

Exhibit P-78

demonstrated. The most common factor, when it was augmented by other factors, and relatively the least common factor when it was the only cause was an inadequate intake of vitamin D. The next most common factor was operative in the group in which hereditary causes were the predisposing ones, the third being old brain injuries.

In conclusion, when the paediatrician is called to treat a case of convulsions he must bear in mind that the cause is quite likely to be more complex than his original diagnosis would indicate. Each case must be studied as thoroughly as the exigencies of the occasion will permit. Treatment must be applied to each case individually. The problem of convulsions challenges the best in the art as well as in the science of medicine.

REFERENCES

- FORD, F. R.: Cerebral birth injuries and their results, *Medicine*, 1926, 5: 121.
- LENNOX, W. G., GIBBS, E. L. AND GIBBS, F. A.: The inheritance of epilepsy, *J. Am. M. Ass.*, 1939, 113: 1002.
- PENFIELD, W.: The Epilepsies: with a note on radical therapy, *New Eng. J. M.*, 1939, 221: 209.
- FAY, T.: Diagnosis in convulsions, *Am. J. Surg.*, 1942, 56: 314.
- DANDY, W. E.: Experimental investigations on convulsions, *J. Am. M. Ass.*, 1927, 88: 90.
- ZIMMERMAN, H. M.: The histopathology of convulsive disorders in children, *J. Paediat.*, 1938, 13: 859.
- MCQUARRIE, I., MANCHESTER, R. C. AND HUSTED, C.: Study of water and mineral balances in epileptic children; effects of diuresis, catharsis, phenobarbital therapy and water storage, *Am. J. Dis. Child.*, 1932, 43: 1519.
- MCQUARRIE, I., HUSTED, C. AND BLOOR, W. R.: Lipids of blood plasma in epilepsy: variations of lipids in relation to occurrences of seizures, *J. Clin. Investigation*, 1933, 12: 255.
- HELMHOLZ, H. F.: Discussion following Peterman, M. G.: Convulsions in childhood, review of one thousand cases, *J. Am. M. Ass.*, 1939, 113: 194.
- JOSEPHS, H. W.: Fasting as a cause of convulsions, *Am. J. Dis. Child.*, 1926, 31: 169.
- WEGMAN, M. E.: Factors influencing the relation of convulsions and hyperthermia, *J. Paediat.*, 1939, 14: 190.
- PETERMAN, M. G.: Convulsions in childhood; review of one thousand cases, *J. Am. M. Ass.*, 1939, 113: 194.
- GELLMORN, E., DARROW, C. W. AND YESINICK, L.: Effect of epinephrine on convulsions, *Arch. Neurol. & Psychiat.*, 1939, 42: 826.
- WYATT, O. S.: Convulsions in children while under general anaesthesia, *Minn. Med.*, 1940, 23: 101.

RÉSUMÉ

Les convulsions infantiles constituent un problème diagnostique très complexe où entrent en jeu des facteurs héréditaires et des facteurs acquis. Parmi les facteurs acquis, il faut signaler les traumatismes obstétricaux et leur conséquence, l'hémorragie intracérébrale; l'anoxie, les méningites et les encéphalites. Il faut aussi noter que les convulsions elles-mêmes causent des lésions cérébrales. Notons encore les troubles de certains métabolismes, notamment du calcium, de l'eau, des sels minéraux, etc.

Sur 224 cas, il existait chez 102, deux facteurs ou davantage qui pouvaient déterminer l'épilepsie. La privation de vitamine D est un facteur fréquemment associé à d'autres causes mieux connues; seule, cette avitaminose est rarement responsable des convulsions. L'hérédité est un facteur nettement prédisposant; enfin, les lésions cérébrales anciennes contribuent aussi pour une large part à l'éclosion de l'épilepsie. Le diagnostic étiologique est donc très difficile et le traitement est variable selon la ou les causes responsables.

JEAN SAUCIER

SENSITIVITY TO PAIN

(WITH AN ANALYSIS OF 450 CASES)

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LIBMAN¹ in his classical contribution on the individual sensitiveness to pain has stressed the importance of gauging the patient's sensitivity to pain in order to properly evaluate the symptoms in formulating a correct diagnosis. The appraisal of the patient's tolerance to pain is also an important adjunct in treatment and prognosis. The variation in symptoms of disease of the same nature in different individuals has principally been responsible for focusing attention on this subject.

Individuals have been classified as: (a) hyposensitive, (b) normally sensitive and (c) hypersensitive. According to Libman, there is a great tendency for the hyposensitive patient to feel less or none of the pain of a given disease and to present unusual and irregular radiations of pain. The hyposensitive patient may have what is called substitution symptoms instead of pain. These symptoms are apparently due to a disturbance of the autonomic nervous system, a number of which symptoms are initiated by reflex mechanisms. Substitution symptoms include burning, numbness, pressure, tingling, prickling and other forms of paraesthesia that may be considered as representative of pain. Libman's hypothesis, after an analysis of his observations, is that in the case of the hyposensitive patient, the pain impulses are delayed or may linger in the autonomic nervous system, while in the hypersensitive patient the impulses travel more directly into the central nervous system. He cites cases of visceral disease characterized predominantly by such manifestations as aerophagia or eructation, yawning, coughing, choking, hiccups and sneezing that may be explained on the basis of the aforementioned theory.

Various methods^{2 to 7} have been devised in an attempt to measure the threshold of pain, e.g., the thermal, electrical and chemical methods. In addition to such objections as extensive equipment and the time-factor, these methods have been found to be impracticable in routine clinical examinations. Because of their simplicity, the following tests described by Libman¹ and Hollander⁸ respectively lend

themselves best to routine use in clinical practice.

Libman's test for sensitivity to pain is carried out by first pressing the thumb against the tip of the mastoid bone and then slipping the finger forward and pushing the styloid process. The mastoid pressure serves as a control. Pressure on the styloid process is painful to some individuals and not to others. The sensitive point is presumed to be not the styloid process but a branch of the auricularis magnus nerve. Hollander,⁸ Wilder⁹ and Pelner¹⁰ have pointed out that the Libman test affords only a rough estimation of the patient's sensitivity to pain, for the degree of pressure exerted by the finger cannot be quantitatively determined and is, therefore, an uncontrolled variable in the test.

Recently Hollander suggested another method for quantitative evaluation of the patient's threshold to pain. The instrument consists of a piece of elliptical metal grater, three inches by four inches in size which is sewed to the contact surface of a blood pressure cuff. The cuff is applied on the patient's arm in the usual way, with the metal grater placed on the medial surface of the arm just above the elbow. The cuff is inflated slowly at the rate of about ten mm. of mercury pressure per second. The pressure on the grater prongs that causes the patient to wince, change expression, or cry out, is recorded as the sensitivity level to pain. The individual is not informed what is being done, so that a spontaneous reaction to the examination is obtained. In hyposensitive individuals, no wincing nor objection to the test occurs, even when the limit of the mercury column is reached. In the hypersensitive patient, the sensitivity level was below 110 mm. pressure. In the normal group, the sensitivity level ranged between 110 to 260 mm. pressure. Wilder in his paper on this subject states that the Hollander test was used routinely on an unselected group of cases, with one exception, namely that patients with moderate to severe hypertension were excluded; because these patients usually have had frequent blood pressure readings and are quicker to notice the unaccustomed sensation when the modified blood pressure cuff is applied. Secondly, it was felt that frequently it would be necessary to increase the manometric pressure to excessively painful levels in these patients in order to obtain the systolic blood pressure.

More recently, Pelner has used a device that he terms a sensometer. It is adapted from an instrument called the Geneva Lens Measure which consists of two peripheral fixed points, and one central point which is attached to a watch dial. This instrument is rested on the skin over the proximal phalanx of the thumb held horizontally with the distal phalanx bent at right angles to it, and the number that it registers on the dial by virtue of its own weight is borne in mind. Then the instrument is pressed until the pressure becomes unbearable, and the number corresponding to this sensation is recorded. The difference between the figure read and after pressure on the skin is taken as the patient's sensitivity level to pain.

An analysis of 450 cases in which the Libman and Hollander tests were carried out is herewith presented. This series consists of 260 cases examined in routine office practice; 150 coal miners employed at the Dominion Coal Company, No. 12 Colliery, New Waterford, Nova Scotia, who were the subject of study of the effects of a hazardous occupation on sensitivity to pain, and 40 Miemae Indians residing at the Reservation, Sydney, Nova Scotia, who were studied in search of racial peculiarities with respect to pain sensitivity.

TABLE I.
TOTAL SERIES (260 CASES)

Normal sensitivity.....	170 cases, 65%
Hypersensitive.....	47 " 18%
Hyposensitive.....	43 " 17%

TABLE II.
FUNCTIONAL DISEASE (130 CASES)

Normal sensitivity.....	70 cases, 54%
Hypersensitive.....	39 " 30%
Hyposensitive.....	21 " 16%

TABLE III.
ORGANIC DISEASE (130 CASES)

Normal sensitivity.....	100 cases, 77%
Hypersensitive.....	8 " 6%
Hyposensitive.....	22 " 17%

In the total series of 260 cases the hyposensitive group constituted 17%. This figure was approximately the same in the functional and organic types. Libman states that in his office practice, 30% of the patients were hyposensitive. Hollander's figures are 27% for the hypersensitive group, and 29% for the hyposensitive group. The hypersensitive group comprised 18% of the total series.

These data are modified when a sub-division of the total series is made into the organic and

functional types. In the functional types, which contained many cases in which organic disease could not be demonstrated and in which complaints were functional, as in cases of nervousness, chronic exhaustion, anxiety neuroses, and vague and ill-defined pains, the hypersensitive group increased to 30%. In the organic group, in which there was present evidence of organic disease, the hypersensitive group decreased to 6% (Table III).

Of the 47 cases of hypersensitivity, approximately three-quarters (72.5%) were women. Of the 43 cases of hyposensitivity, approximately 90% were men and 10% women.

Although these data are not in complete accord with the results obtained by other investigators, it is to be noted that the majority of these patients are within the normal limits of sensitivity to pain, i.e., 65% for the total series, as compared with 45 to 50% obtained in other reports.

It will be seen from Tables IV, V and VI that the threshold of pain is lower for women than for men. In the total series the mean average for men was 199 mm. of mercury and

TABLE IV.
PAIN SENSITIVITY LEVEL FOR TOTAL SERIES
Males Females

Sensitivity level, mm. of mercury	Number	Per cent	Number	Per cent
61- 90	5	3.4	9	8.1
91-110	8	5.4	25	22.5
111-150	14	9.4	16	14.4
151-180	33	22.2	32	28.8
181-210	26	17.4	9	8.1
211-259	25	16.8	15	13.5
260-300	38	25.4	5	4.5
Total.....	149	100	111	100
Average....	199 mm. of mercury		156 mm. of mercury	

TABLE V.
PAIN SENSITIVITY LEVEL FOR PATIENTS WITH
FUNCTIONAL DISTURBANCES
Males Females

Sensitivity level, mm. of mercury	Number	Per cent	Number	Per cent
61- 90	4	5.4	7	12.5
91-110	6	8.0	22	39.3
111-150	13	17.5	9	16.0
151-180	12	16.1	8	14.3
181-210	14	18.9	3	5.4
211-259	8	10.8	3	5.4
260-300	17	23.3	4	7.1
Total.....	74	100	56	100
Average....	186 mm. of mercury		138 mm. of mercury	

TABLE VI.

PAIN SENSITIVITY LEVEL FOR PATIENTS WITH
ORGANIC DISEASE

Sensitivity level, mm. of mercury	Males		Females	
	Number	Per cent	Number	Per cent
61- 90	1	1.3	2	3.6
91-110	2	2.7	3	5.5
111-150	1	1.3	7	12.7
151-180	21	28.0	24	43.6
181-210	12	16.0	6	10.9
211-259	17	22.7	12	21.8
260-300	21	28.0	1	1.8
Total.....	75	100	55	100
Average....	212 mm. of mercury		173 mm. of mercury	

156 mm. of mercury for women. In the organic type there was an increase to 212 mm. for men and 173 mm. for women, and in the functional type there was a decrease to 186 mm. for men and 138 mm. for women. These findings would indicate that patients with organic disease have usually a higher threshold to pain than those with functional complaints.

In the total series the hyposensitive figure for men was 25%, in the functional type the hyposensitive figure for men was 23%, and there was an increase to 28% in the organic type. In the functional type, the hypersensitive figure for women was nearly 52%, as against 13% for men. In the organic type, the hypersensitive figure for women was 9% and 4% for men. In the total series, 81% of the men had a reading of over 150 mm. of mercury.

TABLE VII.
AN ANALYSIS OF THE VARIOUS AGE-GROUPS IS
SHOWN IN THE TABLE BELOW

Age	Normal	Per cent	Hyper-sensitivity	Per cent	Hypo-sensitivity	Per cent
20 and under...	21	60.0	12	34.3	2	5.7
20-50....	108	62.7	30	17.5	34	19.8
50-80....	41	77.4	5	9.4	7	13.2

It will be noted that the age group under 20 had the greatest degree of hypersensitivity, namely, 34%. The oldest age group (50-80) showed in proportion the greatest degree of normaley, (77.4%), with a comparatively small degree of hypersensitivity. However, no definite conclusions or differences between various age-groups could be ascertained. It is possible that further study will yield more significant findings.

COAL MINERS

The Libman and Hollander sensitivity tests were conducted on 150 coal miners who were employed at the Dominion Coal Company, No. 12 Colliery, New Waterford, Nova Scotia. They were all well developed, sturdy and rugged physical specimens. Their appearance indicated that they could tolerate pain of great intensity without complaint. Most of them had worked in the mines from periods ranging from one to over forty years. A considerable number were of Scotch, English and Irish descent, and the remainder were comprised of Russians, Poles, Hungarians, Germans, Italians and Negroes. Their ages varied from seventeen to seventy. They conversed with a devil-may-care attitude and created the impression that they feared nobody. Many of these miners had served in the last war with distinction in the Cape Breton Highlander Regiment which had been noted for its valour. Young men from the age of seventeen were examined and one could note their freshness of youth in marked comparison with the boys of 23 and 24, who looked quite hardened and older than their years, though physically fit. They all agreed that working in the mines for years had toughened them considerably. Most of them on being questioned had had no major illnesses, and spoke very lightly of such ailments as tonsillitis, influenza, wounds or abscesses.

TABLE VIII.
PAIN SENSITIVITY LEVEL FOR MINERS

Males		
Sensitivity level, mm. of mercury	Number	Per cent
150-180.....	3	2.0
181-210.....	7	4.7
211-259.....	27	18.0
260-300.....	113	75.3
Total.....	150	100
Average.....	251.4 mm. of mercury	

An analysis of Table VIII shows that over 75% of these miners (113 out of 150 cases) were hyposensitive to pain, and the remaining 25% had a normal threshold to pain. The lowest reading was 160 mm. by the Hollander test. Eighteen per cent (27 cases) had readings between 211 and 259 mm. of mercury. The average mean reading was 251.4 mm. of mercury. The study of the various age-groups did not show any great significance.

MICMAC INDIANS

It has been noted that the Indians are preponderantly hyposensitive to pain. The Hollander and Libman tests were routinely carried out on forty Micmac Indians at the Reservation, Sydney, Nova Scotia. The average reading for the male was 237 mm. and 230 mm. for the female. Sixty-three per cent of the males were hyposensitive and 46% of the females were hyposensitive. There were no hypersensitive individuals in this group. The lowest reading for the male was 150 mm. and 164 mm. for the female. Boys and girls at the ages of seventeen gave readings from 150 to 210 mm. of mercury. A study of the various age-groups in relationship to sensitivity to pain yielded no definite information.

TABLE IX.
PAIN SENSITIVITY LEVEL FOR MICMACS

	Males		Females	
Sensitivity level, mm. of mercury	Number	Per cent	Number	Per cent
111-150	1	3.7		
151-180	4	14.8	2	15.4
181-210	2	7.4	2	15.4
211-259	3	11.1	3	23.1
260-300	17	63.0	6	46.1
Total.....	27	100	13	100
Average....	237 mm. of mercury		230 mm. of mercury	

METHOD OF EXAMINATION

The Libman test was performed first in all cases, and the findings recorded. This was followed by the performance of the Hollander test. An analysis of the 450 cases reveals the accuracy of the Libman test in grading the cases as normal, hypersensitive and hyposensitive. The findings of the Libman test were corroborated by the Hollander test. There were several cases who were sensitive to the styloid pressure on only one side, and these according to Libman react clinically like those who are hyposensitive to both sides. This observation was substantiated by the Hollander test which showed readings in all cases over 260 mm. of mercury, thus relegating them to the hyposensitive group.

CONCLUSIONS

1. An analysis is made of 450 cases in which the Libman and Hollander tests were performed to gauge their sensitivity to pain.

2. In 260 cases which were examined in the routine procedure of office practice, 65% were found to have normal sensitivity to pain, 17% were hyposensitive, and 18% were hypersensitive to pain.

3. Women have a lower threshold to pain than men.

4. In the hypersensitive group, over 72% were comprised of women.

5. In the hyposensitive group, 90% were comprised of men.

6. Patients with organic disease have a higher threshold to pain than those with functional disease or complaints as shown in the Tables.

7. No effects of age upon sensitivity to pain could be definitely determined.

8. Examination of 150 coal miners revealed that over 75% were hyposensitive to pain, and the remaining 25% were in the upper limits of normal findings. These findings suggest that a hazardous occupation over a period of years may be a predisposing cause in raising a patient's threshold to pain within the hyposensitive range.

9. Examination of 40 Miemac Indians re-

vealed that 57.5% were hyposensitive, and the remainder were normal. No case of sensitivity was found among them. Even youngsters gave high readings. These findings corroborate the statement that the Indians are a preponderantly hyposensitive race, despite the small number of cases examined.

10. The Libman and Hollander tests agreed in the categorization of all patients.

REFERENCES

1. LIBMAN, E.: Observations on individual sensitiveness to pain, with special reference to abdominal disorders. *J. Am. M. Ass.*, 1934, 102: 335.
2. HARDY, J. D., WOOLF, H. G. AND GOODELL, H.: Studies on pain. New method for measuring pain threshold. *J. Clin. Investigation*, 1940, 19: 649.
3. WOOLF, H. G., HARDY, J. D. AND GOODELL, H.: Studies on pain. Measurement of effect of morphine, codein, and other opiates on the pain threshold. *J. Clin. Investigation*, 1940, 19: 659.
4. MARTIN, E. G.: A quantitative study of faradic stimulation. II. The calibration of the inductotherm for break shocks. *Am. J. Physiol.*, 1908, 22: 116.
5. MACHT, D. I., HERMAN, N. B. AND LEVY, C. S.: A quantitative study of the opium alkaloids, individually and in combination with one another in normal men. *J. Pharmacol. & Exper. Therap.*, 1916, 8: 1.
6. HAUCK, A. AND NEUERT, H.: Untersuchungen über die Hautsensibilität die Schmerzschwellen bei elektrischer Reizung des sensiblen Nerven. *Arch. f. d. ges. Physiol.*, 1937, 238: 574.
7. EDDY, N. B.: Studies on morphine, codein and their derivatives. *J. Pharmacol. & Exper. Therap.*, 1932, 45: 339.
8. HOLLANDER, E.: A clinical gauge for sensitivity to pain. *J. Lab. & Clin. Med.*, 1939, 24: 537.
9. WILDER, R. M., JR.: Sensitivity to pain. *Proc. Staff Meet., Mayo Clin.*, 1940, 15: 551.
10. PELNER, L.: The determination of sensitivity to pain. *J. Lab. & Clin. Med.*, 1941, 27: 248.

Case Report

HISTOLOGICAL CHANGES IN CARCINOMA OF PROSTATE FOLLOWING RESECTION AND THE USE OF STILEBESTROL

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A man, H.S., aged 62, with acute complete urinary retention was referred to me by his physician, who stated that the condition was an obstructed bladder due to enlargement of the prostate, which, per rectum, appeared to be due to carcinoma. I palpated this gland and found it to be enlarged, irregular, of firm to stony hardness, and generally fixed—a typical malignant-appearing prostate.

He was admitted to hospital and I carried out prostatic resection. At this time, examination of the bladder disclosed the usual picture of prostatic obstruction without marked complications and little if any evidence of infection, the urine being clear and never showing more than a few white blood cells in the low-

power field. Following this operation micturition rapidly returned to normal so that within a few weeks of his hospital discharge he had no dysuria, was completely emptying his bladder, and had no frequency day or night. He was, however, complaining of a feeling of heaviness which appeared to be within the rectum. This at times would become an aching, and at other times a vague type of irritation. He had no energy, felt tired, and, though he had returned to work, found it to be an effort. He also had not regained weight lost while in hospital.

The pathological report of the sections of prostate removed was "Carcinoma, showing fairly extensive infiltration".

The prostate at the time of leaving hospital was generally smaller than previous to operation, but was still hard and fixed, and made one unhesitatingly think of malignancy.

Fifteen months after his hospital discharge, he was given stilbæstrol to take. During this period of time (from operation until com-