VOL. IV THURSDAY, NOVEMBER 10, 1932 NO. 1

GENERAL STAFF MEETING
MINNESOTA GENERAL HOSPITAL
UNIVERSITY OF MINNESOTA

CONTENTS

PUBLICATION MANAGED BY STUDENT ASSOCIATION

I. [illegible]ENTS:

1. Department of Medicine Seminar, Wednesday, 4:45 P.M., Room 109, Main Building.
Programs:

Nov. 9, 1932 - Cecil Watson - Bile Pigment, Derivatives Excreted in Health and Disease.

Nov. 23, 1932 - Miss D. Simonsen - Cysteine in regard to Cell Growth Stimulation.

Dec. 7, 1932 - Halbert Dunn - Statistical Methods in Medicine.

You are cordially invited to attend.

2. Department of Pediatrics.
Departmental Seminar, every Tuesday, 4:30 P. M., Pediatric Laboratory, W 109, first floor. Clinical Conference twice monthly, Sunday, 9:30 - 11 A.M., Departmental Monthly Meeting, usually first Thursday, two papers, one historical and the other on some subject in pediatrics. Department cordially invites you to attend.

3. Time of Meeting. An attempt is being made to start promptly at 12:15 and stop promptly at 1:15. There is a little difficulty in getting the group together at 12:15. This necessitates extending time as you will notice by weekly reports. We intend to start promptly at 12:15 and stop at 1:15 unless the discussion is of such nature that it is advisable to go on. Your cooperation is solicited.

4. Canti Film
Today, Thursday, next hour, 1:30-2:20. Anatomy Amphitheater. Unusual movie of growth of cells in tissue cultures (light and dark backgrounds) showing effects of radiation. If you have never seen it, this is an unusual opportunity. Don't miss it. Courtesy of American Society for the Control of Cancer.

II. CASE REPORT

PROBABLE PITUITARY BASOPHILISM

Case is that of white female, 15 years of age, admitted to Minnesota General Hospital 3-24-32, discharged 6-3-32 (71 days).

Syndrome of headaches, amenorrhea, obesity of trunk and face, erythema of face, low basal metatolic rate, etc. Negative exploration of adrenals. X-ray treatment of pituitary region.

Headache
12- -27 - About 10 or 11 years of age at this time. Began to have daily supra-orbital headaches which persisted at intervals until admission.

Sinusitis
3- -29 - Sinuses treated (maxillary and frontal?) which relieved headaches for about year. Height at this time was 4'5-1/2". Vague pains in lower extremities.

Obesity
12- -29 - Weight 96 lbs. Gradually gained in weight; at admission weighed 141 lbs.

Pains
3- -30 (about) - Headaches reappeared. Complained of vague pains as follows: (1) vague frequent backaches, (2) daily precardial pain, dull in character and lasting several minutes to 3 or 4 hours, (3) intermittent attacks of epigastric burning after meals.

Hairy
7- -31 - Noted growth of hair on face. Later extremities became hairy up to elbows and knees. Nocturia began and had to get up at least once per night.

Family History
Mother began to menstruate at 17 years of age, 1 sister at 13, another at 17 and another at 16.

Personality traits and interests (Social Service):
Friendly and talkative, enjoys companionship of children of both sexes. Makes friends easily. Presents consistent feminine pattern from early childhood to present. Likes dancing and is fond of music.

Admitted

3-24-32 - Physical Examination reveals a white female, 15 years of age, stocky and overweight. Face is fleshy, round and erythematous, and covered with abundant growth of black hair. Length from head to symphysis - 28-3/4", from symphysis to feet 28-3/4". Hair rather thick and coarse. Breasts under-developed and of masculine type. Some coarse hair around nipples. Pulse 85, B.P. 130/80 (only reading?). Abdomen - very obese girdle type. Mass of subcutaneous fat over lower cervical and upper thoracic regions. No scoliosis. External genitalia - normal; clitoris slightly enlarged; masculine distribution of pubic hair. No acrocyanosis or acrodynia of extremities.

Laboratory

Urine - specific gravity 1.020. Hb.95%, wbc's 10,100, Pmn's 77%, L 20%, M 3%.

X-ray

3-26-32 - of skull, chest, abdomen - Kidneys appear to be within normal limits in size, shape and position. No definite evidence of disease in abdomen. Diaphragms are displaced upward (possibly) but there is no evidence of disease in either lung or heart. Marked decalcification of skull. This is rather diffuse, but no other evidence of disease could be made out. Bony changes in skull are rather atypical. Sella tursica appears to be within normal limits. Plates of hands and feet show normal growth.

Sinuses

3-28-32 - X-ray of sinuses - Sinuses well-developed and appear entirely clear. Conclusions - Negative sinuses. Ear, eye, nose and throat - Clinically, no evidence of sinusitis. Deflected septum may be cause of headaches.

Gynecological consultation

Pelvis - abundant pubic hair of male distribution, sharply angled pubic arch. Clitoris - marked development of glans; clitoris long; prepuce retracted over glans. Labia minor - under-developed (markedly). Pelvic floor - nulliparous. Cervix - small and movable. Corpus - very small.

Sugar tolerance

On fasting -.079, 1/2 hour after 50 gms. of glucose - .150, 1 hour - .129, 2 hours - .069, 3 hours - .069. Blood - wbc's 6,950. B.M.R. - 7%. Temperature 98.2

4-1-32 - X-ray of thymus - Films of chest show no evidence of enlarged thymus or other mediastinal mass. Heart appears just within normal limits in size, although it is on borderline. Conclusions - negative. Spinal fluid - pressure 160/250, clear, colorless, cell count 2 to 3, Nonne negative, Noguchi trace, Colloidal gold and Wassermann negative.

Eye consultation

Media clear, fundi normal. Eyes - no evidence of any nerve changes in either eye. Form field of left eye is slightly contracted temporarily, while that of right eye is normal. In view of fundus findings, that is discounted? It is also likely that patient's reaction time is a little slow when the field on left eye is taken as it is the first eye examined for field changes. Blood calcium - 11.745 mgs.

4-3-32 - Patient had a severe headache. Sphenopalatine ganglion cocainized with relief of pain.

Neurological examination -

Eye grounds - negative. Fields are within normal limits. Eyes dilated. Neurological examination is essentially negative. Patient undoubtedly has some glandular dysfunction. No evidence of any neoplasm by x-ray, spinal puncture or from clinical history (no vomiting, headaches, etc.) Theelin ampules i daily. Put on reducing diet.

4-6-32 - B.M.R. - 27%. Temperature 98.

Spine

4-11-32 - X-ray of cervical spine - Films of cervical spine show no evidence of abnormality. Conclusions - negative cervical spine. Theelin ampules i daily. Thyroid extract gr. i, three times daily. Blood viscostty - 10, viscosity plasma - 2.2. Sedimentation rate - 1 hour and

15 minutes. B.M.R. - 27%. Temperature 98.

Pyelogram

4-19-32 - Only a very fair filling is made out. Kidney shadows and ureters appear normal. There is no evidence of calcification or other disease. Conclusions - Probable negative urinary tract. Theelin ampules i daily. Thyroxin i mg. daily. B.M.R. - 25%.

Pyelogram

4-21-32 - Left kidney pelvis and ureter appear normal. Right kidney pelvis shows some irregularity of middle calyx suggesting possibility of cortical abscess or some inflammatory process. This is not entirely definite. Headaches. Trichlorethylene 10% on cotton put in nostrils to relieve headache. B.M.R. -22%.

Tumor, Adrenal or Pituitary

4-25-32 - Thyroxin i mg. daily. Placental extract gr. v, three times daily. Complains of headache. Cholesterol 210.5. Medical opinion is that patient should be explored for possible adrenal tumor. If nothing is found at operation, pituitary should be x-rayed, as basophilic adenoma should be considered in view of late work of Dr. Harvey Cushing.

Operation

5-6-32 - Preoperative diagnosis - Pituitary dystrophy, possible genital ridge tumor or adrenal cortex tumor. Under spinal anesthesia, supplemented with ether, a right rectus incision was made in the upper abdomen and a thorough exploration was made for palpable tumor mass in the region of genital ridge. Adrenal glands were also palpated for tumor. The pelvic organs were also palpated. The uterus was very small, perhaps 2 cms. in diameter, but about 4 cm. in length. The ovaries were so small that they could not be definitely identified. No tumor was palpable in the broad ligaments on either side and none up along the aorta or along either side of the vertebral column and none in the region of kidneys or adrenal. Patient returned from the operating room in good condition and had uneventful convalescence.

X-ray Treatment

5-24-32 - 133% skin erythema dose to pituitary glands in 4 treatments advised is given.

6-1-32 X-ray of left foot, chest. Diaphragm , mediastinum, heart and pleura are normal. Lungs show no evidence of disease. The left foot shows no evidence of disease. Conclusions - Negative chest and left foot.

6-3-32 - Discharged. Follow-up - Condition apparently unchanged.

History abstract by Bjarne Pearson.

III. ABSTRACT

THE BASOPHIL ADENOMAS OF THE PITUITARY BODY AND THEIR CLINICAL MANIFESTATIONS (Pituitary Basophilism).

Ref. Cushing, H., (Harvard Medical School), Johns Hopkins Hosp., Bull. 50: 137-195, '32.

1. General Statement:

Excellent review of subject with all cards on table indicating difficulty of distinguishing it from tumors of adrenal (or pre-adrenal origin?). Polyglandular syndromes (1912) were defined as secondary functional alterations occurring in ductless gland series whenever the activity of one of glands becomes primarily affected. Term restricted to those cases in which it was difficult to tell where initial fault lay.

Primary derangement of pituitary gland (spontaneous or experimental) is particularly prone to cause widespread changes in other endocrine organs (appreciated in 1912). Author strongly suspected that this centrally placed and well protected structure in all probability represented master-gland of endocrine series.

Much stumbling and speculation occurs in this field. Tumors or other destructive lesions have been described as primarily involving one or another of the organs in endocrine group. Tumors usually prove to be adenomatous. First recognized in thyroid as adenomas which were functional active structures producing hypersecretory effects. It is definitely shown that it is the degree of secretory activity of an

adenoma (which may be out of all porportion to its dimensions) that evokes recognizable symptom-complex in all hypersecretory states.

2. Anatomy and Physiology:

3 types of cells in anterior pituitary body. (1) Chromophobe, (non-granular), (2) cytoplasm) (3) chromophil (acidophilic granules, basophilic granules). Each of these cellular types is apparently capable of producing its own peculiar adenomatous formations? Author reviews controversy in regard to origin and relationship of these cells. Alkaline anterior lobe extract injected in rats (which show no closure of epiphysis during life) and subsequently in dogs (with an epiphysis like man) produced condition of overgrowth comparable in all respects to that characterizing acromegaly. But this is only half the story as multiple hormones are involved. In addition to promoting growth, ovulatory cycles of animals were checked, leading Evans and his associates to believe 2 glandular hormones present and that they were in some way opposed in their action. Some evidence tends to show growth-provoking and sex-maturing principles related to types of cells.

Author believes old concept of hyper and hypo-pituitary states should be abandoned. Tumors of anterior pituitary variously described as sarcomas and strumas really represent adenomas. Working concept at present time states that acidophilic tumors produce overgrowth, basophilic tumors - sex changes, chromophobe tumors - no changes until surrounding structures are affected by tumor growth? Mixed type may occur. Case reports then follow of 12 presumptive examples of basophil hyperpituitarism (using combined terminology.) As one reads these reports, the difficulty in placing origin of endocrine disorder is very evident. Only in cases in which pituitary gland was observed at autopsy is the case clear. Here, again, it must be remembered that Erdheim by careful studies found adenomas in 1 out of every 10 routine autopsies.

3. Clinical Picture:

Ref. - Basophilic Adenoma of Pituitary (Pituitary Basophilism-Cushing Syndrome).

Moehlig, R.C., J.A.M.A. 99:1498-1500, (Oct. 29), '32.

1. Rapidly acquired, peculiarly disposed and usually painful adiposity confined to face, neck and trunk, extremities being spared.

2. Tendency to become round shouldered, kyphotic, even to measurable loss of height associated with lumbo-spinal pains.

3. Sexual dystrophy shown by early amenorrhea of females and ultimate impotence in males.

4. Alteration in normal hirsutes shown by tendency to hypertrichosis of face and trunk in all females as well as pre-adolescent males and possibly reverse in adult males.

5. Dusky or plethoric appearance of skin with purplish lineae atrophicae.

6. Vascular hypertension.

7. Tendency to erythema (erythrocytosis?).

8. Variable headaches, abdominal pain, fatigueability and ultimate extreme weakness.

Less constantly present: 1. Acrocyanosis, 2. Purpura-like ecchymoses from bruising or spontaneous in origin. 3. Aching pains in eyes associated with slight exophthalmus, with diplopia, with suggestive papilloedema, with dimness of vision, with sub-retinal exudate and retinal hemorrhages. 4. Extreme dryness of skin with pigmentation. 5. Polyphagia polydipsia and polyuria. 6. Edema of lower extremities. 7. A susceptibility to pulmonary infections. 8. Albuminuria of slight degree with occasional casts. 9. Sense of suffocation and difficulty in swallowing. 10. Insomnia. 11. Polymorphonuclear leukocytosis.

Cushing Cont'd.

Cushing's report shows young adults (6 to 25 years) undersized females, 2 tall males average duration of life -

5 years, from onset of disease.

4. Pathological endocrine changes:

Secondary endocrine disturbance conceivably affects adrenal gland suggested by hypertension, pigmentation and terminal weakness; on part of pancreatic islands by glycosuria; by thyroid gland by increased basal metabolic rate (present in a few cases). Parathyroid glands involved because of osteoporosis (decalcification) demonstrated by x-ray or at autopsy also spontaneous fractures. No increase of blood calcium in one case studied (Secour case). Hypertrophy of heart noted in some cases. Of 7 reported cases (only opportunities to study) a basophil adenoma pituitary gland was found in 3, undifferentiated adenoma in 2, adenomatous-like structure in fibrosed area in 1, and in 2 the gland was said to be normal. Thyroid slightly enlarged in a few. Suprarenal glands showing cortical hyperplasia, 1. Small adenoma (remember normal presence here too) or no changes in several. Gonads said to be atrophic in most.

Note: In ascribing this polyglandular syndrome to pituitary rather than adrenal source, author states much can be said in favor of latter origin. In our case difficulty in deciding caused exploration to be done, with negative results as far as adrenals were concerned. Is adrenal in functional imbalance as the result of pituitary influence? This disorder is much more common than we suspect?

5. Conclusions: (Author's)

1) Primary anterior pituitary disorders are commonly produced by adenomas.

2) Adenomas of endocrine series are as a whole functionally active lesions.

3) Even minute adenomatous tumors of parathyroid glands and pancreatic islands may lead to serious constitutional derangement of hypersecretory type.

4) Pituitary adenomas are of 3 principal varieties: 1. Neutrophiles, 2. eosinophils, 3. basophiles. No constitutional disorders, heretofore having been definitely ascribed to last.

5) Experimental evidence suggests that basophilic element of anterior pituitary elaborates sex hormone.

6) Polyglandular syndrome hitherto supposed to be of cortical adrenal origin characterized in full blown state by acute plethoric adiposity, genital dystrophy, osteoporosis, and hypertension have been found at autopsy in 6 of 8 instances to be associated with pituitary adenoma, which in 3 (most carefully studied) cases were definitely shown to be composed of basophilic element; lesion in one instance having been clinically predicted before postmortem verification.

7) During past 10 years, innumerable syndromes of so-called polyglandular type, some of them bearing certain resemblance to type under consideration have been described in print.

8) Some of these syndromes are unquestionably due to cortical adrenal tumors, followed in several instances by definite relief of symptoms after removal of tumor.

9) Suprarenal tumors have been found after death in absence of any recognizable abnormality in pituitary bodies in some of these cases. (Although too often the protocol refers to examination of pituitary either briefly or not at all.

10) In absence of any alteration of adrenal cortex other than possible secondary hyperplasia all such cases should have very careful pituitary studies.

IV. CASE REPORT

SIMMONDS DISEASE: POLYGLANDULAR DYSTROPHY. (ANTERIOR LOBE PITUITARY DEFICIENCY).

The case is that of a woman, 33 years old. Admitted to Northwestern Hospital on the service of Paul A. Wilken on the day she died - 2-12-32.

(1912) No Eyebrows

According to her family she was normal to the age of 13; went to school and developed normally except that she had no eyebrows. At this age she developed an acute infectious disease of some sort which was thought by the

physician to be encephalitis. She was in bed 2 years following this and after this did not seem to develop.

1914 - Spastic, slow

There was no paralysis but she seemed slow mentally; did not develop sexually. There was spasticity of the legs. The eyebrows did not grow. At this time she was given pituitary, ovarian extract, and some thyroid and her diet was balanced. After a few months she seemed to develop eyebrows and pubic hair. After about 8 months the limbs seemed less spastic than when seen after the illness.

1925 - Glandular Extracts

Another doctor treated her with glandular extracts. Three years ago she was given thelin but there was apparently no change in her condition; altho she was abnormal in many ways, having never menstruated, being rather sluggish mentally, and not particularly robust physically, she was able to get around the house and carry on ordinary duties.

Not well

2-1-32 - she said she was not feeling well. Glandular extracts were prescribed. On Feb. 7 she was feeling all right. On the 8th she had washed and ironed clothes. On the 9th she felt tired.

Worse

2-11-32 - she was home alone all day and when her brother came home in the evening he found her in bed. She did not complain much and said she was all right. The doctor called on the 12th and sent her to the hospital. She grew weaker and died at 4 P.M.

There is a history that a nephew has glandular trouble and has been treated for diabetic coma recently.

Blood chemistry on the morning of death: urea 21 mg; creatinin 2.6 mg; blood sugar .29 mg. Urinalysis on the morning of death, 9 o'clock: small amount of albumin; no sugar; no acetone; no diacetic; a few casts; 10 to 12 granular casts; 1 to 3 pus cells per high power field; 2 to 5 blood cells per high power field; specific gravity 1030. Blood: leucocytes 10,100.

Autopsy

The body is that of a moderately developed, obese white woman, 158 cm long, and weighing about 175 lbs. The body measures 90 cm from the bottom of the foot to the anterior superior spine and 60 cm from the anterior superior spine to the crown of the head. There is a peculiar girdle distribution of adipose tissue. The face is edematous. The eyes are moderately wide apart. The hair on the head is coarse and thick, fairly scanty. There is no pubic hair and no axillary hair to be seen. The face looks like that of a cretin. The feet are small. The fingers are small and tapering; the nails are normal. There is no rigor, edema, cyanosis, or jaundice; there is hypostasis in the dependent parts. The pupils are regular and equal.

The peritoneal surfaces are shiny and smooth. There is no distension of the gut. The appendix is normal. The liver edge is 2 fingers below the rib margins.

There are a few adhesions on the right upper lobe. The pericardial sac contains 25 cc of clear, straw-colored fluid; no adhesions.

The heart weighs 250 grams. The valves are entirely normal. The coronaries are patent. The root of the aorta is entirely normal.

The right lung weighs 350 grams, the left 300 grams. There is normal crepitation thruout. The cut surfaces exude a small amount of fluid.

The spleen weighs 325 grams. It is slightly softer than normal; slightly congested.

The liver weighs 1500 grams. It cuts with slightly increased resistance. The gallbladder is slightly distended, containing 200 cc of light yellow bile.

The stomach is not dilated. The mucosa of the gastrointestinal tract is normal thruout. The pancreas is normal.

On section of the perirenal tissues before the kidneys are taken out it is impossible to find the adrenals. Numerous small masses of tissue are taken for microscopic examination.

Each kidney weighs 100 grams. The cut surfaces are normal. The capsules strip easily. The bladder is normal.

The uterus is free and movable; it is very small, infantile in type. The ovaries are of normal size but hard and smooth; apparently no ovulation had taken place at any time.

The aorta and lymph nodes are normal. Two small pieces of tissue, about 1 cm each in diameter, thot to be the thyroid, are taken for microscopic examination.

On putting the clamps to the skull it is noted that the skull is extremely thin; the points of the clamp crush thru it. On sawing the skull it is noted that in some places it is almost as thin as paper. The whole brain weighs 1375 grams and appears entirely normal. On section there is no gross lesion. The region of the tuber cinereum seems normal. On cutting away the dorsum sella, the sella turcica is seen to be slightly enlarged and irregular; it measures 12 x 12 mm and within it there appears to be a small yellow cyst about 1.5 cm in diameter. This is removed completely for microscopic examination.

Microscopic Examination:

Ovary: dense fibrous connective tissue capsule; there are several primordial cells present but no mature follicles; there are several corpora albicantia. Thyroid: some lymphocytic infiltration; extreme flattening of the secretory epithelium and tremendous atrophy of the gland as a whole. Hypophysis: cyst with thin walls, lined with ciliated columnar cells with abundant mucus; there are no cells that can be identified as anterior gland cells; in the wall of the cyst are several small vesicles with colloid that are interpreted as being remnants of the pars intermedia. This is supposed to be a cyst arising from the lumen of Rathke's pouch and compressing the pars anterior and the pars intermedia. Liver: moderate fatty metamorphosis. Pancreas: apparently normal pancreatic acini; the islands of Langerhans appear normal.

Diagnosis:

Simmond's disease (atrophy of thyroid and ovaries) due to pituitary insufficiency.

Report of case thru courtesy of Leo Zon, Fellow in Pathology, University of Minnesota.

V. ABSTRACT

ANTERIOR PITUITARY INSUFFICIENCY (SIMMOND'S DISEASE).

Ref.: Calder, R.M. (Duke University, School of Medicine), Johns Hopkins Hosp. Bull. 50:87 -114, '32. Excellent review of subject with 115 references, including brief summaries of 70 reported cases (1899-1931). Submitted for publication December 1, 1931.

1. Historical:

1884 Fritsche and Kleb. Recorded enlargement of pituitary body in case of gigantism.

1887 Minkowski. Suggested pituitary might be related to acromegaly.

1894 Tamburini. First series of cases showing enlargement of hypophysis to be of etiological significance in cases of pathological overgrowth.

1904 Erdheim. Suggested injury to tuber cinereum might cause adiposity.

1908 Paulesco. Removal of pituitary in dogs followed by train of symptoms (weakness, loss of weight, death). Called it cachexia hypophyseopriva.

1909 Cushing. Attempted to confirm this work.

1910 Crowe, Cushing and Homans. Again attempted experiment. Probably inconclusive because of subtotal removal. Rapid involution or actual degeneration of thyroid and gonads and adiposity followed, probably due to injury of surrounding structures.

1912 Cushing. Monograph on pituitary body and its disorders now acknowledged by author to be superseded.

1914 Simmonds. Described first clinical case exhibiting syndrome observed in Paulesco's experimental animals. Female 46, at 38, victom of puerperal sepsis. Following illness, cessation of menses, muscular weakness, premature senility. Autopsy - atrophy of kidneys, ovaries, pancreas, and liver, with necrosis and scar-tissue replacement of anterior lobe of hypophysis.

1916 Simmonds. 2 more clinical cases not quite so conclusive.

1920 Camus and Roussy. Polyuria, adiposity, disturbance of temperature regulation, sexual dystrophy produced by focal lesions of tuber cinereum without coincident injury to pituitary body.

1921 Baily and Bremer. Same results.

1925 Graubner. Review of clinical literature on anterior pituitary insufficiency prior to 1925. Found 6 cases before Simmond's report.

1927 Smith. Ingenious operative procedure proved that cachexia hypophyseopriva is due to anterior lobe deficiency and dystrophia adiposogenitalis is due to lesion of hypothalamic region. Research substantiates on experimental basis clinical syndromes described by Simmonds.

Author (Calder) then reviews briefly 70 reported cases.

2. Symptomatology. (Hibernation plus premature senility).

Emaciation. Constant.

Changes in integument (premature senility).

Teeth and hair fall out.

Nails show trophic change.

Skin dry and wrinkled.

Mental: Listlessness, apathy, pathological sleep, coma (death), mild personality disorders to gross delusions (non-specific?).

General muscular weakness:

Skeletal

Gastro-intestinal (constipation, vomiting, food distress).

Temperature (subnormal with chilliness).

Basal metatolic rate - lower than normal.

Blood pressure - lower than normal.

Sexual: Females - amenorrhea and sterility. Males - impotence.

Lack of sexual desire both.

Metabolism - salt and water changed - too few observations.

3. Cause.

Always destruction of anterior lobe of hypophysis (no exceptions). First case due to puerperal sepsis. Arteries in anterior lobe are end-arteries, infarcts and scars result from embolic plugging - in posterior lobe, because of different vascular arrangement, abscesses result.

Sex: 70 cases, 47 females, 18 males, 5 not stated.

Pregnancy: 20 of 47 cases associated with pregnancy; 18 others, not so associated. Specific changes in anterior lobe during pregnancy result in increased susceptibility to injury or disease or cause faulty involution. Scars usually present in lobe. Of 1700 consecutive necropsies (Simmonds) following lesions found in pituitary glands, metastatic carcinoma 17, syphilis 9, tuberculosis 9, emboli 20. Note - large number of vascular origin.

Tuberculosis: not common. May be difficult to distinguish symptomatology of 2 diseases as both have many features alike.

Syphilis - probably rare.

Tumors and cysts of fair size usually press on surrounding structures, complicate interpretation. Cushing does not believe tumors are very often the cause of this syndrome.

Miscellaneous. Acute inflammation, fractures, etc.

4. Changes in organs other than hypophysis:

Changes in integument, thickening and loss of luster of skin, falling of hair and teeth, and trophic changes in nails, have already been mentioned. Conspicuous changes occur in other glands of internal secretion: macroscopically, thyroid, parathyroid, suprarenal cortex, and reproductive glands are markedly decreased in size, and microscopically this decrease in size is seen to be due to an actual atrophy of glandular structure. In addition, regressive changes in all abdominal viscera, so that the liver, spleen, kidneys, and pancreas are much smaller than normal. To emphasize etiological importance of pituitary insufficiency in this condition Simmonds has used the term "Splanchnomikrie", in contrast to the splanchonomegaly which accompanies over-functioning of gland.

5. Pathological Physiology: In order to interpret symptomatology of any endocrine disturbance, it is necessary to remember that glands of internal secretion are mutually interdependent, and that injury to one may lead to secondary changes, functional or anatomical, in others. Endocrine system, moreover, consists of a series of checks and balances, of pressors and depressors, the proper coordination of which is necessary for normal hormonal activity; and it therefore follows that symptoms may be produced not only by absence of a given hormone but perhaps also by the release of a second hormone to which first is normally antagonistic.

These circumstances make the untangling of any endocrine syndrome difficult, and, although some of the symptoms may be explained with a fair degree of certainty, there remain many gaps in our knowledge. Especially is the symptomatology of cases of pituitary disuse difficult of interprestation.

Note: Author next discusses in detail relationship between anterior pituitary lobe and thyroid, suprarenal cortex, islands of Langerhan's, reproductive glands and higher nervous centers. See original for details.

6. Treatment: Inasmuch as primary destructive factors responsible for injury to the anterior lobe are, for the most part, not subject to therapeutic attack, our efforts must be concerned with supplying the missing hormone. Experimentally, as has been able by the use of transplants and extracts to effect repair of most of the disabilities incident to pituitary removal, and has thereby established the rationale of therapeusis in these cases.

Reye seems the first to have succeeded in producing clinical improvement. He used an anterior lobe extract, "Praephyson", (Passek and Wolf, Hamburg), the exact nature of which is not indicated in his reports. Improvement, according to his accounts, was so striking that he proposed use of this material as a diagnostic procedure in a suspected case.

In a case which has come under our observation, improvement followed the use of "Antuitrin", an acid extract of the anterior lobe prepared by Parke-Davis, the material being given hypodermically in daily doses of 1 cc. Although good results were obtained under this treatment, it cannot be concluded that every sample of this material will be found potent. As a matter of fact, recent experimental work on the subject points to the unstable character of these extracts, and no doubt much work remains to be done before stable preparations are available for clinical application. In the absence of adequate methods of biological assay of potency, it must be considered a fortunate accident that a fresh and potent supply of the required hormone was available for our use.

It is important to know whether similar results are to be expected from oral administration of these extracts? Numerous experiments aimed at the production of acromegaly by feeding anterior lobe substance have been failures. Smith found that the daily feeding of fresh bovine anterior pituitary glands to experimental animals does not cause any increase in body weight, nor does it restore, in the slightest degree, the atrophied genital system, thyroids, or suprarenal cortex of the hypophysectomized rat. The clinical implication is obvious.

Whether extracts of other glands, notably the thyroid, may be required to supplement the pituitary extracts, depends most likely on the duration of the disease. Thus, it is reasonable to assume that in the early stages the insufficiency of the thyroid rests on a functional basis, and accordingly supplying the missing pituitary hormone should re-activate the structurally competent thyroid. Such a state of affairs seemed to exist in our case (and Dr. Zon's). That the thyroid, if not permanently damaged, may be stimulated by injections of anterior lobe extract is further indicated in a case recently studied by Dr. Jean Craven of this hospital: The patient was a girl of 12 presenting signs of pituitary gigantism, whose basal metabolic rate was raised from 2% below normal to 33% above normal by the use of "Antuitrin". If, on the other hand, the disease has endured for a long time, then anatomical changes of the nature of disuse atrophy will have set in, and in such event it is reasonable to assume that not only the

pituitary hormone but also those of the secondarily involved glands may be required in order to relieve the symptoms."

Impressions:

1. Knowledge of pituitary gland and its disorders has increased greatly in last 10 years.
2. Anterior lobe insufficiency cases "hibernation" and premature senility.
3. Most occur in females, often following pregnancy.
4. Commonest causes are emboli, metastatic tumor, tuberculosis, syphilis, primary tumors and cysts.
5. Marked changes occur in other organs ("splanchnomikrie") the opposite of "splanchnomegaly" seen in hyper-secretory states of the anterior lobe.
6. Disturbance in other endocrine glands are striking and irregular. Effects of other organ changes may dominate picture.
7. Treatment is replacement therapy and results are indefinite.

VI. MEETING

Date: November 3, 1932.

Place: Interns' Lounge, 6th Floor, West Building.

Time: 12:18 to 1:29

Program: Medical Economics.
Pathogenesis and Treatment of Acute Pancreatitis (Pancreatic Necrosis)

Present: 87

Discussion: Frank L. Rector
Leo G. Rigler
Edward A. Boyden
O. H. Wangensteen
Angus Cameron (Minot)

Theme: Medical Economics a persistent question without a ready answer. Demonstration of reverse peristalsis in man and cats (in biliary system). Cause of anomalies in this region explained. Possibility of reflux in man greater than 3-5% - probably 66%. Treatment: Do not remove gall bladder during acute attack. Do not tamper with pancreas itself. Do not expect any result from interference in fulminating cases. You can drain biliary system thru gall bladder if stones (or jaundice) are present, or relieve "abscess" by drainage but the real condition (tryptic digestion) is the problem. We were honored by presence of Angus Cameron (Minot), former University Hospital Surgeon.

Gertrude Gunn,
Record Librarian.