They all looked at it, and said it must be a frog, for it looked like a frog, and behaved like a frog, particularly in its ability to jump. But when they heard its origin they were all amazed, and each one gave his explanation of the occurrence. One said, "It is a changeling; it is not what it looks to be." Another said, "It was surely made to swim, for its feet are webbed, and, having no water to swim in, it has acquired the habit of jumping." A third said, "It has been gingered." A fourth said, "Some restraint must have been taken off it to enable it to jump." And the professor himself said, "No, it has a flea inside which lives within it as its familiar spirit, and that gives it the power of jumping."

Then the professor said to the little object: "We are very sorry for you. You are neither animal nor vegetable, for neither animal nor vegetable can be created from the sands of the desert. There is, therefore, no place for you among living creatures."

The little creature jumped and crawled away. But as it did so it looked back at the group of learned men, and said: "There is no place in the living world for me owing to the misfortune of my birth. Thank you, gentlemen, but I have already found a place for myself, and you will find it very difficult to oust me from it."

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SOME MANIFESTATIONS OF PITUITARY GROWTHS.*

BY

J. JAMESON EVANS, M.D., F.R.C.S.,

SURGEON TO THE BIRMINGHAM AND MIDLAND EYE HOSPITAL.

BEFORE proceeding to discuss the signs and symptoms of pituitary growths, it may be well to refer very briefly to some points in the anatomy and physiology of this ductless gland.

The pituitary body, or hypophysis cerebri, is a small rounded organ situated at the base of the brain in the depression of the sphenoid bone known as the sella turcica.

It is made up of two parts—a larger anterior lobe developed from an ectodermal upgrowth from the stomodeum (Rathke's pouch), and a smaller posterior lobe derived from a downgrowth from the floor of the third ventricle with which the gland is connected by a stalk called the infundibulum.

A third subdivision is also described under the name of the pars intermedia, which seems to be formed by the fusion of the anterior or ventral wall of the posterior lobe and the invaginated posterior or dorsal wall of the anterior lobe. Histologically the anterior lobe consists of vascular glandular epithelium; the pars intermedia is formed of less vascular epithelium secreting a colloid substance, and the posterior lobe or pars nervosa consists mainly of neuroglia with a few colloid-producing cells.

The physiological functions of these parts have not been definitely worked out. The anterior lobe appears to be related to calcium metabolism, and the growth of skeletal tissues—bone, cartilage, and connective tissues generally—to the deposit of fat and the development of the sexual organs. Physiologists have not been able to define these functions, and the chief evidence in support of these statements has been derived from observations made in pathological conditions of the organ.

The pars intermedia produces a colloid which affects blood pressure and urinary secretion. As a general rule, this colloid material raises blood pressure by causing con-

traction of the blood vessels, and increases secretion of urine, but it may, on the other hand, have precisely the opposite effect in each case. Extracts of the infundibulum also cause contraction of non-striped muscle, such as that of the uterus, intestine, and dilator pupillae. The pituitary body appears to be a vital organ, and its complete removal results in death.

These anatomical and physiological data enable us to classify and correlate many of the varied signs and symptoms of pituitary growths, but it must be admitted that the pathogenesis of the manifestations is as yet by no means established, and it has even been said that the most striking condition ascribed to pituitary growths—namely, acromegaly—may occur without any apparent disease of the hypophysis cerebri.

For the purposes of this paper I propose to classify the manifestations of pituitary neoplasms into:

1. Those which may be ascribed to excessive action of the glandular epithelium of the anterior lobe—*Hyperpituitarism*.
2. Those which may be ascribed to a diminished functional activity of the anterior lobe—*Hypopituitarism*.

In view of our incomplete knowledge of the physiology and pathology of the pituitary and other ductless glands, it is possible that these two classes of symptoms may be due to perverted action of the hypophysis—*Dyshypophysis*—or to perverted action and interaction of several ductless organs—*Polyglandular syndrome*.

3. The mechanical effects of an intracranial tumour showing definite localizing symptoms, which can be explained by the anatomical relationships of the enlarged organ. These symptoms are common to Class 1 and 2 as long as the pathological condition of the gland is associated with its enlargement. In cases of atrophy these symptoms will be absent.
4. Confirmatory evidence of enlargement or atrophy of the hypophysis is supplied by radiographs of the sella turcica, though naturally the size of the gland and its bony recess is no guide as to the functional activity of the gland. Hypopituitarism, at any rate, may apparently be the result of either enlargement or atrophy of the gland.

I. HYPERPITUITARISM.

Under this heading we place *Acromegaly* and *Gigantism*. The pathological processes seem to be the same in these two morbid conditions, and the difference in their clinical characters is dependent on the period of incidence of the disease. "Gigantism is the acromegaly of the growing period; acromegaly is the gigantism of the period of completed development; acromegalo-gigantism is the result of a process common to gigantism and to acromegaly, overlapping from the period of adolescence into that of maturity."

The essential feature in each case is exaggerated growth of the skeletal tissues, hard and soft, especially of the extremities, associated with alteration in the physiognomy and in the contour of the skull. These symptoms have been so fully described by Marie and others that it is almost superfluous to repeat them. I would point out, however, that, according to Launois and Casbron, the changes in the skull demonstrable by radiography constitute the only positive signs of acromegaly. These changes consist in very irregular thickening of the cranial parietes, which gives rise to a polygonal appearance of the skull. The external and internal tables are separated by an abnormal and irregular space owing to an alternate separation and approximation of the tables. The frontal and maxillary sinuses are increased in height and depth. The post-lambdoidal prominence is exaggerated, and there is more or less marked increase in the antero-posterior dimensions of the pituitary fossa. The sexual organs also show hypertrophy, though this is often associated with impotence, and may later be followed by atrophy of the organs and loss of pubic hair.

The symptoms which may be ascribed to the mechanical effects of the intracranial tumour (3) may include headache, vomiting, vertigo, tinnitus, polyuria or glycosuria, convulsive or apoplectic attacks, certain psychoses,

* A paper read before the Midland Medical Society.

including delirium, delusions, perverted or excessive appetite, and melancholia. Mental and physical torpor are often complained of, and whereas the pulse may be accelerated the temperature of the body is lowered.

The localizing symptoms of the intracranial growth are mainly exhibited in connexion with the eyes and the ocular muscles.

Impairment of vision in one or both eyes is often complained of, and in cystic or vascular tumours, which may vary in size or burst, the vision may be definitely variable. The impairment of sight may be associated with the appearance of a blue haze over everything. As a general rule the impairment of sight slowly but surely progresses to almost complete blindness.

Alterations in the *visual fields* are a striking feature of pituitary enlargements, and bitemporal hemianopia is the most common and most characteristic of these alterations. In the advanced stages of these conditions the patient feels as if he were walking between two high walls. In many cases the temporal hemianopia is unilateral, owing to complete loss of sight in one eye; this is as might be expected when we remember that the growth is often irregular and is liable to press on one nerve more than the other. For the same reason the boundary line between the blind and the seeing parts is hardly ever regular or vertical. When the boundary line is vertical, or approximately so, it generally passes through the point of fixation—a fact which helps to distinguish chiasmal lesions from lesions of the optic tract and cortical centres, in which the macular field is spared.

The other more common variations in the visual field are concentric contraction and central scotoma, but homonymous hemianopia and the loss of the whole field, with the exception of one quadrant, have been described. The contraction progresses from above downwards and inwards as a rule, but a surer guide as to the probable type the contraction will eventually assume is to be found in the character of the *colour fields*. It will often be found that the colour fields are definitely hemianopic, while the fields for white are almost full (see Fig. 1). Accentuation of the defect in the field can also be shown by Bjerrum's method.

The usual condition of the optic nerve is one of partial or complete primary atrophy (50 per cent.), but papillary oedema and post-neuritic atrophy have also been recorded (15 per cent. each). Large growths involve other structures than the optic nerve, and give rise to such symptoms as oculomotor paralysis, including paralysis of the third nerve, paralysis of the sixth nerve, total ophthalmoplegia, nystagmus. Trigeminal lesions are exceptional, but when present may lead to neuro-paralytic keratitis. Exophthalmos, prominence of the eyebrows, with pigmentation and thickening of the eyelids and hypertrophy of the palpebral glands, have been noted.

Pupil reactions are of little diagnostic value. The hemiopic pupil phenomenon of Wernicke can seldom be elicited, and in any case it is of somewhat uncertain import. Anosmia is not an infrequent symptom in advanced cases.

The following case of acromegaly is a fairly typical illustration of hyperpituitarism:

CASE I.

D. H. E., aged 29 years, a policeman, was first seen in 1905, when he complained of a heavy feeling in the head, of three or four years' duration. There was no definite headache. He found work a burden, and was very depressed. During this

time he also noticed that he was increasing in size, and in those four years he had grown $1\frac{1}{2}$ in. in height, and his hands and feet had become so large that he had to get special sizes in gloves and boots. When he came to see me his height was 6 ft. 1 in., and his weight was 18 st. 1 lb. His large face, heavy jaws, thick, broad nose, prominent overhanging eyebrows, broad shoulders, with slight stoop, attracted attention and suggested the disease at once. The hands and feet were of remarkable size, and both soft and hard tissues were involved.

There was no enlargement of the thyroid or lymphatic glands. The patient suffered from sexual delusions, and was impotent.

Ophthalmoscopically: The fundi were normal, except for a slight haze of the nasal side of the disc in each eye. R.V. = $\frac{1}{2}$, L.V. = $\frac{1}{2}$. Both visual fields were contracted above, the left decidedly so. The colour fields showed a relatively greater degree of contraction, and were almost hemianopic on the temporal side (see Fig. 1).

Under treatment with pituitary extract his weight diminished a stone in a month, and on combined pituitary and thyroid extracts his weight fell another stone in six months.

This patient was examined again in 1911, and there was no change in his condition. He had been able to follow his occupation all the time, and had been married for two years.

II. HYPOPITUITARISM.

Under this heading I would include those weird cases of retarded skeletal development or infantilism designated ateliosis by Hastings Gilford, and also certain cases in which there is excessive development of fat with mental and physical torpor, and disturbance of sexual functions—*dystrophia adiposo-genitalis* of Fröhlich.

It is also possible that *adiposis dolorosa*, the excessive adiposity of the menopause, diabetes in fat people, and, after fracture of the skull, cretinism and achondroplasia, may be more or less closely related to a condition of hypopituitarism.

Ateliosis.

The characteristic symptoms of this condition, which have been so fully described by Hastings Gilford,²

form a striking contrast to those of acromegaly, and may thus be tabulated:

Ateliosis.	Acromegaly.
Childish facial appearance.	Heavy, repulsive face.
Diminutive stature, with short, small extremities.	Gigantic stature, with lengthened and enlarged extremities.
Delicate, soft skin.	Coarse, thick, darkened skin.
Thin, piping voice.	Deep, hoarse voice.
Small bones and muscular prominences ill-developed.	Large bones and hypertrophied muscular ridges.
Diminutive jaw bones with incompletely erupted teeth.	Enlarged jaw, often prognathous.
Diminished urinary secretion.	Polyuria or glycosuria.
Impaired appetite.	Voracious appetite.
Insomnia (?)	Somnolence.
Low arterial tension and slow pulse.	Increased arterial tension.

It must, however, be remembered that symptoms of hypopituitarism may be associated with those of hyperpituitarism and vice versa, and in both conditions symptoms may be modified by the interaction of impaired or overacting associated ductless glands, such as the thyroid and adrenal bodies.

According to Hastings Gilford, ateliosis may begin: (1) During fetal life; (2) during infancy or early childhood; (3) between the ages of infancy or early childhood and puberty. The ateliotic patient shows throughout life the physical characteristics of his age at the time when he first developed his symptoms. At any rate, his development shows a remarkably retarded rate of progress—that is, he might grow in ten years to the same extent that an ordinary child would grow in one year. It will thus be

Fig. 1.—Case I. D. H. E. Fields in acromegaly. red. ---- blue. The blackened area shows the contraction of the field for white (10 mm.).

found that the epiphyses are not united to the diaphyses (Fig. 6), and the teeth are not completely erupted at 50 years of age. The facial type of the child is retained, though the skin shows evidence of age. The fontanelles remain open for years when the disease begins in early infancy; the testicles are undescended, the sexual functions are undeveloped, and the sexual organs rudimentary when the disease begins during intra-uterine life of the patient.

The mental development is better than the physical, but is hardly up to the standard of a normal person of the ateliotic's age.

There is lack or absence of hair on the face and covered parts of the body, but there is generally a fair amount of hair on the head.

Although the general symptoms in hypopituitarism are in the main the exact opposite of those of hyperpituitarism, the mechanical effects (symptom-group 3) are much the same in each case, because they depend on the enlargement of the gland, which is the usual state both in diminished and increased functional activity. In cases of atrophy of the gland these symptoms would be absent (Case III).

Judging by published records, it would appear that in hypopituitarism (as compared with hyperpituitarism) bitemporal hemianopia is somewhat less frequent, and papillary stasis and atrophy and oculomotor symptoms more frequent. It has also been noted that nystagmus is very exceptional in these cases.

The ocular conditions of the cases reported by Gilford and others do not seem to have been very carefully investigated, so it is difficult to estimate their comparative frequency in cases of pure ateliosis, and the above-mentioned comparisons refer to pituitary enlargements without acromegaly and those with acromegaly.

Dystrophia

Adiposo-genitalis.

This symptom-complex described by Fröhlich does not differ to any great extent from ateliosis, except that it may affect adults, and that excessive deposit of subcutaneous fat and somnolence are pronounced symptoms. If the disease appears before puberty, the sexual organs remain in an infantile condition, and probably also the epiphyses remain as in ateliosis; whereas, if the onset is delayed till adolescence, amenorrhoea and impotence, and probably atrophy of the genitalis and loss of hair result. In these cases the skin is apt to become coarse, whereas in ateliosis it remains

smooth, and in older cases shiny and parchment-like. In some cases mild symptoms of myxoedema or acromegaly may be associated with symptoms of pituitary insufficiency.

The following cases illustrate the main features of hypopituitarism:

CASE II.—*Ateliosis.* (See Fig. 2.)

C. H., aged 51 years, single, formerly a lapidary, now of no occupation. Family history of no particular interest. Had a severe fall on the forehead when he was 5 years of age; there is a scar at the root of the nose which he ascribes to that fall. Until the age of 12 years he was like other boys, except that he had attacks of headaches and drowsiness since his fall, or at any rate since he was 10 years of age. At the age of 12 to 14 years he stopped growing altogether. He seems to have lived comfortably and followed the occupation of a lapidary without difficulty or discomfort until about the year 1903, when he began to notice failure of sight and to complain of headache and giddiness. In 1906 he was seen at the Birmingham Eye Hospital, and optic atrophy and bitemporal hemianopia diagnosed. Dr. Lowry of Toronto, who was then one of our resident surgeons, took notes of the case at that time, and I am indebted to him for a record of the visual fields (Fig. 4).

In 1908 he came under my care. By this time there had been further depreciation of sight—the vision in the right eye having been entirely lost—his headache and giddiness were somewhat worse, and he had developed visual hallucinations, which were evidently causing him a good deal of mental distress, and apparently keeping him awake at nights. The "visions," as he called them, were

generally in the form of flames and clouds of varying brightness, red in the right (homonymous) field and green in the left; he also saw figures such as men walking about, horses, dogs, and landscapes. These were sometimes pleasant, sometimes disagreeable—for example, ugly grinning faces, snakes, etc. They were generally worse in artificial light, and he

often sought dark corners because "the visions became worse when they were allowed to see him." The hallucinations involved the field of the blind (right) eye, as well as that of the blind temporal half of the left. The right side of faces, etc., seen also appear red and the left green. Since that date he has been under my care more or less regularly, and his condition has not materially changed. The following are the main points of interest in the case at the present time:

His general appearance, build, and voice suggest those of a boy of about 14 years of age, but his pale, sallow, shiny skin shows slight scaliness and the wrinkles in it suggest advancing age. The thyroid gland is not palpable. Abdomen somewhat

protuberant. Breasts rather prominent. Slight scoliosis. The penis is small and infantile-looking; the testicles are small and soft and have no testicular feeling; sexual feeling in abeyance. He has no hair on any part of his body except his head, and this is somewhat fine and scanty, especially over the vertex. His height is 4 ft. 7½ in., his weight

Fig. 2.—Case II. Patient (on right), aged 51 years; and his young brother, aged 32 years.

Fig. 3.—Case II. C. H. Showing enlargement of the sella turcica.

5 st. 7 lb. to 6 st. Muscular development is slight and corresponds to his puerile appearance. The right leg is decidedly less developed than the left, the right calf being $\frac{1}{2}$ in. less in circumference.

Hg; pulse 74; temperature 97.4°; blood count showed nothing abnormal.

Cerebration is slow and his intelligence is distinctly below that of a man of his age. He is apt to be irritable, bad-tempered,

Fig. 4.—Case II. C. H. 1906. Fields for white.

Fig 5.—Case II. C. H. 1911. red. — blue. Shaded area = relative scotoma.

The head is small but long and the post-lambdoidal protuberance is very marked; jaw small; teeth good.

Fronto-occipital measurement	...	14½ in.
Mento-occipital	...	18½ "
Arm	...	12 "
Forearm	...	9½ "
Chest	...	26 "
Chest expansion	...	3½ "
Pelvis circumference (ant. sup. spines)	...	28 "
Thigh (ant. sup. spine to int. condyle)	...	18 "
Symphysis pubis to ground	...	28 "

Fig. 6.—Case II. C. H. May 12th, 1911. No fusion of epiphyses and diaphyses.

Urine: The amount of urine passed daily has been very difficult to measure as the patient resents having it collected, but the average was apparently considerably under 20 oz. a day; specific gravity 1019, acid; no albumen, sugar, or casts. Digestion and appetite are good, but he suffers much from constipation. Cardio-vascular system: No heart lesion; blood pressure 95 mm.

and lethargic, and, though he is awake a good deal at nights, he is often drowsy during the day. It is interesting to note that efforts made to relieve his symptoms by x rays increased the hallucinations and sleeplessness at night. Knee-jerks are normal, and there is an extensor toe reflex on each side.

Ophthalmic Examination.—The right eye is divergent and amaurotic, the nasal field having been lost between 1906 and 1908. The media are clear, and the optic disc shows advanced primary atrophy. R.V. = no P.L. The left eye shows a similar state of primary atrophy of the optic nerve. L.V. = $\frac{5}{20}$; temporal hemianopia (Fig. 5). Colour fields are of the same type but smaller, and there is a central scotoma for colours of $\frac{20}{200}$ for red and green and $\frac{5}{200}$ for blue. Convergence is lost, and there is no contraction of the pupils when an attempt at convergence is made. The right pupil does not react directly to light, but responds when light is thrown into the other eye. The left pupil reacts directly to light but not consensually.

Fig. 7.—Case III, aged 15 years, compared with boy aged 7 years (standing on the left). This patient has no optic atrophy and no hemianopia.

Radiographic Examination is highly instructive. An extensive excavation of the sella turcica is noticeable (Fig. 3); all the epiphyses of the long bones (upper and lower extremities are still unossified (Fig. 6). During the last two years he has been on a variety of medicaments, including pot. bromid., iron

quinine, and arsenic, didymin, thyroid, thymus, pituitary extract and x rays. Nothing seems to have had much effect upon him, and x rays seemed to aggravate the hallucinations. Thyroid gland only reduced his weight and so was soon discontinued. Pituitary extract seemed to quieten him for a time, and increased the quantity of urine, and apparently also the systolic blood pressure which sometimes went up to over 100 mm. Hg a day or two after injections of pituitary extract, but even these results were by no means consistent and might have been ascribed to normal variations. The one satisfactory feature of the case is that the vision and extent of the field in the left eye have not materially diminished during the last five years. The vision is decidedly variable and on some occasions it gets as low as counting fingers at 3 metres—this in fact was the record of the vision in the left eye in 1906 when that of the right eye was given as $\frac{3}{8}$. It is seldom less than $\frac{3}{8}$ at the present time.

CASE III.—*Ateliosis* (?) (Fig. 7).

Frank L., aged 15 years. Family history unexceptional. Patient was like other children until he was 6 years of age. From that time on he has been physically at a standstill and has retrogressed mentally. Latterly he has been under treatment for *tabes mesenterica*. At the present time he is 3 ft. 7 in. in height, and weighs 3 st. 2½ lb.

His general appearance suggests feeble mental and physical development. The skull is dolichocephalic, with marked frontal eminences; bridge of the nose undeveloped; mouth large, tongue pale and flabby; teeth good; heart and lungs normal. He has scoliosis, lumbar lordosis, and genu valgum. The abdomen is very prominent—23 inches in circumference at umbilicus. There is a fine growth of hair in the lumbar hollow, but there is no deformity of the neural arches.

There is complete testicular descent, and external genitals are normal. The skin over the abdomen and front of the thighs is markedly mottled (see photograph, Fig. 7), and the fingers and toes are of slight purplish tinge, but are quite warm to the touch. Intellectually he is very backward. He speaks, but will not answer questions. Eyes: Beyond having had phlyctenular keratitis, which has now healed up, there is nothing to note with regard to the eyes. There is no optic atrophy, and, as far as we can judge, no defect of the visual fields.

Radiographic examination shows that the sella turcica is smaller than usual, and is apparently encroached on by a bony spicule (Fig. 8).

There seems to be delayed ossification of epiphyses also, as

Fig. 8.—Case III. Radiograph showing small-sized sella turcica encroached upon by a bony process.

there is no union between the ischial and pubic rami. It will be easier to judge of the state of his bony development when he reaches the age when the epiphyses of the long bones are due to join the diaphyses.

The foregoing cases indicate the type of nutritional and other disturbances which result from pituitary insufficiency during the growing period.

The following cases kindly reported to me by Dr. Duncan Lawrie, of Oldham, show the results of hypopituitarism in the adult.

CASE IV.

Miss A. B., aged (?), complained of failure of sight, with frequent headaches and amenorrhoea of three years' duration.

In appearance she was a tall, broad-shouldered woman, and her hands and feet were large, but only in proportion to her size. She was bigger than her mother and sister.

Mentally she was normal or above the average of her class. The thyroid was markedly enlarged.

Pupils dilated, react sluggishly to light, active to accommodation and convergence. Left eye divergent. Nystagmus on fixation. Primary optic atrophy each eye.

R.V. = $\frac{3}{8}$, L.V. = $\frac{3}{8}$.
Reads J. 4.

Charts of visual fields show bitemporal hemianopia. Colour vision for red, green and blue good in parts of fields retained. Thyroid administration rapidly gave rise to tachycardia and tremors and did not improve other symptoms. She died with symptoms of cerebral growth. No autopsy.

CASE V.

Mrs. B., aged 35 years. Had noticed failure of sight for three years; menses, which were regular previously, became arrested four years ago.

Physically and mentally she shows nothing abnormal, and beyond the complaints mentioned feels perfectly well. The right pupil is larger than the left. Neither pupil reacts to light. The right eye is divergent. There is primary atrophy of the optic nerves, the right being more markedly atrophic.

R.V. = Fingers at 6 in.
L.V. = $\frac{3}{8}$.

Bitemporal hemianopia. The case has been lost sight of since.

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THE VACCINE TREATMENT OF GONOCOCCAL ARTHRITIS.

By RALPH STOCKMAN, M.D.,

PROFESSOR OF MATERIA MEDICA AND THERAPEUTICS IN THE UNIVERSITY OF GLASGOW AND PHYSICIAN TO THE WESTERN INFIRMARY.

THE occurrence of gonococcal arthritis signifies an infection through the blood stream, usually from the urethra or vagina, very exceptionally from the conjunctiva. The vitality of the gonococcus on these mucous membranes and the obstinacy of the local infection are well recognized, but from the comparative infrequency of visceral infections it is evident that the micro-organism has great difficulty in maintaining its existence in the blood serum. The tissues which it attacks from the blood, though very widely spread, are few in number, chiefly the fibrous structures of the joints, muscles, and fasciae, and the synovial membranes of joints and tendon sheaths, although the valves of the heart and the pleura are not exempt. All these structures, in fact, consist chiefly of white fibrous tissue.

Fibrous Tissue.

Once established in fibrous tissue the gonococcus may maintain itself very obstinately, but as a rule local reaction occurs, characterized by formation of new fibrous tissue, and after some weeks the organism dies out, leaving behind it a local fibrosis which is pathological in structure and gives rise to chronic muscular stiffness, pain or aching, contracture of joints, flat-foot, and other effects. Sometimes, but rarely, an abscess forms, and yields pure cultures of the gonococcus.¹

Joints.

In joints the fact that increased secretion takes place from the synovial membrane determines to a great extent the local symptoms. The gonococcal inflammation is often transient, although it can be very prolonged. Thus we find that many patients give a history of one or more attacks of polyarthritis which have cleared off in a few days, and frequently, when several joints have been affected, these cure spontaneously with the exception of one or two, which remain more or less obstinately inflamed. The exudation into the cavity of the joints contains many polymorphous leucocytes, and is rather