in his sinuses ran a definite risk of developing a more serious form of the infection. In actual fact, 7 of the 88 patients (2 children, 5 adults) have had proved pneumococcal or lobar pneumonia, and there are possibly more, as the significance of the association has hitherto not been

TABLE II.

Year.	Children.			All Cases.			Crude Death rate from Lobar Pneumonia per Million Living England and Wales.		
	Examinations.	Pneumococcal Infection.		Examinations.	Pneumococcal Infections per 100 Examinations.	Lobar Pneumonia at Necropsy per 10,000 Infirmity Patients.			
		Per 100 Children.	Per 100 Examinations.						
1920 ...	51	}	5.7	4.0	245	}	...	}	220
1921 ...	75		...	...	326		2.1		
1922 ...	6	...	...	165	...	...			
1923 ...	28	}	15.0	10.6	235	}	...	}	246
1924 ...	47		...	...	343		5.3		
1925 ...	32	}	0	0	385	}	...		
1926 ...	37		...	...	298		0.7	12.5	
1927 ...	65	8.9	4.6	368	2.2	...	...	270	
1928-29*	165	16.3	12.0	611	7.0	26.4			

* Fourteen months.

appreciated nor have special inquiries been directed to the point; two cases of pneumococcal meningitis and one of pneumococcal mastoid disease also are recorded.

By the kindness of Dr. A. D. Fraser I have been able to obtain the figures for lobar pneumonia from the *post-mortem* indexes of the Bristol Royal Infirmary. Treating

these as an index of the local incidence of the disease, and the Registrar-General's returns as a national index, we see that there has recently been a close association between the incidence of pneumococcal infection of the sinuses and that of pneumonia. All four sets of figures show a low value for 1920-21, a high value for 1923-24, a low value

for 1926, and a subsequent rise. We appear now to be in a period of high incidence of pneumococcal infection; certainly the local figures for lobar pneumonia are high, and I feel tempted to predict that 1928 and 1929 will eventually show high national incidence. At least with local figures, the rise and fall of sinus pneumococcal infection tends to precede that of pneumonia; and it will be interesting to observe in the future whether variation in the nasal sinus infections (and particularly in children, in whom it seems to be greater and to appear rather earlier than in adults) forms a reliable guide to forecast the trend of mortality from lobar pneumonia. The accompanying graph illustrates the association recorded in the last ten years.

CONFUSIONAL INSANITY WITH EMPYEMA OF THE SPHENOIDAL SINUS.

BY

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(With Special Plate.)

THE association of a sphenoidal sinusitis with definite macroscopic change and microbic invasion of the pituitary gland in a case of insanity is described below, and is illustrated by sketches and photomicrographs; its importance to psychiatry is emphasized by a consideration of pituitary-hypothalamic metabolic disorders in 69 cases of insanity in which a sphenoidal sinusitis had been demonstrated clinically.

A man, aged 51, died four months after admission to hospital. His early history was indefinite, but there was concussion at the age of 26. The first onset of mental disorder occurred when he was 31; from this he recovered, but relapsed again ten years later. He was suffering from confusional insanity, was talkative, disorientated, and maniacal. He had auditory hallucinations, bilateral otitis media, bilateral ptosis, and his blood pressure was 210. The Wassermann and Widal reactions were negative. Three days before death he developed epileptiform fits, after sixty-eight of which he died in status epilepticus.

Post-mortem Examination (seventy-five minutes after death; the tissues as removed were immediately placed in fresh Kaiserling solution).—There were slight superficial haemorrhages in the pia arachnoid, the largest being over the left frontoparietal area. The cerebro-spinal fluid was slightly blood-stained in the posterior cisterns only. The dural surface of the base of the skull was clear and shiny. There was pus in the pharynx, which could be traced to the left sphenoidal ostium. The sphenoidal sinus was literally full of yellowish pus, the cavity being a large one and almost surrounding the pituitary gland. The pituitary contained large masses of colloid. There was a mucous polypus in the left antrum. The right lung was adherent to the chest wall; there was some perihepatitis, perisplenitis, and a well-marked hydronephrosis.

EXPLANATION OF THE FIGURES.

Fig. 1 is a sketch of the sinus (actual size), and illustrates the following:

(a) Empyema of the sinus. Thick, glairy, yellow pus was attached firmly to the posterior inferior wall, from which it extended to and through the ostium. The sketch gives a poor idea of the actual amount originally present, fixation having caused a very marked shrinkage, and handling of the specimen the detachment of a quantity of smaller particles.

(b) The pituitary fossa with its contained gland projects into, and is almost surrounded by, the cavity of the sinus. The importance of this anatomical relationship is obvious by inspection of Figs. 1 and 2. It has already been emphasized¹ that actual bone does not offer so much resistance to the spread of organisms as might be supposed, this function being the property of, first, the sinus membrane, and, secondly, the dural pericistern on the other side of the bone. Hence we really have a condition in which the most important endocrine gland of the human body is suspended in a bath of pus.

(c) Macroscopic abnormality of the pituitary gland is evidenced by the abnormal appearance, which is irregular, and does not show the normal colour difference between the anterior and

posterior lobes, the anterior usually having a uniform reddish colour and being of loose texture, whilst the posterior part is firmer and considerably paler but uniform. The dividing line between the two lobes should be very narrow and distinct. In the present instance the pars intermedia is swollen, and contains masses of colloid. (In another case this colloid material has been shown to be associated with the presence of micro-organisms²; and in yet another case of our series, as yet unpublished, an enormous mass of colloid, almost as big as the pituitary gland itself, was found. The case was one of severe epilepsy, and the patient, who had recovered, was without fits for nearly a year before death.) The irregularity of the capsule and occurrence of adventitious fibrous tissue should also be noted.

Fig. 2 is a diagrammatic sketch superimposed upon the sinus to show the close relationship of the infected sinus and pituitary to that part of the brain concerned with various metabolic processes³ (and which is often acutely involved in lethargic encephalitis). As the path of secretion is toward the brain stem it is obvious that toxic bacterial products in pituitary infections also find their way into this most important region of the brain, actual organisms having been demonstrated in the pituitary stalk of our case M. L.¹

Fig. 3 is a photograph of the sinus membrane (Gram's stain). In the upper part of the figure can be seen ciliated epithelium, whilst the long, well-formed chains of a diplococcal streptococcus are below the surface. Although there was considerable pus in the sinus there seemed to be very little leucocytic reaction in the membrane, a point which must be emphasized, as it has an important bearing on the finding of the organisms still deeper in the tissues—either the organism seen was "non-pyogenic" or the biological immunity reaction by leucocytic infiltration was suspended. No other organisms were found in the sinus membrane. It has been said by an eminent histologist that granules in the tissues should never be taken for micro-organisms unless surrounded by cellular reaction. In the present instance undoubted streptococci are seen without even a lymphocytic reaction of any magnitude; *post-mortem* invasion can certainly be definitely excluded. This figure and all the remaining figures are direct reproductions from untouched photomicrographs.

Figs. 4 and 5 show the streptococcal chains in the submucosa and adjacent to the bone surface (black). Note especially that the morphological appearance of these still undoubted streptococci is now becoming less typical. The chain formation is distinct, but the size, shape, and spacing of the stainable part of the organism are distinctly irregular as contrasted with the diplococcal streptococcus nearer the surface.

Fig. 6 is a minute canal in the bone in which streptococcal chains are viewed "end on," the chain characteristic being verified by the microscopical examination of successive horizontal fields.

Fig. 7 shows streptococci in the vessel wall of the anterior pituitary, the arrows indicating a vertical and a horizontal chain respectively.

Fig. 8 shows the organisms adjacent to the eosinophile cells of the pituitary, the latter recognizable as large dark masses.

Fig. 9 shows small granules, in rows in the wall of the cavernous sinus, which are at least suggestive of their being partly digested streptococcal chains.

Fig. 10 is a vessel from the hypothalamus (stained by Gram's stain) showing granules in its wall, the significance of which, however, is as yet doubtful. The large dark mass consists of mucinoid material, which probably indicates a degenerative lesion of the nervous tissue in that region.

Fig. 11 is another vessel of the mid-brain showing a large collection of granules of varying sizes in its accompanying lymphatic space.

Fig. 12 shows a mass of spirochaetes, not syphilitic, but of the oral type, in the centre of a small lymphatic nodule adjacent to the upper part of the internal carotid, which was removed through the skull with the sphenoid block. Its interest lies in the fact that it clearly demonstrates the distance that a septic extension may proceed when the organisms are relatively avirulent and of the type usually regarded as non-pathogenic. Its proximity to the internal carotid may, given the assumption of a toxic or septic spread along the artery, explain the mental symptoms of confusion, since such spread would affect chiefly the cortical layer of the brain.

COMMENT.

The clinical picture suggested by the case is therefore that of a man having had an accident to the skull followed by infection, the nature of which remained obscure for years. Mental disorder was sufficiently marked to necessitate certification five, ten, and twenty-five years afterwards. The later finding of empyema of the sphenoidal sinus and otitis media strongly suggests that there had been an insidious chronic infective process of long duration involving both. We know from anatomical considerations that the carotid artery is in intimate relation both with the middle ear and the sphenoidal sinus.⁴ From this it is

obvious that the lymphatics accompanying the carotid would at least occasionally contain deleterious toxic products, and perhaps even on occasion organisms; such a condition, by an assumption of further distal spread by the wave-like arterial pulsation along the course of the carotid, would account for the cortical haemorrhages, especially that over the left fronto-parietal area, and also explain the mental confusion. The pituitary involvement renders impairment of the pituitary-hypothalamic region of the brain a logical conclusion. In view of the hydronephrosis one must consider uraemia in connexion with the status epilepticus, but it is noteworthy that in our collection of specimens with gross involvement of the sphenoidal sinus and pituitary most of them were epileptics, suggesting a more intimate relation between the status epilepticus and mid-brain disorder—in this case through the medium of an infected sphenoidal sinus.

A consideration of this case naturally suggests that pituitary disturbances should regularly occur when the infective process affects the tissues deeper than the membrane on the roof of the sphenoidal sinus. Well-marked cases showing such disturbance are often met with in general practice, and Ferreri⁵ quotes a case with typical pituitary symptoms and early acromegalic signs which improved following drainage of the sphenoidal sinus. In such cases the pathological effects of the sinusitis presumably do not influence nervous tissue beyond the pituitary. It is not at all improbable, however, that in some cases there is a further extension to the brain stem via the pituitary stalk. The pituitary may not be affected in quite the same way as in the above cases, but a toxic disturbance of the pituitary secretion occurs leading to symptoms of hypofunction (with consequent overaction of other endocrine glands) rather than the more commonly recognized hypersecretion following irritation by tumour. In mental hospital cases there probably occur phases of hypersecretion and hyposecretion due to variations in the infection and resistance, leading to a disturbed balance of endocrine gland functions, which is a well-recognized feature of mental disease.

Gigantism, acromegaly, and dystrophia adiposo-genitalis are often recognized as occurring in mental hospitals;⁶ but of much more importance in the present consideration are the *minor* changes which may occur due to dysfunction of the pituitary gland and the sympathetic centre of the brain with which it acts in various metabolic functions. The demonstration of such minor pituitary disturbances in mental hospital patients is difficult for several reasons. The co-operation of the patient is often wanting; the history, even from the patient's relatives, is deficient; the mental attitude itself of the patient demands such attention and study that minor endocrine signs and symptoms, though noticed, do not usually find their proper place in the clinical picture of the case; and also characters which we usually associate with pituitary disturbances are limited to those due to an irritation by a tumour of the pituitary rather than a toxic disturbance of its secretion.

Table I, collected from Schafer, gives various functions of the pituitary; Table II, from various sources, gives the nerve centres of the hypothalamus. These should be studied in conjunction with Tables III and IV, in which the symptoms of pituitary-hypothalamic dysfunction have been tabulated in 69 cases of insanity in which a pyogenic infection was clinically demonstrated in the sphenoidal sinus by Mr. W. Stirk Adams. The clinical symptoms were collected with the aid of Dr. T. C. Graves, Dr. Elizabeth Selkirk, and Dr. C. W. Forsyth, superintendents of the Birmingham mental hospitals. These tables afford evidence of the coexistence of metabolic disorder and mental disorder, the one often improving parallel with the other. It is also a matter of common experience that nearly every case of insanity where the pathological processes concerned are active, shows metabolic defects⁷; these are referable to the pituitary and hypothalamus acting as an endocrine nervous centre. It should be noted that, although the symptoms of refusal of food, delusions of poisoning, and abnormal hunger are at least partly referable to a disordered condition of the intestinal tract, they do afford some evidence for a coexisting disturbance of the function of the pituitary-hypothalamic region. It is therefore evident that a sphenoidal sinusitis may in certain circumstances affect the pituitary-hypothalamic region of the brain even although no macroscopic perforation of the pituitary fossa is present, such as occurred in the case M. L.¹; this is supported by the comparison of symptoms and mental improvement which occurred subsequent to treatment following the demonstration of a pyogenic infection of the sphenoidal sinus in the 69 cases investigated.

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OF THE SPHENOIDAL SINUS.

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

FIG. 5.

FIG. 6.

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OF THE SPHENOIDAL SINUS.

FIG. 7.

FIG. 8.

FIG. 9.

FIG. 10

FIG. 11.

FIG. 12.

TABLE I.—*Pituitary Gland Function.* (From Schafer.)

Absent.	Deficient.	Excessive.	Injection of Extract.
Anencephalics	Dwarfs	Skeletal overgrowth	
Paralysis C.N.S.	Hibernation		
Somnolence	Drowsiness		
Lethargy	Lethargy	Mental depression and stupor	
Loss of muscle tone	(Lassitude)		
Metabolic depression	Lowered basal metabolism		Increased basal metabolism.
Subnormal temperature	Low temperature		Rise in temperature.
Respiratory failure	(Sub-breathing)		
Rapid loss of weight	Fat storage		Stops water diuresis.
Refusal of food	(Alimentary dysfunction)	Inordinate appetite	Alimentary stimulation.
Polyuria or oliguria	Polyuria	Polydipsia and polyuria	Glycosuria.
	Atrophy of endocrines, sex characteristics, and functions	Coarsening of features	Nitrogen retention phosphorus and calcium increased.
	Skin and hair feminine	Excessive hair	Prevents experimental oedema.

TABLE II.—*Nerve Centres of the Hypothalamus.*

Control the smooth muscles of: Eye, bladder, uterus, blood vessels, ?stomach, ?small intestine. Also: Striped skeletal muscle (involuntary), plastic muscle tonus.

Control the secretion of: Sweat, saliva, tears, urine, pancreatic secretion, ?gastric secretion, ?cerebro-spinal fluid.

Control the metabolism of: Sugar, protein, water, temperature, fat, trophic skin, sex-gland activity, sleep, mineral salts of the body fluids, ?acid-base equilibrium, ?digestion.

Symptoms of dysfunction: Glycosuria, albuminuria, polydipsia, pyrexia, subnormal temperature, obesity, sudden loss or gain of weight, amenorrhoea, impotence, insomnia, drowsiness, apathy, trophic ulcers, abnormal hunger, catalepsy, marasmus, hyperidrosis, salivation, seborrhoea, lacrymation, polyuria, constipation, polypnoea, retention of urine, ?achlorhydria, ?cyanosis, ?dilatation of stomach, ?dilatation of small intestine, ?sudden lassitude, ?hypochondria.

Pathological changes occur in: Diabetes insipidus, dystrophia adiposo-genitalis, narcolepsy, Graves's disease, encephalitis lethargica, Parkinsonism, ?some forms of epilepsy, ?some forms of mental disease.

TABLE III.—*Clinical Symptoms, possibly Referable to Pituitary Hypothalamic Disturbance, in 69 Cases of Insanity with Pus in Sphenoidal Sinus.*

A. PITUITARY-HYPOTHALAMIC DYSFUNCTION.

Symptoms.	Before Treatment.				After Treatment or Recovery.			
	0	+	++	+++	0	+	++	+++
Cyanosis	22	5	16	26	44	23	2	0
Pallor	19	5	15	30	45	21	3	0
Oedema	41	5	16	7	60	7	2	0
Stupor	31	8	13	17	54	12	3	0
Drowsiness	32	9	13	15	54	11	4	0
Refusal of food	26	2	12	19	64	3	1	1
Delusions of poisoning	48	2	4	15	67	1	1	0
Abnormal hunger	61	3	2	0	68	0	0	1
Constipation	6	3	20	40	33	31	2	3
Sub-breathers	3	20	22	24	21	34	13	0
Coarsening of face	48	8	11	2				
Variations of weight	31	17	16	5				

Other Common Symptoms—Vasomotor defect; subnormal temperature; gross fattening; asthenia (suprarenal); thyroid (excess and deficit); retrogression of sex characteristics.

0=Absent or normal. +=Slight. ++=Moderate. +++=Very marked symptoms.

TABLE IV.
B. MENTAL DISORDER, ETC.

Symptoms.	Before Treatment.				After Treatment or Recovery.			
	0	+	++	+++	0	+	++	+++
Mental disorder... ..	0	4	11	54	22	26	13	8
Confusion	11	7	12	39	43	15	7	4
Apathy	20	12	20	17	47	13	7	2
Catalepsy	48	4	11	6	64	3	2	0
Insomnia	19	5	6	39	42	22	4	1
Headache	17	6	12	34	48	15	2	4
Naughtiness	54	3	2	10	57	6	3	3
Fear processes	20	6	14	17	41	8	6	2
Influenza	39	4	19	16				
Family history	31	20	12	3				

Mental Classification.

Dementia praecox	25	Epileptic	4
Confusional	14	Mania	2
Imbecile	3	Melancholic	14
Paranoia	3	Alternating mania, melancholic	4

0=Absent or normal. +=Slight. ++=Moderate. +++=Very marked symptoms.

My thanks are due to Dr. J. M. Mackenzie for kindly showing me the case and for the clinical notes, and to the Medical Research Council for incidental help from Mr. A. T. Rennie, my laboratory assistant.

REFERENCES.

¹ Pickworth: *Journ. Laryngol. and Otol.*, March, 1928. ² Pickworth: *Proc. Roy. Soc. Med.*, 1928, xxi, 74. ³ Graves and Pickworth: *Proc. Roy. Soc. Med.*, 1928, xxi, 55. ⁴ Pickworth (in the press). ⁵ Ferreri: *Riv. Oto. Neuro. Ophthalmol.*, 1927, B.4, S.21-28. ⁶ Weygandt: *British Medical Journal*, 1928, ii, 283.

WOUNDS OF THE HEART.

A STUDY OF THREE CASES.

BY

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WOUNDS of the heart have been recorded from classical times, and though they were then regarded as being invariably fatal, it is now well recognized that the heart is an organ which is able to tolerate mechanical interference reasonably well. Not only have wounds of the myocardium been successfully sutured,¹ branches of the coronary arteries ligated,² and foreign bodies extracted,³ but in more recent years even the cavities of the heart have been explored in the hope of alleviating the mechanical handicap of a stenosis of the valve leaflets.⁴

TYPES OF FATAL CARDIAC INJURY.

While this is true, yet in war many combatants must die instantaneously from the immediate effect of wounds of the heart. In these days such injuries as result from the use of bullets, shrapnel, fragments of high explosive shells, and the like, are probably a more frequent cause of immediate cardiac arrest than statistics would indicate. Death, when it occurs instantaneously, is the result of a number of factors, notable amongst which must be the extent and severity of the lesion produced in the heart. The momentum of such missiles may be very great and the damage to the heart may be beyond all hope of repair. Sudden gross destruction with gaping lacerations of a wide area of ventricle or auricle is incompatible with life. Even a large proportion of the wounded in whom the damage is less severe must die before surgical aid can be made available, and in these shock and haemorrhage may be profound. Others, again, may survive a matter of minutes to hours, and die from the effect of the accumulation of blood within the pericardium. Blood leaking from a wound of

* Working under the Medical Research Council.