HEAT REGULATION IN DEMENTIA PRÆCOX REACTIONS OF PATIENTS WITH DEMENTIA PRÆCOX TO COLD *

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THE responses of a homoeothermal organism to an extremely low environmental temperature and their adequacy in maintaining the body temperature at its normal level are measures of heat regulatory efficiency. A study of the reactions of schizophrenics exposed to extreme cold may reveal defects of ætiological importance. Experiments on heat regulation are particularly applicable for the discovery of any inadequacies in dementia præcox at the physiological level because the stimulus (cold) may be made sufficiently intense to tax the central thermogenetic apparatus to the utmost.

Lavoisier,¹ in 1777, observed that a man consumes more oxygen when the temperature of the air is 15° C. than he does when the environmental temperature is 32·5° C. Rubner,² among others, has demonstrated by calorimetric experiments that the heat production of the body is increased when there is a fall in the external temperature, the body temperature remaining constant. This phase of heat regulation was termed by Rubner 'chemical regulation' in contradistinction to 'physical regulation' which consists in an adjustment of the heat loss of the body when exposed to ordinary environmental temperature changes. Chemical regulation consists of a reflex increase in heat production in response to a very low external temperature when physical regulation or diminution of the heat loss no longer suffices to maintain the body near its constant temperature.

Variations from the normal in the oxygen consumption rate of schizophrenics have been reported by Hoskins.³ However, the lower oxygen consumption rate under basal condition that he reported may be interpreted as being due to the inactivity of the schizophrenic or may be consequential to the disease, a factor which Hoskins did not omit in his interpretation. On

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the other hand, a study of changes in the rate of oxygen consumption induced reflexly by an intense stimulus of short duration and dependent upon the activity of the central nervous system and neuromuscular apparatus may reveal factors of ætiological significance. Moreover, patients with dementia præcox, who in their usual environment show only slight or no physiological variations from the normal, may react to extreme environmental changes in a manner indicative of a profound physiological disturbance.

METHOD

Fifty female patients diagnosed as cases of hebephrenic dementia præcox by the staff of the Elgin State Hospital were tested in the manner described below. They were all free from organic disease and were fairly cooperative with the procedure. Their median age was 30. Only 44 per cent. of the group were over 30 years of age and only five patients were over 43 years. The range was from 18 to 64. Their weights ranged from 83 to 193 lb., with 60 per cent. of the group weighing between 110 and 150 lb. The median weight was 121.5 lb. The duration of hospitalization was from 12 days to 15 years, with an average of two and a half years, 60 per cent. of the group having been in the hospital less than two years.

The oxygen consumption rate was determined for each patient under as nearly basal conditions as possible. The patients had had no food for 15 to 16 hours and rested from one to two hours before the tests were made. Fifteen or 20 minutes prior to immersion in cold water the oxygen consumption rate was determined on each patient. It was decided to immerse the patients in as cold water as possible. Four of the patients were tested in water at 58° F., one at 54° F. and one at 57° F. A temperature between 60° and 62° was finally found to be the most satisfactory and was used for 72 per cent. of the patients. Nine, or 18 per cent., of the patients did not cooperate in water at this temperature but did cooperate when the temperature was raised to 68° or 70° F.

At this point it is advisable to mention the fact that water has a greater heat conductivity than air and a considerably greater heat capacity. Heat from the body is lost much faster when exposed to cold water at a given temperature than in a medium of air at that temperature. Stated in another way, water at 90° F. feels cool, whereas air at that temperature feels very warm. Water at 60° F. is an extremely intense cold stimulus and is comparable with experiments in air at a much lower temperature. As soon as the patient was resting quietly in the water, the oxygen consumption rate was determined. The subject was then taken out, wrapped up in a warm blanket and put to bed. The total time spent in the water was usually from 15 to 20 minutes. Oral temperatures, pulse, complete blood counts and blood sugar determinations were taken in about 40 per cent. of the patients. No selections of patients were made for these additional observations. The

scope of the tests was merely enlarged as the work progressed. These determinations were made immediately after the oxygen consumption was tested in bed and in the water.

The recovery reactions of the patients were then tested and the above-mentioned observations were repeated after the patient had rested in bed, covered with blankets, 45 minutes to one hour after emergence from the cold water.

Twelve patients with chronic encephalitis and 26 healthy nonpsychotic subjects were subjected to the same procedures and served as controls. The patients with chronic encephalitis were tested twice within several weeks—once under treatment with atrophine and again after treatment had been discontinued for about a week. The control subjects included both men and women. A detailed analysis of the controls is given in papers to be published.^{4,5}

RESULTS AND COMMENT

The reactions of the three groups are charted and tabulated. Fig. 1 shows that schizophrenics as a group differ from the normal control group in the rate of oxygen consumption when exposed to extreme cold. Fifty-six per cent. of patients with dementia præcox react to cold with an increase in oxygen consumption rate between 10 and 40 per cent., whereas 50 per cent. of nonpsychotic controls are grouped between 33 and 68 per cent. A histogram was not made from the results in chronic encephalitis because of the small number of subjects. However, a glance at Table V shows that the median change in oxygen consumption was similar in dementia præcox and in treated postencephalitic parkinsonism (21.00), and lower than the median in the nonpsychotic group (36.50). Table V also shows that the median temperature change on exposure to cold in the dementia præcox group was -0.8°F. as compared with a median change of -0.7°F. in chronic encephalitis (untreated), -0.6°F. (treated), and a change of -0.2°F. in the normals.

Reactions of the individual cases are given in Tables I to IV. Sixteen patients with dementia præcox, or 84.2 per cent. of the group in which temperatures were taken, lost from 0.2°F. to 3.0°F. , with an average loss of 0.94°F. Only one patient showed a gain in temperature (0.2°F.). Two patients showed no change. Forty-four per cent. of the nonpsychotic subjects gained from 0.2°F. to 0.9°F. , with an average of 0.3°F. Sixty-six per cent. lost from 0.2°F. to 1.2°F. , with an average of 0.73°F. All of the untreated chronic encephalitics showed a decrease in temperature varying from 0.2°F. to 1.2°F. , with an average of 0.73°F. The treated patients with chronic encephalitis had the lowest increase in oxygen consumption rate and showed the most marked decrease in temperature. A detailed comparison of the treated and untreated chronic encephalitics forms the subject-matter of another paper.⁵

FIG. 1.—Histogram showing the gain or loss in oxygen consumption in 50 patients with hebephrenic dementia praecox as compared with 26 nonpsychotic healthy subjects, while placed for 15 to 20 minutes in cold water of about 60° F. The solid line represents the patients with hebephrenic dementia praecox. The broken line represents the nonpsychotic subjects.

The reactions of patients with dementia præcox, in general, resemble those of the chronic encephalitics. They are of a lesser intensity than the responses of the nonpsychotic subjects, and are greater than the reactions of chronic encephalitics treated with atropine. It is evident, then, that schizophrenics as a group are defective in chemical heat regulation when compared with nonpsychotic subjects. Patients with dementia præcox have an inadequate response when exposed to cold. In only one of the schizophrenics

TABLE I. THE EFFECT OF COLD ON OXYGEN CONSUMPTION AND ON BODY TEMPERATURE

Hebephrenic Dementia Præcox

Patient	Oxygen consumption Gain or loss in cold water	Oxygen consumption Gain or loss 45 min. to 1 hr. after exposure in cold water	Temperature Gain or loss in cold water °F.	Temperature Gain or loss 45 min. to 1 hr. after exposure in cold water °F.	Difference between temperature readings during exposure and 45 min. to 1 hr. following exposure °F.
F.D.	81	2	— 0.2	0	0.2
F.A.	63	—	— 0.4	—	—
F.R.	62	— 9	— 1.0	— 0.4	0.6
L.E.	53	0	— 1.0	— 0.2	0.8
R.R.	50	3	0.2	0.1	— 0.1
E.K.	48	—	— 0.8	—	—
H.S.	45	11	— 0.8	— 0.6	0.2
A.W.	39	— 35	— 0.6	— 1.3	— 0.7
I.W.	35	— 8	— 1.0	— 0.6	0.4
M.R.	28	0	— 1.5	— 1.2	0.3
F.Rh.	28	0	0	0	0
A.N.	22	—	— 0.8	—	—
V.B.	21	0	— 3.0	— 2.4	0.6
E.D.	17	0	0	—	—
E.W.	17	— 8	— 0.4	— 0.6	— 0.2
M.M.	16	—	— 1.4	—	—
D.H.	10	— 7	— 0.2	— 0.8	— 0.6
B.W.	7	14	— 1.0	— 2.8	— 1.8
B.S.	5	3	— 0.9	—	—

was there an overcompensation in heat production to cause a slight increase in temperature over the basal level (Table I). Eight of the 18 nonpsychotic subjects whose temperatures were taken in water showed an increase in temperature as a result of overcompensation in metabolic response to cold (Table II).

Our observations are in apparent contradiction to those recently reported by Cameron.⁶ However, by employing an extremely low temperature we tested responses of increased heat production or chemical regulation, whereas Cameron exposing his patients to a temperature of about 20 degrees higher

than we used did not induce a reflex increase in metabolism. Physical heat regulation was studied by him and he concluded that although heat production in the schizophrenic reaction is low, the mechanisms of heat control are slightly more active in a schizophrenic than in a non-schizophrenic group. 'This overactivity was sufficient to compensate for the poor heat production even on exposure to cold.' One may, therefore, conclude from our observations that chemical regulation is defective in dementia præcox, and from

TABLE II. THE EFFECT OF COLD ON OXYGEN CONSUMPTION AND ON BODY TEMPERATURE

Nonpsychotic Controls

Patient	Oxygen consumption Gain or loss in cold water	Oxygen consumption Gain or loss 45 min. to 1 hr. after exposure in cold water	Temperature Gain or loss in cold water °F.	Temperature Gain or loss 45 min. to 1 hr. after exposure in cold water °F.	Difference between temperature readings during exposure and 45 min. to 1 hr. following exposure °F.
M.B.	100	51	— 0·6	— 2·0	— 1·4
C.W.	67	9	—	—	—
F.K.	62	— 5	— 1·0	— 2·0	— 1·0
A.S.	57	41	0·2	— 0·4	— 0·6
L.A.	54	0	0·5	— 0·7	— 1·2
A.A.	50	7	— 0·3	— 0·3	0
H.S.	45	21	— 1·2	— 1·4	— 0·2
L.S.	37	32	— 1·1	— 1·0	0·1
M.W.	36	— 11	0·2	— 0·8	— 1·0
F.N.	33	1	0·6	— 0·2	— 0·8
T.W.	23	3	—	—	—
M.A.	21	—	— 1·1	—	—
I.F.	19	— 13	0·2	— 1·4	— 1·6
M.S.	14	8	0·6	— 0·2	— 0·8
M.B.	12	— 8	0·9	0	— 0·9
M.F.	10	—	— 1·0	—	—
M.Y.	5	— 4	— 0·6	— 0·6	0
W.S.	0	— 5	0·4	0·4	0
M.L.	— 15	—	— 0·2	—	—
W.H.	— 14	— 4	— 0·2	— 0·8	— 0·6

Cameron's observations that physical regulation is more active. The conclusion that physical regulation is more active in the schizophrenic reaction may be correct, but the fact that his patients were tested only two hours after a meal introduces another factor into the interpretation. Rubner,² in experiments on fasting and well-fed animals, has shown that food compensates for metabolism that is induced reflexly by cold. He has also criticized the results of Johansson⁷ because the latter tested the reaction of his subjects only three hours after a meal. Moreover, Cameron himself has noted that the

heat response to the ingestion of food is more marked although less well sustained in the schizophrenic.

As mentioned above, we enlarged the scope of our investigation during its progress, adding, among other observations, temperatures during all test periods, and oxygen consumption rates 45 minutes to one hour after the bath. It so happened that the patients with dementia præcox on whom the additional observations were made fell in the group that had the higher range of oxygen consumption increase in cold water. Thus, a glance at Tables I and II reveals the fact that this smaller group of schizophrenics shows similar reactions to the nonpsychotic subjects in oxygen consumption gain or loss in cold water (col. 2). Nevertheless, these patients differ from the nonpsychotic controls in the reactions tabulated in the remaining columns of Tables I and II. Thus, none of the patients with dementia præcox showed a gain in oxygen consumption rate above 15, whereas four of the nonpsychotic subjects showed an increase (51, 41, 21 and 32 per cent.). The schizophrenics, then, did not maintain their increased metabolic response that they had on exposure to cold, whereas some of the normal subjects who had a similar metabolic reaction in cold water had a continued effect of the cold water 45 minutes to one hour later. The results tabulated in cols. 2 and 3 in Tables I and II further reveal the fact that the schizophrenics do not maintain the metabolic stimulation of the cold water. The patients with dementia præcox had a much greater drop in oxygen consumption rate after exposure from the high rate during exposure as compared with the normals.

The differences between the two groups are even more strikingly revealed in the last two cols. of Tables I and II. In these two columns are tabulated the gain or loss in temperature 45 minutes to one hour after exposure in cold water and the differences between the temperature readings during exposure and 45 minutes to one hour following exposure, respectively. Before we analyse these results we wish to mention briefly a physiological effect noticed after emergence from a cold bath and known as the 'after-effect.'^{8, 9} After a person comes out of a cold bath and is wrapped up in a warm blanket it is found that his inner temperature is lower than it was in the bath. According to Liebermeister,⁸ this lowering of the inner temperature depends obviously on the fact that the temperature of the peripheral part which became considerably cooled during exposure to cold tends to equalize itself with the inner temperature by means of the circulation. As a result of exposure to cold the superficial layer of the body is cooled to a considerable depth. After the subject is again exposed to a warm environment there occurs a reactive hyperæmia, the inner heat being conducted by means of the dilated blood vessels to the surface of the body. Thus, the inner temperature falls while the surface temperature rises until a normal gradient in the temperatures of the skin and the subcutaneous tissue is again set up.¹⁰ If one studies the results given in the last column on Tables I and II, it becomes obvious that dementia præcox as a group does not have this reactive hyperæmia, as

shown by a failure of the inner temperature to fall. In fact, it is possible that a vasoconstriction occurs. Whereas seven out of 13 schizophrenics whose temperatures were taken showed a rise in temperature after the bath as compared with the temperature in the bath, only one of the normals (who also had hypertension) showed a slight rise (0·1° F.). The evidence adduced from the lack of a lowering of the inner temperature indicates that in dementia præcox there is no reactive hyperæmia observed in normal individuals, but instead there is a vasoconstriction. In this respect, also, the schizophrenics have reactions similar to the postencephalitics (Table III).

TABLE III. THE EFFECT OF COLD ON OXYGEN CONSUMPTION AND ON BODY TEMPERATURE

Postencephalitics (Untreated)

Patient	Oxygen consumption Gain or loss in cold water	Oxygen consumption Gain or loss 45 min. to 1 hr. after exposure in cold water	Temperature Gain or loss in cold water °F.	Temperature Gain or loss 45 min. to 1 hr. after exposure in cold water °F.	Difference between temperature readings during exposure and 45 min. to 1 hr. following exposure °F.
F.B.	121	— 22	— 0·2	0	0·2
W.K.	85	— 1	— 0·9	— 0·3	0·6
H.H.	83	22	— 0·2	— 0·8	— 0·6
A.G.	49	35	— 0·2	0	0·2
F.P.	33	—	— 1·9	0·6	2·5
W.B.	29	7	— 0·7	— 0·6	0·1
R.F.	19	— 6	— 1·4	— 0·8	0·6
F.M.	17	— 4	— 0·4	— 0·6	— 0·2
C.C.	12	— 11	— 0·4	— 1·0	— 0·6
E.P.	— 18	—	—	—	—
T.H.	27	— 5	— 0·8	— 0·8	0
C.B.	— 46	— 43	— 0·7	— 1·1	— 0·4

Tables VI, VII, VIII and IX give the individual reactions of the patients as to pulse, respiration, leucocyte count and blood sugar. Table X is a statistical summary of the pulse and respiration in the three groups. There was no consistent reaction as to pulse in any of the groups. But a greater percentage of the schizophrenics reacted with an increase in pulse rate and the increase was greater than in the normals. There was a tendency towards a slight increase in respirations in all groups. Upon first entering the cold water the nonpsychotic subjects experienced a respiratory shock. This was not present in the schizophrenics, who breathed regularly and without effort from the very beginning. The observations on all subjects were made after the respiratory shock disappeared and breathing became regular. Loewy¹¹ observed this respiratory shock which soon disappeared and then the regular type of breathing was resumed. In 43 observations Loewy noted a lower

respiratory rate in 20, no change in 16, and a rise in seven on exposure to low temperatures. The respiratory frequency was lowered in a smaller number of patients in our experiments. There were insignificant differences in the respiratory changes in schizophrenia as compared with the control group.

The leucocyte count as a rule was increased on exposure to cold in all groups. An increase in the white blood count in cold baths was first reported by Thayer.¹²

There was no significant change in the blood sugar level on exposure in all groups. Swift,¹³ who exposed 21 human subjects to cold air at 2° C. for

TABLE IV. THE EFFECT OF COLD ON OXYGEN CONSUMPTION AND ON BODY TEMPERATURE

Postencephalitics (Treated, Atropine Sulphate to Tolerance)

Patient	Oxygen consumption Gain or loss in cold water	Oxygen consumption Gain or loss 45 min. to 1 hr. after exposure in cold water	Temperature Gain or loss in cold water °F.	Temperature Gain or loss 45 min. to 1 hr. after exposure in cold water °F.	Difference between temperature readings during exposure and 45 min. to 1 hr. following exposure °F.
F.B.	74	—	— 1.0	—	—
W.K.	2	— 9	— 3.0	0	3.0
H.H.	16	—	— 0.1	—	—
A.G.	20	— 20	—	—	—
F.P.	22	9	— 1.4	— 0.4	1.0
W.B.	35	7	— 2.2	— 1.4	0.8
R.F.	29	7	— 2.2	— 1.2	1.0
F.M.	3	4	— 0.6	— 0.6	0
C.C.	27	8	— 0.4	— 1.2	— 0.8
E.P.	18	—	— 0.5	—	—
T.H.	38	— 14	— 0.6	— 0.2	0.4
C.B.	7	—	0.6	—	—

one hour and a quarter, found the blood sugar level unchanged and concluded that epinephrin secretion is not involved in the increased heat production. Grollman¹⁴ concluded from his study on the effects of variations of the environmental temperature on various circulatory reactions in normal individuals that 'The quantity of blood thus diverted from the skin must be small and the absence of any increase in the total blood flow at low temperatures must be taken as evidence against the view that epinephrin plays the predominant part in producing the increased oxygen consumption observed at low temperatures.'

Thus, our observations corroborate those of Swift¹³ and Grollman¹⁴ and do not support the views of Cannon¹⁵ and his pupils. Epinephrin, however, may play a predominant rôle in the defence against cold in the lower animals.

TABLE V.
COMPARISON OF OXYGEN CONSUMPTION IN

	Hebephrenic dementia præcox				Postencephalitis untreated				Postencephalitis treated ; atropine sulphate to tolerance				Nonpsychotic healthy subjects			
	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range
Under basal conditions	50	-0.56	-0.50	-24 to 23	12	25.25	22.00	1 to 77	12	15.58	12.00	-9 to 60	26	-2.70	-1.50	-30 to 23
Gain or loss in tub of cold water	50	30.50	24.00	-14 to 115	12	34.25	28.00	-46 to 121	12	24.25	21.00	2 to 74	26	36.38	36.50	-14 to 114
Gain or loss after 45 min. to 1 hr. rest in bed following exposure to cold	15	-2.13	0	-35 to 14	10	-2.80	-4.50	-43 to 35	8	-1.0	5.50	-20 to 9	17	7.23	1.00	-13 to 51

COMPARISON OF TEMPERATURE °F.

	Hebephrenic dementia præcox				Postencephalitis untreated				Postencephalitis treated ; atropine sulphate to tolerance				Nonpsychotic healthy subjects			
	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range
Under basal conditions	20	98.40	98.40	97.40 to 99.20	11	98.20	98.40	97.30 to 99.00	11	98.20	98.40	97.60 to 98.80	19	98.10	98.00	97.40 to 99.00
Gain or loss in tub of cold water	19	-0.80	-0.80	-3.00 to 0.20	11	-0.70	-0.70	-0.20 to 1.90	11	-1.03	-0.60	-3.00 to 0.60	18	-0.20	-0.20	-1.20 to 0.09
Gain or loss after 45 min. to 1 hr. rest in bed following exposure to water	13	-0.80	-0.60	-2.80 to 0.10	11	-0.50	-0.60	-1.10 to 0.60	7	-0.70	-0.60	-1.40 to 0	15	-0.80	-0.70	-2.00 to 0.40
Gain or loss from temperature in tub after 45 min. to 1 hr. rest in bed	13	-0.02	0.20	-1.80 to 0.80	11	0.20	0.10	-0.60 to 2.50	7	0.80	0.80	-0.80 to 3.00	15	-0.70	-0.80	-1.60 to 0.10

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TABLE VI. EFFECT OF EXPOSURE TO COLD ON PULSE, RESPIRATIONS, LEUCOCYTE COUNT AND BLOOD SUGAR IN HEBEPHRENIC DEMENTIA PRÆCOX

Patient	Pulse Gain or loss in tub of cold water	Respirations* Gain or loss in tub of cold water	Pulse Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Respirations Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Leucocyte Count			Blood Sugar		
					Before being placed in cold water	While in tub of cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water	Before being placed in tub of cold water	While in cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water
F.D.	10	4	— 1	1	11,000	9,400	10,100	69.82	68.92	66.66
F.A.	22	4	—	—	7,200	10,700	11,200	68.93	66.66	—
F.R.	8	1	1	1	6,800	7,800	7,800	72.72	71.43	66.66
L.E.	24	6	6	4	6,200	9,500	8,500	72.43	69.82	69.82
R.R.	15	2	1	0	8,400	11,200	8,400	80.00	78.50	78.04
E.K.	— 1	0	—	—	13,000	16,000	—	80.00	80.39	—
H.S.	— 2	3	— 19	— 2	7,400	11,000	6,800	62.50	63.10	63.00
A.W.	— 3	4	— 3	0	9,000	11,000	12,400	74.07	74.07	73.52
I.W.	— 1	2	— 11	3	8,600	9,100	9,000	76.92	80.00	76.92
M.R.	— 7	3	— 3	0	6,200	5,600	7,000	76.59	77.22	76.92
F.Rh.	12	2	— 4	— 1	9,000	11,200	9,000	65.50	65.50	62.50
A.N.	4	3	—	—	—	—	—	—	—	—
V.B.	3	— 2	— 8	— 6	5,600	8,600	7,000	66.66	72.72	—
E.D.	— 6	0	—	— 1	8,000	10,800	8,100	64.51	74.07	66.66
E.W.	5	— 5	5	— 7	6,100	8,150	5,200	—	—	—
M.M.	4	2	—	—	—	—	—	—	—	—
D.H.	— 2	— 2	— 8	2	5,065	7,200	4,400	62.50	64.51	65.00
B.W.	— 3	2	— 9	2	5,000	9,600	8,800	71.43	69.40	—
B.S.	— 3	4	— 10	— 1	6,000	7,000	9,200	75.47	76.92	76.33

TABLE VII. EFFECT OF EXPOSURE TO COLD ON PULSE, RESPIRATIONS, LEUCOCYTE COUNT
AND BLOOD SUGAR IN NONPSYCHOTIC CONTROLS

Patient	Pulse Gain or loss in tub of cold water	Respirations Gain or loss in tub of cold water	Pulse Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Respirations Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Leucocyte Count			Blood Sugar		
					Before being placed in cold water	While in tub of cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water	Before being placed in tub of cold water	While in cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water
M.B.	- 6	0	- 8	0	6,000	7,000	5,000	71.21	76.93	76.03
C.W.	- 3	1	9	1	6,000	13,800	7,300	68.91	71.43	71.43
F.K.	6	2	- 6	0	7,500	11,000	8,500	66.66	67.50	67.12
A.S.	0	2	- 8	2	6,600	7,000	7,200	76.92	76.33	76.33
L.A.	- 5	2	- 14	2	5,950	8,200	8,200	74.10	74.80	74.90
A.A.	5	0	- 11	1	7,800	12,000	5,600	66.61	68.90	68.70
H.S.	- 11	5	- 11	4	6,300	11,050	7,250	—	—	—
L.S.	4	1	8	1	5,000	9,200	7,500	81.30	85.83	81.30
M.W.	- 5	0	- 1	—	7,500	9,500	4,500	73.26	73.26	77.51
F.N.	- 2	0	- 11	1	6,200	8,000	7,800	81.30	66.60	—
T.W.	2	2	0	2	6,000	9,500	8,900	85.10	—	86.95
M.A.	4	0	—	—	9,000	10,000	11,000	82.98	85.10	—
I.F.	12	1	- 18	1	5,500	6,400	6,000	78.04	68.92	88.92
M.S.	- 4	2	- 2	4	6,700	6,600	5,000	74.60	—	74.00
M.B.	1	2	- 4	2	7,200	10,000	5,000	63.40	63.50	60.50
M.F.	- 6	3	—	—	9,100	9,300	—	69.65	68.92	71.43
M.Y.	- 9	1	3	1	5,000	6,800	6,500	81.30	75.18	83.83
W.S.	6	2	2	2	5,700	13,000	9,000	71.43	66.66	71.43
M.L.	- 5	- 3	—	- 4	—	—	—	—	—	—
M.H.	- 6	- 3	- 7	- 3	9,100	11,000	9,100	66.66	64.51	64.51

TABLE VIII. EFFECT OF EXPOSURE TO COLD ON PULSE, RESPIRATIONS, LEUCOCYTE COUNT AND BLOOD SUGAR IN POSTENCEPHALITICS (TREATED)

Patient	Pulse Gain or loss in tub of cold water	Respirations Gain or loss in tub of cold water	Pulse Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Respirations Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Leucocyte Count			Blood Sugar		
					Before being placed in cold water	While in tub of cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water	Before being placed in tub of cold water	While in cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water
F.B.	— 7	2	—	—	—	—	—	—	—	—
W.K.	3	1	6	0	10,500	11,500	6,400	67·12	67·50	68·92
H.H.	—	—	—	—	—	—	—	—	—	—
A.G.	7	2	—	—	11,000	17,000	10,500	80·00	83·33	83·33
F.P.	— 15	0	1	0	8,300	15,600	15,000	67·12	64·51	66·66
W.B.	— 4	0	—	—	9,800	7,300	7,600	72·10	70·66	72·10
R.F.	— 3	—	—	—	4,400	5,000	4,500	76·92	76·92	80·00
F.M.	— 4	—	—	—	6,600	7,000	6,200	83·33	83·33	90·90
C.C.	— 2	3	—	—	6,100	10,800	6,800	74·07	72·72	72·72
E.P.	— 7	—	—	—	—	—	—	—	—	—
T.H.	9	1	—	2	5,000	6,400	4,500	76·92	72·99	76·92
C.B.	17	2	—	—	6,200	9,000	7,100	67·12	66·66	62·50

TABLE IX. EFFECT OF EXPOSURE TO COLD ON PULSE, RESPIRATIONS, LEUCOCYTE COUNT AND BLOOD SUGAR IN POSTENCEPHALITICS (UNTREATED)

Patient	Pulse Gain or loss in tub of cold water	Respirations Gain or loss in tub of cold water	Pulse Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Respirations Gain or loss to 1 hr. rest in bed following exposure in cold water	Leucocyte Count			Blood Sugar		
					Before being placed in cold water	While in tub of cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water	Before being placed in tub of cold water	While in cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water
F.B.	19	3	- 1	1	6,500	9,000	4,800	68.92	68.92	64.51
W.K.	6	4	6	1	7,750	9,800	8,200	85.10	66.90	—
H.H.	—	2	- 1	—	7,050	8,800	9,000	83.80	84.70	85.10
A.G.	18	7	0	0	6,000	8,900	7,200	71.43	65.62	74.04
F.P.	7	0	8	—	11,000	13,000	8,800	74.10	75.40	75.40
W.B.	- 8	3	- 7	—	6,000	9,100	10,000	86.90	88.80	90.90
R.F.	- 18	0	- 24	0	4,400	5,000	4,500	76.92	76.92	80.00
F.M.	- 5	1	- 8	1	6,500	7,700	5,400	100.00	95.20	100.00
C.C.	- 4	0	- 12	—	8,200	10,200	6,800	68.50	76.90	76.90
E.P.	—	7	—	—	—	—	—	—	—	—
T.H.	0	6	- 11	3	10,600	12,700	13,400	100.00	88.80	—
C.B.	- 7	- 1	- 15	—	10,000	13,750	9,100	80.00	76.90	80.00

TABLE X. COMPARISON OF PULSE IN

	Hebephrenic dementia præcox				Postencephalitis untreated				Postencephalitis treated ; atropine sulphate to tolerance				Nonpsychotic healthy subjects			
	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range
Under basal conditions	43	72.41	72.00	48 to 96	11	83.00	84.00	73 to 94	11	80.00	79	72 to 91	20	69.50	66.00	54 to 94
Gain or loss in tub of cold water	41	1.14	0	-16 to 24	10	0.80	-2.00	-18 to 19	11	0.54	-3	-15 to 17	20	-2.30	-3.50	-12 to 6
Gain or loss after 45 min. to 1 hr. rest in bed following exposure to cold	14	-4.50	-3.50	-19 to 6	11	-5.90	-7.00	-24 to 8	8	-5.75	-7	-15 to 6	17	-4.00	-6.00	-18 to 9

COMPARISON OF RESPIRATIONS IN

	Hebephrenic dementia præcox				Postencephalitis untreated				Postencephalitis treated ; atropine sulphate to tolerance				Nonpsychotic healthy subjects			
	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range
Under basal conditions	49	16.02	16	8 to 28	12	16.60	16.00	12 to 22	12	16.58	16.00	12 to 22	26	13.31	13.50	7 to 20
Gain or loss in tub of cold water	49	1.00	1	-7 to 11	12	2.66	2.50	-1 to 7	12	0.42	0.50	-2 to 3	26	1.65	1.50	-3 to 10
Gain or loss after 45 min. to 1 hr. rest in bed following exposure to cold	15	-0.50	0	-7 to 4	10	0	0	-2 to 3	8	-1.25	-0.50	-8 to 2	18	1.00	1.00	-4 to 4

Our findings do not indicate either an increased or diminished response in epinephrin in dementia præcox and do not support the conclusions of Freeman and Hoskins¹⁶ that there is some adrenal deficiency in schizophrenia. However, these authors were eliciting the reactions of schizophrenics to a glycerin extract of adrenal cortex. Hartman, Brownell and Crosby¹⁷ in experiments on rats concluded that the cortical hormone is concerned with heat production to maintain the body temperature.

In addition to observing that the schizophrenics, as a rule, did not have any respiratory shock on entering the cold bath, we observed that fewer of the patients with dementia præcox shivered than normals, and of those that shivered, the intensity of the shivering movements was considerably less than in the nonpsychotic subjects.

DISCUSSION

There is an agreement in the recent literature in ascribing to the hypothalamus the rôle of principal heat regulatory centre. From experiments on cats, Bazett, Alpers and Erb¹⁸ concluded that the hypothalamus just cephalic to the corpora mamillaria was necessary for temperature control. This area included the nuclei surrounding the walls of the third ventricle and the infundibular nuclei. The patients with dementia præcox, considered as a group, on exposure to cold, did not respond with as intense heat production as the normals and had a greater drop in temperature. This inadequacy in heat regulation may be due to a disturbance in the physiology of the hypothalamus. The deficient response in shivering is further evidence that the disturbance is in the hypothalamus. Sherrington,¹⁹ who observed dogs with a spinal transection, under extremes of temperature, noticed that when the animals were exposed to extreme cold there was an absence of shivering in the region innervated from behind the transection. Shivering occurred only headward of the spinal lesion. Shivering was concluded by Sherrington to be of central (diencephalic) origin. Keller and Hare²⁰ observed that animals in which the hypothalamus had been removed and the rest of the brain left intact could not be made to shiver and showed a release from control of the heat loss mechanism.

The failure of the schizophrenics to react with a vasodilatation when exposed to a warm environment is further evidence that the disturbance is in the hypothalamic nuclei. Davison²¹ attributes the function of heat regulation to the nuclei tuberis proper and the mamillary bodies.

The reactions in dementia præcox resembled those elicited in post-encephalitic parkinsonism as a group. In view of the fact that the hypothalamus and the grey matter round the third ventricle are the seat of lesions in many cases of epidemic encephalitis,²² the evidence for a physiological disturbance in that region in dementia præcox becomes more conclusive. One of us, however (Finkelman²³), from a study of viscosity of muscles in catatonia and parkinsonian rigidity, has concluded that the

difference between the muscle tonus curves of chronic encephalitis and catatonia is evidence that the muscle rigidity in these two conditions is not due to physiological interruption at the same levels. This work does not invalidate our conclusions, as the cerebrospinal pathways that subserve muscle tonus are not involved in the experiments reported here. In other words, the hypothalamic centres to which we are attributing the physiological disturbance in dementia præcox as to defective heat regulation are probably not primarily involved in the mechanism of rigidity in catatonia.

The conclusion that there is a central disturbance in dementia præcox in the mechanism for heat regulation may be further strengthened if deficiencies in the peripheral mechanisms involving afferent and efferent pathways are eliminated. First we shall consider the afferent pathway. It is commonly held that in dementia præcox there is insensitivity to pain. Thus, one may prick the patient's tongue with a pin and notice that the tongue is not withdrawn. The conclusion that the pain is not felt is erroneous. Although the patient's outward demeanour does not betray his feeling of pain, there occur the usual respiratory changes with pain. What one observes is a poor defence reaction. The tongue is not withdrawn or it is withdrawn hesitatingly from the noxious stimulus. According to Huston,²⁴ there is no significant difference in the sensory threshold to direct current stimulation between a schizophrenic group and a comparable normal one. Temperature sensations are associated with reflex response to temperature. According to Ebbecke,²⁵ the sensation of cold depends on the difference established between the temperature of the cold end-organ in the skin and the layers surrounding it which are supplied with blood. A difference between the temperature of warm blood and a cooled skin around the cold end-organ will cause a sensation of cold. Even assuming a very slow blood flow, the temperature of the skin in our experiments was made so extremely cold (on exposure to 60° F.) as to set up a temperature gradient even with a slow blood flow. The threshold value was exceeded.

The next peripheral pathway to be considered and one which may be defective in dementia præcox is the efferent system. In a recent publication we have reported some observations on the reactions of patients with dementia præcox to dinitrophenol.²⁶ Schizophrenics react to dinitrophenol with as great an increase in oxygen consumption rate as that reported in the literature for nonpsychotic individuals. Dinitrophenol is a metabolic stimulant which acts peripherally. It is evident, then, that schizophrenics do not have a defective effector apparatus for metabolic activity. Spinal reflex pathways, including the afferent arc, a spinal centre and the efferent arc, are not physiologically interrupted in dementia præcox. In fact, Dorsey and Travis²⁷ reported experimental evidence of an increased activity of the lower neural level in catatonic stupor. In schizophrenics the reflex conduction rate (patellar reflex) was greatly increased over that of the normal subject.

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There is one more possible localization of the deficiency in the mechanism for heat regulation, and that is the cortical component. Pinkston, Bard and Rioch, reporting observations made on dogs and cats which survived the removal of portions of the forebrain by six weeks to 28 months, could not decide 'whether or not there is a single centre in the brain responsible for the coordination of excitatory and efferent mechanisms' (for heat regulation), but concluded that several levels of the nervous system, including the cortical, are necessary for normal temperature control. One might suppose that the disturbance in dementia præcox is in the association pathways that subserve heat regulation; that there is a dissociation between the feeling of cold which is a cortical function and the motor innervation for increasing the metabolism. In other words, in dementia præcox there is an inadequate 'defence' reaction to extreme cold. Man, through use of clothing and artificial heat, has become accustomed to a very narrow temperature range. The degree of cold to which we exposed our patients was a very uncomfortable, noxious stimulus, against which nonpsychotic individuals (not in the experimental situation) make an adequate defence. The schizophrenics as a rule stepped into the cold water unconcernedly. Bender and Schilder, reporting on unconditioned and conditioned reactions to pain in schizophrenia, state that it was characteristic of all the reactions (to pain) that the patients never actively attempted to escape or defend themselves. These authors conclude that the defence of the patient is no longer integrated. There is a dissociation between the appreciation of pain and the defence mechanism. We can similarly speak of a dissociation between the appreciation of cold and the defence mechanism. But since the 'defence mechanisms' in heat regulation are involuntarily controlled reactions (shivering, vasomotor changes), the disturbance in heat regulation in dementia præcox is probably in the hypothalamus.

SUMMARY AND CONCLUSIONS

The reactions to extreme cold of a group of 50 patients with hebephrenic dementia præcox were observed. The oxygen consumption rates, temperature readings, blood sugar determinations and pulse, respirations, shivering, and other responses were noted before exposure, during exposure to water at 60° F. and during rest in bed after the bath. These reactions were compared with those observed in nonpsychotic subjects and in a group of chronic encephalitics exposed to the same experimental conditions. The patients with dementia præcox react to cold as a group with a lower heat production than the normals. The drop in temperature in the schizophrenics was greater than in the normals. Some of the nonpsychotic subjects maintain their metabolic stimulation for some time following exposure. This continued increased metabolic response was not found in schizophrenia. In the normal subjects there occurs a reactive hyperæmia, as evidenced by a drop in the inner temperature, after emerging from the cold bath into warm surroundings.

The inner temperature drops, the heat being conducted to the cooled body surface. This 'after-effect' does not occur in dementia præcox as a group.

Schizophrenics do not have any respiratory shock on immersion in cold water, as a rule. This transient respiratory phenomenon was observed in most of the normal subjects. In schizophrenia there was an absence of, or a very slight shivering response. Many of the nonpsychotic subjects shivered, and some very intensely. There was no significant change in the blood sugar level in any of the groups, indicating that epinephrine, at least in human subjects, does not play a rôle as a calorogenic agent on exposure to cold. Many of the reactions were similar in schizophrenia and in post-encephalitic parkinsonism.

We can conclude that in dementia præcox there is a low heat production in response to cold. The heat production is not maintained after exposure and there is no reactive hyperæmia. Evidence is adduced that there is a physiological disturbance in the hypothalamus in schizophrenia.

BIBLIOGRAPHY

¹ LAVOISIER and SEGUIN, 'Premier mémoire sur la respiration des animaux ; Premier mémoire sur la transpiration des animaux,' in *Oeuvres de Lavoisier*, 1862, 2, 688, 704.

² RUBNER, M., *Die Gesetze des Energieverbrauchs bei der Ernährung*, 1902.

³ HOSKINS, R. G., and WALSH, ANNA, 'Oxygen consumption ("Basal metabolic rate") in schizophrenia,' *Arch. Neurol. and Psychiat.*, 1932, 28, 1346.

⁴ FINKELMAN, I., and STEPHENS, W. MARY, 'Heat regulation ; the effect of cold on oxygen consumption,' to be published.

⁵ FINKELMAN, I., and STEPHENS, W. MARY, 'Heat regulation in postencephalitis,' to be published.

⁶ CAMERON, D. E., 'Heat production and heat control in the schizophrenic reaction,' *Arch. Neurol. and Psychiat.*, 1934, 32, 704.

⁷ JOHANSSON, J. E., 'Ueber den Einfluss der Temperatur in der Umgebung auf die Kohlensäureabgabe des menschlichen Körpers,' *Skand. Arch. f. Physiol.*, 1897-98, 7-8, 122.

⁸ LIEBERMEISTER, C., *Handbuch der Pathologie und Therapie des Fiebers*, 1875.

⁹ STRASSER, A., 'Die warme Regulation und ihre Bewertung,' *Wien. Arch. f. inn. Med.*, 1923, 6, 215.

¹⁰ BAZETT, H. C., 'Physiological responses to heat,' *Physiological Reviews*, 1927, 7, 531.

¹¹ LOEWY, A., 'Über den Einfluss der Abkühlung auf den Gaswechsel des Menschen,' *Pflüger's Arch.*, 1878, 46, 189.

¹² THAYER, W. S., 'Note on the increase in the number of leucocytes in the blood after cold baths,' *Johns Hopkins Hosp. Bull.*, 1893, 4, 37.

¹³ SWIFT, R. W., 'The effects of low environmental temperature upon metabolism : II. The influence of shivering, subcutaneous fat and skin temperature on heat production,' *Jour. Nutrition*, 1932, 5, 27.

¹⁴ GROLLMAN, A., 'The effect of variations in the environmental temperature on pulse rate, blood pressure, oxygen consumption, arteriovenous oxygen difference and cardiac output of normal individuals,' *Amer. Jour. Physiol.*, 1930, 95, 263.

¹⁵ CANNON, W. B., QUERIDO, A., BRITTON, S. W., and BRIGHT, E. M., 'The rôle of adrenal secretion in the chemical control of body temperature,' *Amer. Jour. Physiol.*, 1927, 79, 466.

- ¹⁶ FREEMAN, H., and HOSKINS, R. G., 'Comparative sensitiveness of schizophrenic and normal subjects to glycerin extract of the adrenal cortex,' *Endocrinology*, 1934, **18**, 576.
- ¹⁷ HARTMAN, F. A., BROWNELL, KATHERINE A., and CROSBY, A. A., 'The relation of cortin to the maintenance of body temperature,' *Amer. Jour. Physiol.*, 1931, **98**, 674.
- ¹⁸ BAZETT, H. C., ALPERS, B. J., and ERB, W. H., 'Hypothalamus and temperature control,' *Arch. Neurol. and Psychiat.*, 1933, **30**, 728.
- ¹⁹ SHERRINGTON, C. S., 'Note on temperature after spinal transections, with some observations on shivering,' *Jour. Physiol.*, 1924, **58**, 405.
- ²⁰ KELLER, A. D., and HARE, W. K., 'Hypothalamus and heat regulation,' *Proc. Soc. Exper. Biol. Med.*, 1932, **29**, 1067.
- ²¹ DAVISON, C., and SELBY, N. E., 'Hypothermia in cases of hypothalamic lesions,' *Arch. Neurol. and Psychiat.*, 1935, **33**, 570.
- ²² WEIL, ARTHUR, *Neuropathology*, 1933, 142.
- ²³ FINKELMAN, I., 'A comparison of the viscosity of muscles in catatonic and parkinsonian rigidity,' *Arch. Neurol. and Psychiat.*, 1934, **31**, 87.
- ²⁴ HUSTON, P. E., 'Sensory threshold to direct current stimulation in schizophrenic and in normal subjects,' *Arch. Neurol. and Psychiat.*, 1934, **31**, 590.
- ²⁵ EBBECKE, U., 'Über die Temperaturempfindungen in ihrer Abhängigkeit von der Hautdurchblutung und von den Reflexzentren,' *Arch. f. d. g. Physiol.*, 1917, **169**, 395.
- ²⁶ FINKELMAN, I., and STEPHENS, W. MARY, 'Dinitrophenol in dementia præcox,' *Jour. Neurol. and Psychopath.*, 1935, **15**, 230.
- ²⁷ DORSEY, JOHN M., and TRAVIS, L. E., 'Reflex response latencies in manic and depressive cases of the cyclothymic group and in cases of catatonic stupor of the schizophrenic group,' *Arch. Neurol. and Psychiat.*, 1932, **27**, 687.