Summary

One hundred and thirteen patients with acute staphylococcal infections have been treated with daily doses of a preparation consisting of 300,000 units of procaine penicillin in oil with 1% aluminium stearate and 100,000 units of sodium penicillin. The results have been found to be as satisfactory as those in a similar series of patients treated with 300,000 units of procaine penicillin daily or 300,000 units of sodium penicillin in saline twice daily.

Levels of penicillin in the blood of 81 of these patients during treatment are recorded.

We would like to thank Professor Sir James Paterson Ross and Professor L. P. Garrod for their advice and criticism, Miss Deal, sister in charge of the surgery, and the nursing staff for their co-operation, and Miss M. Rhodes for technical assistance. We are indebted to Messrs. Glaxo Laboratories Ltd. for all the preparations of procaine penicillin used.

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CANCER OF THE UTERUS IN ADRENOGENITALISM

BY

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[WITH PHOTOGRAPHIC PLATE]

Tumour formation is not uncommon in the course of adrenogenitalism, but the following case is unusual in that carcinoma of the uterus with the rare features of adenocarcinoma developed in the thirteenth year of illness.

Case Report

The patient, an unmarried woman aged 31, first reported to Professor A. P. Thomson's clinic in 1937. During the previous four years she had doubled her weight to 280 lb. (127 kg.), while menstruation had ceased in 1936. She was grossly obese and hirsute; her blood pressure was 170/110. Within two years a restricted diet with 2 gr. (0.13 g.) of thyroid a day reduced her weight to 145 lb. (66.8 kg.) and her blood pressure to 145/90. Normal menstruation restarted at the outset of treatment.

In 1942 her weight increased by 30 lb. (13.6 kg.) despite her reduced diet and 2 gr. of thyroid a day. She was given 3 gr. (0.2 g.) of thyroid daily, and this, with the work involved in nursing her father in a terminal illness, brought her weight to normal. For the first time, however, her general health then broke down. She was depressed and listless, and became fatigued on slight exertion. She also suffered from vertigo and bouts of left-sided headache.

First Admission

When admitted to hospital on July 21, 1943, the patient was mentally depressed and apathetic. Her face was highly coloured and she had marked generalized hirsuties and acne vulgaris. Visual fields, fundi, x-ray film of pituitary fossa, B.M.R., fractional test meal, and blood Wassermann reaction were all normal. Her weight was 148 lb. (66.7 kg.); serum chlorine ions, 359 mg. per 100 ml.; and serum potassium, 320 mg. per 100 ml.

Her condition was serious enough to cause anxiety, and Mr. H. H. Sampson, honorary surgeon, Queen Elizabeth Hospital, finally agreed to explore her adrenal glands. At a

preliminary laparotomy an enlarged left adrenal gland was felt and a follicular cyst about the size of a hen's egg was removed. Ten days later the enlarged gland was removed without difficulty through a loin incision. Post-operative shock, often described after this operation, was absent.

The gland weighed 13.3 g. and consisted of diffuse cortical hyperplasia with areas of nodular hyperplasia of the zona fasciculata.

Result.—The most striking effect was the great improvement in the generalized acne vulgaris, and this may have contributed to her improved mental state. She became cheerful and regained her usual energy, returning to full work as a clerk. Four weeks before operation her 24-hour urinary androsterone level was 12.4 mg.—that is, within the normal range. Five days after adrenalectomy it fell to 4 mg.

Second Admission

On August 20, 1947, the patient was admitted to the University gynaecological unit on account of continuous uterine bleeding for the previous 12 weeks. She was grossly obese (220 lb.—99.8 kg.); hirsuties was pronounced over the face, areolae of nipples, and legs. There were mild acne vulgaris of her highly coloured face and many healed acne scars over her back and chest. Fat striae were present over the legs and abdomen, while the left tibial region had been swollen and oedematous for the past five months (Figs. A and B). Her voice was hoarse and croaking, but she asserted that this was normal.

FIG. A.—A single woman aged 41 with adrenogenitalism for 13 years. Weight variable, at present 180 lb. (81.6 kg.). Note the fat striae. The deep abdominal scar resulted from a mild infection of the very obese abdominal wall at hysterectomy.

FIG. B.—Same case as Fig. A. Marked hirsuties but without acne vulgaris. The hair is coarse and dry.

General examination showed that the systems and urinary analysis were normal. There was no obvious explanation for the swelling over the left tibial region. Her blood pressure was 160/80; pulse 72. Visual fields and fundi were normal; the red blood cells numbered 4,600,000; haemoglobin, 100%; white blood cells, 4,600; differential count, normal; B.M.R., minus 10%; radiographs of long bones revealed no osteoporosis; the pituitary fossa was normal.

The biochemical findings were as follows:

Blood chlorides (before operation)	359 mg. per 100 ml.
Serum sodium	318 " " " "
" " (15 months after operation)	286 " " " "
" " chloride ions (before operation)	369 " " " "
" " (15 months after operation)	372 " " " "
" " calcium (after operation)	10.6 " " " "
" " phosphorus	3.3 " " " "
" " alkaline phosphatase	7.5 units " " " "
Total calcium (1,631 ml. urine in 24 hours) ..	277 mg.

Gynaecological findings, apart from a bulky uterus, were normal, with female hair distribution and normal clitoris.

Operation (September 18, 1947).—After curettage had shown carcinoma of the uterus, total hysterectomy with removal of the remaining tube and ovary was performed. The uterus, which was 4 in. (10.16 cm.) long, was also bulky, chiefly owing to hypertrophy of the lateral muscular walls (1½ in.—3.8 cm.—thick). The postero-lateral wall of the uterus was infiltrated with an area of carcinoma 1 by 1 in. (2.5 by 2.5 cm.) in area.

On microscopy the myometrium was penetrated by masses of typical adenocarcinoma, through which were scattered areas of paler-stained cells (Plate, Fig. 1). These pale areas proved to be typical of adeno-acanthoma—that is, cellular metaplasia of glandular carcinoma gave a superficial (low-power) resemblance of cell-nests. Fig. 2 shows that the metaplasia affects both epithelial and stromal tissue. From the epithelial cells arise clusters of bizarre cells, irregular in shape and size, with pale-staining cytoplasm and nuclei containing little chromatin apart from fragments at the periphery. The stromal degeneration was of hyaline type.

Hormone Assays

These were made by Dr. A. M. Hain, of Manchester University. Two factors apart from hysterectomy could have influenced the readings: first, the patient has had 2 gr. of thyroid every day for the past six years; and, secondly, during the ninth month after operation she had 17,000 mg. of alphatocopherol (vitamin E) to control and finally cure her severe menopausal flushings. The readings are shown in the accompanying table.

Hormone Assays

	Pre-operative	2 Weeks Post-op.	15 Months Post-op.	17 Months Post-op.	Normal Readings
Follicle-stimulating hormone	38–40 M.U.	48 M.U.	?	Over 40 M.U.	Cyclical: 15–20 M.U. 40–80 mid-cycle and menopause
Oestrogens ..	Nil (2 tests)	Less than 30 I.U.	?	"No excess"	15–50 I.U. Peak at mid-cycle 120 I.U.
17-ketosteroids (per 24 hours)	18.9 mg. (2 tests)	18.9 mg.	20.6 mg.	21.2 mg.	8–17 mg.
Pregnanediol	Trace: 3–4 mg.	Nil, only "pregnane" metabolite	?	Nil	Cyclical: 1–5 mg.

Gonadotrophins (Follicle-stimulating Hormone).—The readings (see table) cannot be correlated with the clinical condition of flushing, since they do not cover the period of severe symptoms. According to Nathanson *et al.* (1940) and Sharpey-Schafer (1940) a high level of excretion of anterior pituitary hormones might then have been expected. The final excretion level of over 50 M.U., however, was at the high level associated with the menopause.

Oestrogens.—At no time was evidence of excessive oestrogen secretion obtained either by complicated extraction from the urine or by direct injection of the natural urine.

17-Ketosteroids.—The normal limits of excretion vary from 8 to 17 mg. in 24 hours, and this level is generally exceeded in women with virilism not associated with an adrenal cortical

tumour. There are, however, many cases of virilism on record with excretion levels within normal limits (Douglass, 1947).

Pregnanediol (Venning, 1938).—After hysterectomy a "pregnane" metabolite was present; its chemistry has not yet been elucidated. Miss Hain (1947) has extracted this substance on several other occasions, but its significance is not yet clear.

The Vaginal Smear as a Rough Mirror of Hormone Activity (McLaren, 1941).—Pre-operative smears and biopsy corresponded fairly well, the histology showing subacute vaginitis—that is, superficial mucosal desquamation with areas of sub-epithelial infiltration. Despite a prolonged search no cancer cells or cells resembling those seen in sections of the tumour were discovered. Fourteen months after operation her vaginal smear clearly reflected castration, containing mainly small basal and spinosum cells with many polymorphs.

Conclusions.—No unusual hormone excretion level was observed before or after operation. The level of gonadotrophin remained at the relatively high figure commonly found in menopausal women; the excretion of 17-ketosteroids (at between 18 and 21 mg. per 24 hours) probably reflected the hypertrophy which had been taking place in the remaining adrenal gland during the four years that had elapsed since unilateral adrenalectomy was performed.

Discussion

This case shows clearly the various phases of the vaguely defined endocrine illness which we have labelled adrenogenitalism. It is interesting that adrenalectomy led to improvement in the patient's acne vulgaris and to improvement in her general condition, although this may have been quite fortuitous after operation and rest in hospital. The enlarged adrenal (clinically assumed to be a tumour) and the follicular cyst probably represented only a phase of adrenogenitalism.

One is tempted to speculate on the reason why cancer of the uterus developed, although it may have been mere chance in a nulliparous woman approaching the climacteric. On the other hand, it seems certain that women suffering from adrenogenitalism are especially liable to develop tumours, not only in the pituitary but also in the adrenal, thymus, or ovary. Thompson and Eisenhardt (1943) have surveyed 98 cases from the literature with records of simple and malignant tumours in 76. Rare types of carcinoma have also been recorded. Crooke (1946) reviewed three cases of basophilism and recorded one of his own in which the pancreas (not Langerhans cells) was the site of carcinoma, while McLetchie and Scott (1942–4) reported carcinoma of an adrenocortical rest in the pancreas with bilateral adrenocortical hyperplasia and pronounced hypophysial abnormality.

The genital tract was involved in our case on three occasions: (1) amenorrhoea for a year, when the patient weighed 280 lb.; (2) six years later, when a follicular ovarian cyst was removed with her adrenal gland; (3) ten years later, when uterine bleeding led to a diagnosis of adeno-acanthoma of the uterus.

From the facts at our disposal we cannot say whether or not this patient's endocrine disturbances or the surgical removal of her adrenal gland had any bearing on the development of uterine cancer. Adrenalectomy seemed to have a temporary lowering effect on the excretion of 17-ketosteroids, but any operative procedure might do this. It is unlikely, moreover, that any temporary alteration of adrenal secretion after adrenalectomy would operate as a factor in the development of cancer three to four years later.

From the facts available, therefore, we must simply record the case as one of a fat, hirsute woman whose weight and blood pressure rose and fell over the years, and who at one stage developed carcinoma of the uterus with the

unusual features of adeno-acanthoma. Whether her ill-defined endocrine disturbances or surgical intervention had any bearing on the development of carcinoma is mere conjecture.

Summary

A case of adreno-genitalism is described in which over a period of 16 years surgery was necessary on three occasions: (1) to remove a hypertrophied adrenal gland; (2) to remove an egg-sized follicular cyst of the ovary; and (3) to remove the uterus for carcinoma (adeno-acanthoma). Hormone excretion levels were recorded before and after hysterectomy, but no unusual level was obtained.

I wish to thank Professor Hilda Lloyd, P.R.C.O.G., and Professor A. P. Thomson for the opportunity of reporting this case, and also Dr. A. M. Hain for the biological assays and help in their interpretations. Drs. W. St. C. Symmers and C. W. Taylor reported on the pathological sections, which were prepared and photographed by Miss M. E. Attwood.

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ERYSIPELOID OF ROSENBACH EIGHT CASES TREATED WITH PENICILLIN

BY

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Erysipeloid, while not a common condition, occurs often enough for it to be borne in mind, particularly in any large clinic dealing with septic hands. Recently there have been several papers on this subject in this country (Hodgson, 1945; Singer, 1946; Barber, Nellen, and Zoob, 1946; King, 1946; Bush, 1949), and in America, Klauder (1938) records his experience on 100 cases which he has observed.

It is significant that, in spite of the increasing awareness of this entity, many cases must be missed or misdiagnosed, and the condition is not even mentioned in the second edition of Handfield Jones's *Surgery of the Hand*. I therefore wish to record eight cases occurring over the past 12 months (December, 1948, to December, 1949) among a total number of 385 septic hands seen at the clinic—that is, 2% of cases.

The responsible organism is *Erysipelothrix* (or *Bacillus rhusiopathiae*) (Browning and Mackie, 1949), which causes a disease in pigs known as "swine erysipelas." It is a Gram-positive bacillus, and human infection is mainly manifest by an erythematous lesion of the skin of the fingers, hand, or forearm. The bacillus is found among decomposing nitrogenous products. The condition is particularly prevalent amongst fishmongers, butchers, and housewives, who contract the infection by minor traumata to the fingers or hands while handling meat bones, poultry, or fish.

Case Reports

Case 1.—A man aged 32 punctured his left little finger while handling boxes of fish on December 12, 1948. He was seen by his own doctor on the 14th, when he complained of swelling

of the finger. There was no constitutional upset. Injections of penicillin were given by his doctor twice daily, 200,000 units at a time, from December 17, when the condition appeared to settle, and he was allowed to use his hand from the 21st. The condition recurred on December 24, and his doctor then sent him to the casualty department as a "query bone infection of the finger." The little finger was swollen along its whole length, with a typical erythematous reaction of the skin. There was no heat in the part, the site of injury was healed, and there was no constitutional upset. The x-ray film of the finger was negative. He was given procaine penicillin, 300,000 units daily, from December 28 to January 5 inclusive, the hand being rested in a sling. On January 6 the condition had cleared, leaving a slight residual tenderness over the terminal interphalangeal joint.

Case 2.—A fishmonger aged 15 first attended the out-patient department on July 20, 1949. He had pricked his right index finger with a fish-bone on July 14, and had had intermittent inflammation since. On examination typical redness and swelling of the right index finger characteristic of erysiploid were seen, and pronounced tenderness was present over the terminal interphalangeal joint. There was no lymphangitis, glandular enlargement, or constitutional upset. He was given 300,000 units of procaine penicillin daily by intramuscular injection for five days, when the condition rapidly subsided.

Case 3.—A butcher aged 20 first attended the casualty department on September 28, 1949, with a "septic" left middle finger, sustained from a scratch from a bone eight days previously. The day after injury the finger felt sore, but it improved until September 27, when it became inflamed. On examination of the middle finger of the left hand there was the typical erysiploid reaction, localized particularly over the proximal interphalangeal joint. There was no fluctuation, lymphangitis, or lymphadenitis. He was given 300,000 units of procaine penicillin daily, antiphlogistine was applied to the finger, and the hand was rested in a sling. Penicillin was discontinued on October 1, and the patient was discharged on the 3rd. He returned the next day with a recurrence of the erysiploid on the third finger, but this time spreading also to the fourth finger over the dorsum of the hand. After a further course of penicillin for five days the condition cleared completely.

Case 4.—A butcher aged 21 first attended hospital on October 5, 1949, having scratched his right hand with a meat bone in the region of the dorsum of the metacarpo-phalangeal joint of the little finger on September 26. He had swelling and pain in the hand, with the usual erysiploid reaction. He was given 500,000 units of procaine penicillin immediately, and continued with 300,000 units daily for five days. He was then discharged cured.

Case 5.—A housewife aged 36 first attended hospital on October 5, 1949. She had scratched the third finger of her left hand on September 30 while cutting up fish. There was an erythematous infiltration of the finger. The customary dosage of 300,000 units of procaine penicillin was given daily up to and including October 12. The patient was discharged cured on October 13.

Case 6.—A fishmonger aged 38 attended hospital on October 16, 1949, having injured the dorsum of the proximal interphalangeal joint of his left ring-finger on October 9 while cleaning out ice from a fish box. The typical erythematous appearance of the skin was present. Procaine penicillin, 300,000 units daily, and local antiphlogistine were given. He was discharged on October 27 with the condition healed. There was a scaly desquamation of the skin, and full movements of all the finger-joints were present.

Case 7.—A fishmonger aged 22 attended hospital on November 1, 1949, with a swollen and reddened left forefinger. He could not bend the finger. There was no constitutional upset, enlarged glands, or lymphangitis. A week previously he had pricked his finger on the volar aspect of the base of the second phalanx. The finger swelled several days afterwards and was painful and red. After poulticing, the swelling subsided, but it recurred again and 300,000 units of procaine penicillin were given daily for seven days. The condition cleared, leaving no residual effects.

J. G. SCADDING: SARCOIDOSIS, WITH SPECIAL REFERENCE
TO LUNG CHANGES

FIG. 8.—Case 11. Radiograph of chest; January, 1948.

FIG. 9.—Case 11. Radiograph of chest; April, 1949.

FIG. 10.—Case 16. Radiograph of chest; June, 1949.

FIG. 11.—Case 16. Radiograph of chest; August, 1949.

G. H. JENNINGS: AMYLOIDOSIS IN RHEUMATOID ARTHRITIS

FIG. 1.—Case 2. Spleen ($\times 85$). Methyl violet stain shows amyloid in central arteriole of Malpighian corpuscle and in smaller arteriolar branches around periphery.

FIG. 2.—Case 2. Liver ($\times 85$). Dark-staining amyloid material between sinus endothelium and compressed, degenerated liver cells.

FIG. 3.—Case 2. Kidney ($\times 85$). Amyloid changes in glomeruli and afferent arterioles; tubular degeneration; replacement fibrosis.

H. C. McLAREN: CANCER OF
UTERUS IN ADRENOGENITALISM

FIG. 1.—Adeno-acanthoma with circumscribed pale area. ($\times 480$.)

FIG. 2.—Metaplasia. Cytoplasm of irregularly shaped epithelial cells is pale staining with hæmatoxylin-eosin; some of the nuclei are fragmented. ($\times 480$.)