection : " Head and temper feel good. Am much more settled and can work hard all day now and get no dizzy spells at all. Am enjoying life."

13th injection : " Been home and now feel reasonable with everyone. I feel quite different."

CASE 2.—Admitted 31.x.44 ; discharged 12.i.45.

Complained of headaches, frontal, at times occipital, which came on many times daily, lasting 10–30 minutes ; depression, irritability, dizzy attacks, especially on bending. Concentration impaired. Had lost memory on two occasions for short periods. History of two head injuries.

(1) January, 1942. Shell splinter hit L. occipital region ; sustained cerebral contusion and fractured skull. Was unconscious until the following day, when he came to in hospital. Felt hazy and foggy—" things hard to recollect." In bed for five weeks. On getting up was unable to concentrate, felt irritable, had severe headaches and could not stand noises.

(2) March, 1943. R. malar bone damaged by shrapnel. Operation R. temporal area to repair same. Was unconscious on this occasion for five hours. Afterwards felt " all sense of what he was doing had been taken away from him." Had lapses of memory and forgot to carry out orders. On admission stated he had " lost interest in everything and had become resigned to headaches."

Notes.

" On admission I was feeling very depressed and suffering from severe headaches. I was very irritable and quarrelled all the time I was at home."

2nd injection : " After this I went to sleep and when I awoke I found that I felt better with my head easier."

4th injection : " I must admit that I am feeling more cheerful and am beginning to get my confidence back. Headaches have become much milder. Feel depression is going. I am not so jumpy."

6th injection : " I am feeling much fitter and quite lively and don't jump at every sound. I can concentrate now."

10th injection : " Am feeling much more confident and cheerful than I have done for a long time. There has been great improvement. Feeling much better all round."

12th injection : " When I go home I feel in a fine mood. Am feeling fitter than I have for a long time and much more happy. My memory is all right now,"

CASE 3.—Admitted 13.vi.45 ; discharged 17.viii.45.

This patient was admitted from the general side of the hospital in a very serious mental condition. He was very agitated and depressed, had severe headaches, much irritability, bad temper and nocturnal restlessness. Felt suicidal at times, that all hope was lost, that nothing could be done for him. He was unable to concentrate or think clearly ; memory was much impaired for recent events. Stated his mind often " went blank for a long time." Thoughts were confused and " often mixed up at times." Had impulsive attacks of bad temper, with a tendency to violence. History of three head injuries.

(1) France, July, 1944 : Fell down a German man-trap. Unconscious 1½ hours. In hospital for a month, where he developed headaches.

(2) September, 1944 : When driving ammunition lorry explosion occurred which blinded him. Lorry went over a ditch ; he struck his head. Was unconscious for seven hours and very hazy for days afterwards. Was in hospital for three months. Head was " driving him mad all the time." Boarded B1 on 3.iv.45. Returned U.K.

(3) May 24, 1945 : Following quarrel with a soldier was knocked out and left unconscious on road. Was unconscious for several hours. Very confused afterwards and subsequently admitted to Sutton. This man's improvement was dramatic.

Notes.

2nd injection : " Fewer headaches and more confidence seem to be the effect these two injection have had on me."

4th injection : " I feel much better and more settled. Dizziness is passing off and headaches seem to be under control. The injections do me a lot of good ; it is not a drugged feeling. Am a lot less depressed and bad tempered."

6th injection : " I now have a full night's sleep. Spend the mornings in the workshop and can now go to the pictures. Before these injections I could not bear the thought of anything like that. Now everything seems different, and I can enjoy myself with no ill-effects, such as headaches. No sway between moods as there was at first. Have much more confidence and seem to be getting back to my original self."

10th injection : " These injections have certainly made me feel very much better. I can concentrate and think clearly and now feel equal to anyone."

INTELLIGENCE TESTS.

Fifty-four of the cases (unselected) were given the 20-minute Progressive Matrices Test on admission and on completion of the treatment. Group mean scores and standard deviations for the two tests are as follows :

	First test.	Second test.
Mean scores	33.37	38.93
Mean percentile scores	(41.26)	(65.84)
Standard deviation	13.15	12.61

These figures show a substantial increase after treatment. By the following formula it is possible to calculate the significance of this increase without recourse to controls :

$$\sigma_D = \sqrt{\sigma^2 M_1 + \sigma^2 M_2 - 2r_{12} \sigma M_1 \sigma M_2} \quad . \quad . \quad . \quad (20)$$

The critical ratio obtained from this formula is 5.55/1.45 or 3.82, and the probability that the obtained difference is significant is almost 100 chances in 100, i.e. virtual certainty.

Confirmation is demonstrated by a comparison—by grade—with 107 control cases tested on admission and after discharge on the same test.*

Gr.	I	II	III	IV	V	Expected %	Control group. (107 cases.)		Treatment group. (54 cases.)	
							First test. %	Second test. %	First test. %	Second test. %
							3	10	9	17
20	14	15	18	28						
50	48	42	41	39						
20	25	25	30	16						
5	10	8	2	0						

	Control group. %	Treatment group. %
Two grades up	5.6	3.7
One grade up	25.2	37.1
Unchanged	53.4	55.5
Down one grade	14.9	3.7
Down two grades	0.9	0.0

* The cases used as control group were neurotics from a similar population. We are indebted to Mrs. H. T. Himmelweit of Mill Hill Emergency Hospital for the figures.

The treatment group also show less score deviation on retest—unlike the control group, which shows a slight increase. The coefficient of variation $\frac{100\sigma}{M}$ for the treatment group is 18 per cent. less on the second test than on the first test (32.43 against 39.38).

The improvement shown after the injections was evident not only in the enhanced speed and accuracy, but also in the men's demeanour, when they assembled for the retest: they were brighter and more cheerful.

DISCUSSION.

The results obtained from the use of Afenil for the relief of the distressing symptoms of the post-concussive syndrome help to throw a new light on the aetiology of the disorder.

The administration of the preparation produces a powerful vasodilatation of the organism, which supports Malone's (15) theory that the syndrome in part has as its aetiological basis an altered vasomotor activity. He put forward the hypothesis that in the relief of symptoms by prostigmine the ensuing vasodilatation acted on the labyrinthine and cranial blood vessels. Perlow (22) has found this dilatation to be primarily arterial rather than arteriolar or capillary.

Helfand (23) found in a series of 22 cases of the syndrome that many of the findings were of a functional (reversible) nature, and believes that they were primarily vasomotor in origin.

Zacks (8) has described degenerative changes in the nuclei of the cochlear and vestibular nerves, as well as an altered irritability of the vasodilators and vasoconstrictors, with resultant areas of localized altered circulation.

Wolff (24) concluded that intracranial pain is due to an alteration in the tonus of the involved arteries and of the meningeal arteries in particular. This goes to support the results obtained with Afenil. It is possible that such vasodilatation may result in the mechanical breaking-up of organic changes, such as adhesions.

Further to the vasodilatation produced one might ascribe to the calcium content of Afenil a checking influence on conditions of excitation of the nervous system. Calcium ions have a general sympathicotonic effect. The investigations of Jansch on the eidetic constitution, and Peritz (25), who traces a part of the schizothymic dispositions of Bleuler and Kretschmer to spasmophile dynamics of the organism, suggests that calcium therapy acts by way of the epithelial bodies.

In reference to other calcium mobilization agents, notably those containing vitamins B and D, some of these latter medicaments were substituted with practically no result at all. Intravenous application is indicated in all cases.

The effect of Afenil on post-concussive states is unmistakable, and its employment is to be recommended for its undoubtedly favourable effect upon the course of the cure. The results suggest that the symptoms of the post-concussive syndrome are probably produced through pathophysiologic

mechanisms involving an alteration in the vasomotor tonus with resultant muscular tension and vascular instability.

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