More especially should he be taught the principles that underlie the prevention of deformities and their correction. At this clinic the instruction should be of the simplest kind, and the student should not be burdened by material of a controversial character. He should not leave this clinic until he has mastered the simpler and more efficient methods of treating fractures. He should also be made familiar with the uses of plaster-of-Paris. This course of education should be carefully planned, and week-end visits should be made to the country hospital. In my opinion the out-patient departments of the general hospitals in London should lay themselves out for the reception of the undergraduate, and a hospital such as the Royal National Orthopaedic, in alliance with the Shepherd's Bush Hospital, should be equipped for the training of the post-graduate. Post-graduate teaching has hitherto been of a very unsatisfactory kind. Practitioners have come for, at most, a month or six weeks, and the arrangements, on the side of both teacher and student, have been of a most casual kind. The glamour of the operating theatre has overshadowed the out-patient department from which the bulk of his training should come.

Systematic instruction should be offered the post-graduate, and should consist of short courses for the practitioner who merely wants to be familiar with modern methods. Even this tuition should be carefully planned so that the education may prove intensive. The post-graduate who can only spare three months should be encouraged, for he is the type of man who feels the responsibility of not being competent. The post-graduate school should, however, be prepared with higher courses of training as applied to men who wish to become thoroughly efficient orthopaedic surgeons. These courses should extend some over one and others over two years, and graduates should be given every opportunity to familiarize themselves by practice both with mechanical and operative technique. At the end of the first year, if the work of the graduate has been satisfactory, he should be granted a diploma in orthopaedic surgery, and if he elects to train a second year he may take his university degree in the same subject. The higher courses should offer the advantages of the anatomical, the physiological, and the pathological departments, and for a degree original research work should be essential. I sincerely hope that a progressive university will favourably consider such a scheme.

There is one more point in connexion with training that I would like to suggest—namely, that the orthopaedic surgeon attached to teaching hospitals should be granted a lectureship, and that he be asked to deliver certain of the systematic lectures dealing with his specialty.

At present, alas! there are not enough orthopaedic surgeons to meet the hospital demands, but in many hospitals surgeons will be found who are interested in the surgery of the extremities. The results of the hospital treatment of injuries leave very much to be desired, and an effort should be made in all hospitals to segregate these cases into special wards. They are too often left in charge of the most junior member of the staff. A segregation of such cases in order that comparisons may be drawn will soon lead to better methods of treatment, and the surgeon who shows the greatest aptitude will ultimately obtain control.

In conclusion, I need scarcely emphasize the fact that on the personality not less than on the efficiency of the surgeon will the success of the orthopaedic department depend. Friendships and discussions with the staff will all make for higher education, and a feeling of comradeship will immensely add to the efficiency of hospital work. We can never forget the delightful spirit that dominated our orthopaedic centres during the war, where we each spoke to the other of our failures, and where any advance made by any member of the staff became at once the property of all. The secretive mind had no place amongst our workers. No member of a team was jealous of the other, and light hearts tempered responsibility. Uppermost in our thoughts springs Shepherd's Bush—a hospital so closely associated with His Majesty King Manuel, to whom we as orthopaedic surgeons owe so much, who accompanied us with unerring instinct through deep and troubled waters, and who devoted four years of his life in self-sacrifice and devotion to the cause of the wounded soldier. We welcome him amongst us to-day, proud that we can count him an honorary fellow of the British Orthopaedic Association.

ULCERATING GRANULOMA OF THE PUDENDA CURED BY INTRAMUSCULAR INJECTIONS OF ANTIMONY TARTRATE.

BY

H. LOVETT CUMMING, M.D., CH.B. EDIN.,
D.P.H., D.T.M. AND H.CAMB.,
SHANGHAI.

THE disease known as "ulcerating granuloma of the pudenda," "granuloma inguinale," "granuloma venereum," etc., is fairly prevalent in South China, British Guiana, West Indian Islands, India, West Africa, South Africa, and Northern Australia; it is less frequently seen in Ceylon and Central Africa. I have met with a number of cases in Malaya, but chiefly among coolies from India and China. It does not seem to be common among Malays and Javanese.

Ulcerating granuloma is now generally considered a venereal disease. In the great majority of cases it commences somewhere on the genitals, usually on the penis or labia minora, or on the groin, as a papule or small nodule. The epidermis over this gradually becomes inflamed, thinned out, and excoriated, and the surface breaks down to form an ulcer. The resulting ulceration is seldom deep. The disease either spreads by eccentric peripheral growth or by auto-infection from an opposing surface.

The affection is probably of protozoal origin, but so far nothing definite has been established. Some writers have described a spirochaete as the cause, while Donovan found present in the lesions certain bodies resembling "gigantic bacilli with rounded ends." Siebert found, in all instances, similar bodies in material from various countries, but called them diplococci.

On the other hand, spirochaetes have only been found in a certain number of cases, and when these have disappeared after salvarsan treatment the disease has still continued. In fact, salvarsan and allied preparations in the treatment of this disease have been either altogether useless or extremely disappointing.

I have seen several cases where the disease was quite uninfluenced by intravenous injections of salvarsan, which, with the more extensive experience of other writers, goes far to prove that, in any case, the origin of the affection is unlikely to be spirochaetal. The incubation period is uncertain. It is not referred to in any of the well known textbooks. In the case about to be described it was at least four weeks. Probably, in most cases, it is never likely to be much shorter than that period.

It is only within very recent years that antimony tartrate has come to be used in various diseases, chiefly tropical, which have hitherto resisted, almost completely, all previously known forms of treatment. This drug has been given with great success in kala-azar, Delhi boil, trypanosomiasis, bilharziosis, yaws, certain forms of syphilis, and in ulcerating granuloma of the pudenda.

During the summer of 1916 the writer saw a very advanced case of the latter disease cured at the Albert Docks Hospital by intravenous injections of antimony tartrate. This case was fully reported by Low and Newham in the BRITISH MEDICAL JOURNAL of September 16th, 1916, p. 387.

The following case is of particular interest on account of the method of treatment used and its complete success with comparatively small amounts of the drug introduced into the system.

S. H., an American, first consulted me on September 8th, 1919. He was suffering from chronic gonorrhoeal discharge—a thick yellow "bonjour drop"—which had been present off and on for nearly a year; also from several soft sores, three in number, with hard edges, situated on the dorsum of the penis in and behind the balano-preputial furrow, and involving to a slight extent the proximal end of the glans penis. There was a considerable amount of inflammation and infiltration present round the sores but no definite induration. The glands of the groin were neither enlarged nor tender.

The patient, who is a very observant and intelligent man, stated that he had first noticed on March 3rd, 1919—about six months previously—what appeared to be a slight abrasion, "similar to a hair-cut," which he himself treated steadily for about five days with alternate applications of silvol and potassium permanganate crystals, placed between layers of damp gauze and applied directly to the suppurating area—about two fresh applications of each drug every twenty-four hours. As a result by March 10th—a week later—there was closure of the

raw area, but a slightly swollen and inflamed area appeared, larger than the original open area.

This condition—an inflamed, hard, raised area—continued in a varying degree until it reopened and formed a fresh sore about the end of July, 1919. At this time three distinct sores developed. He treated the condition as before, with the addition of zinc ointment. The treatment was ineffective over a period of nearly a month—that is, up to September 9th, 1919, when he consulted me.

Source of Infection.—With regard to date and circumstances of exposure, nothing very definite was known. There were two possible exposures in the four weeks preceding March 3rd, 1919, one being a European and the other a Chinese (Cantonese) woman. Neither was a professional prostitute, to the best of his knowledge. This occurred in Hong Kong from December 18th, 1918, to February 1st, 1919. Ulcerating granuloma is quite common in South China, and amongst Cantonese prostitutes. The writer has since seen in Shanghai a Chinese woman from Canton who is suffering with this disease in a very advanced form.

Condition Present at First Examination, September 9th, 1919.—On close examination, the sore presented three definite and separate ulcerations, but the surrounding inflamed areas were practically contiguous, and the inflammation and infiltration were more pronounced at the parts more remote from the actual raw centres.

Thinking the condition was one of simple "soft sores," I prescribed "black wash" and a powder consisting of iodoform, calomel, and boric acid, in equal parts.

September 17th. The sores were cleaner and smaller in appearance, and there was less inflammation present. Solution of silver nitrate, 10 per cent., was painted on the affected parts. This treatment was continued until September 30th, when a decided improvement was noted. Only one sore remained unhealed; this affected the balano-preputial furrow, and extended on to the posterior rim of the glans penis.

October 2nd. Thinking the continued gonorrhoeal discharge might be the cause of the persistence of the ulcer, I passed the urethroscope. The urethra bled readily; inflammation extended back to the internal sphincter, from $1\frac{1}{2}$ in. behind the meatus; there were no signs of infected follicles. Bi-daily douches of potassium permanganate (1 in 4,000) were ordered, and a soothing diuretic mixture to be taken after meals three times a day.

October 11th. Less discharge from urethra; the remaining ulcer still unhealed, but apparently healing in parts; edges ragged and irregular; same treatment continued.

October 24th. Ulcer spreading slowly anteriorly, with breaking down and irregular edges, like modified granulations, deeper than before; healed and healing at the proximal end and opening up distally; no discharge. On this occasion I definitely diagnosed the condition as "ulcerating granuloma," owing to the general appearance, chronicity, and manner of spread, absence of enlarged inguinal glands or constitutional symptoms. Nothing very definite was revealed by bacteriological examination, although some typical Donovan's bacilli were found.

Treatment.

The treatment by intravenous injections of antimony tartrate was suggested, but, owing to pressure of business, the patient was unwilling to go into hospital for treatment. Ordinary intramuscular injections of antimony tartrate were not contemplated, as I had just seen in consultation a marked case of the same disease in a Chinese woman, where antimony tartrate in saline solution, intramuscularly, had caused abscess formation at the seat of injection.

Local applications of various kinds were tried, with only slight improvement in the condition. At best the progress of the disease was merely checked. The application which was attended with best results was a solution of salicylic acid in ether (4 drachms to the ounce), combined with mercury perchloride (0.2 per cent.) in absolute alcohol— aa 1 oz. This reduced the granulations and dried up considerably the spreading open sore at the distal end of the ulcer. The application was painted on morning and evening.

November 4th. No further spread of ulcer, but no further healing. Antimony tartrate ointment was applied for two nights in succession, but the pain and subsequent discomfort, which lasted for hours, caused the patient so much distress and loss of sleep that it was at once discontinued. Salicylic acid in creosote ointment (gr. xxx to 1 oz.) was next tried, and applied regularly for several days, but the result was unsatisfactory. At the same time he was given m v to m xx of vinum antimoniale, in gradually increasing doses, internally three times a day.

November 14th. Healed part of scar appears larger and flattened out, about the size of a farthing. Unhealed part (distal) no larger, but not closing up. Looks like a crack with ragged, irregularly curved edges. A very little thin yellowish discharge present in the sore.

December 13th. A month later there was very little, if any, improvement. The depression scar appeared larger, but the open sore was still present and seemed to be increasing in length. This was typical of the complaint and sufficiently diagnostic.

On December 6th, 1919, Dr. Daniels, of the Colonial Office, called on me when he was passing through Shanghai, and, on mentioning this case to him, he suggested intramuscular injections of antilueticin. Unfortunately, this drug could not be procured locally, and the patient was still unwilling to go into hospital for a course of intravenous treatment.

January 12th, 1920. Whole scar on dorsum of glans penis was larger—a little bigger than a farthing. The unhealed distal crack was larger, with convex anterior edge. The whole appearance was now quite diagnostic of ulcerating granuloma. No other symptoms were present; no pain or enlarged glands. Discharge from urethra was slight and thin in consistency.

Treatment by Antimony Tartrate (Intramuscular).

The patient was becoming very disheartened at the apparent obstinacy of the condition and at the absence of complete healing. Just at this time I received from home the latest edition of Castellani and Chalmers's *Manual of Tropical Medicine*, and discovered there, under treatment for yaws and oriental sore (vide p. 2174), a formula for administering antimony tartrate by intramuscular injection without any unpleasant results. This had been used successfully in the treatment of yaws even in young children.

Castellani's No. 1 formula consists of antimony tartrate with carbolic acid and glycerin—for example:

B Tartar emetic	...	...	...	...	gr. viii
Acid. carbol.	...	...	...	...	℥ x
Glycerin	...	...	...	...	3 ij
Distilled water	to	...	...	...	3 j

Dose: $\frac{1}{2}$ to 1 c.cm.

He also recommends a solution by the mouth:

B Tartar emetic	...	...	...	...	gr. v
Sodii bicarb.	...	...	...	...	gr. xxx
Glycerin	...	...	...	...	3 j
Aq. chloroformi	...	...	...	...	3 ij
Aquae	...	...	...	...	3 ij

Dose: 2 to 4 drachms three times a day after food.

Castellani holds that these combinations of antimony tartrate prove comparatively non-irritant to the muscles (intramuscularly) and to the stomach (internally), and in my experience this proved to be the case.

January 14th. First intramuscular injection given—about 9 minims of Castellani's solution, equal to about gr. $\frac{1}{2}$ of antimony tartrate. This was followed by a slight bruised feeling, with some pain and stiffness in the hip and down as far as the knee, lasting for an hour. Later, the same evening, a transient rash came out on the thighs, like mosquito bites.

January 15th. He commenced taking the mixture, 2 drachms thrice daily. Each dose is roughly equal to gr. $\frac{1}{2}$ of antimony tartrate—that is, gr. $\frac{1}{2}$ daily.

On January 16th antimony tartrate gr. $\frac{1}{2}$ was injected into the left hip; on the 18th and 20th gr. $\frac{1}{2}$ into the right hip; and on the 22nd gr. $\frac{1}{2}$ into the right hip.

The left hip still remained a little swollen and tender on pressure after No. 2 injection on January 16th, but it was possible to go on injecting into the right hip without any unpleasant effects. The sore showed now, after the fourth injection, definite signs of healing. There was less thickening present at the edges and the appearance was healthier.

January 25th. Owing to an attack of influenza, further local treatment was postponed. The last injection was most painful of all. Right hip very tender. Still signs of healing locally. Raised border beginning to contract and flatten out, while the sore was drying up at the same time.

January 31st. Nine days since last injection. No pain or discomfort in either hip. Locally, sore healed, with exception of small area, about a quarter of an inch in length; whole area looks healthier and practically no discharge. Antimony tartrate gr. $\frac{1}{2}$ was injected into the left hip.

On February 2nd antimony tartrate gr. $\frac{1}{2}$, and on the 4th gr. $\frac{1}{2}$, was injected into the right hip. On the latter date there was only a tiny place about $\frac{1}{2}$ in. unhealed; ulcer more shallow. On February 7th gr. $\frac{1}{2}$ was injected into the right hip, and on the 10th the same amount into the left hip; the sore was clean, red, and healing well—less than $\frac{1}{2}$ in. long. On the 14th, gr. $\frac{1}{2}$ was injected into the right hip; sore almost healed; no pain or swelling in either hip.

February 16th. Small white pustule present on dorsum of glans penis, probably due to action of the drug. This dried up and disappeared in two days and there was no recurrence.

February 18th. Antimony tartrate gr. $\frac{1}{2}$ was injected into the left hip. A small fissure of the sore was still present, unhealed. This was treated with strong solution of salicylic acid and mercury deep into the fissure and along the right rim of healed ulcer. On this occasion there was painful swelling of the glands in both groins, but not much enlargement. There was still a slight yellowish urethral discharge in the morning.

February 25th. Scar practically healed. Salicylic lotion painted on, as before. Two days later the scar showed only a slight redness of the edge, so the above lotion was again applied.

February 29th. Scar on penis completely healed and looking well. After this the antimony tartrate mixture, by mouth, was continued for another week. On this date, as the glands of the right groin were still enlarged, also very tense and tender, and as there was still a slight urethral discharge, the patient was put on a course of injections (subcutaneously behind the deltoid muscle of each arm alternately) of Neisser's serobacterin (Mulford), beginning with $\frac{1}{2}$ c.cm. and working up gradually to $1\frac{1}{2}$ c.cm. until 5 c.cm. had been given. There was an interval of two to five days between each two injections, according to the amount of reaction present. At first douches of potassium permanganate were taken (1 in 4,000) twice daily, but after a week these were replaced by acriflavine douches of the same strength, with the result that the urethral discharge gradually disappeared.

April 28th. The penile sore remained healed, and the surface had assumed an almost normal appearance, except for a small shallow depression remaining to show where original sore had been.

June 17th. Nearly four months after actual healing of sore; no sign of any recurrence.

Undoubtedly the gonorrhoeal complication helped to aggravate the condition and retarded the healing of the ulcer. At the same time it is not unlikely that the antimony tartrate injections and the antimony tartrate taken by mouth helped to light up the old gonorrhoeal trouble. It is, however, unquestionable that the antimony tartrate was the only drug which had any effect upon the sore. Definite signs of healing were observed after the fourth injection, although the patient himself declared that he found improvement after the second injection.

All other local treatment was suspended while the injections were being given, with the exception of an antiseptic wash, night and morning, for the sore, followed by the application of a little dusting powder composed of equal parts of calomel, boracic acid, and iodoform, which had been previously used without the slightest effect.

Altogether, about 3 grains of antimony tartrate were injected intramuscularly over a period of thirty-six days. Only twelve injections were given. Castellani recommends $\frac{1}{2}$ to 1 c.cm. as the dose of his No. 1 formula of antimony tartrate. I began with 9 minims (about $\frac{1}{4}$ gr. antimony tartrate), and gradually went up to 1.2 c.cm., or $\frac{1}{2}$ gr. antimony tartrate, for the last five injections. By mouth, roughly 27 to 30 grains of antimony tartrate were taken over the same period. How much of the cure can be attributed to the oral administration of the drug is difficult to calculate, but it was noted that although the patient was taking 5 to 20 minims of antimony wine three times a day, in gradually increasing doses, from November 4th, 1919, to January 14th, 1920—a period of seventy-one days—without any appreciable effect on the condition of the sore, it is reasonable to conclude that only a very small amount of the drug, subsequently given by mouth, had any definite effect on the process of healing. On the other hand, very definite improvement took place after the fourth intramuscular injection, that is, before the drug given orally could have had time to have much constitutional effect. It is stated that:

"Antimony is slowly absorbed and is taken up from the blood and stored in the liver. It does not appear to have any important influence upon the corpuscles, but diminution in red cells, leucocytosis, and decrease of alkalinity have been recorded." Also, "it is excreted in the intestine, and by the liver, kidneys, and skin" (vide Bruce and Dilling, *Materia Medica*, p. 139).

Some authorities state that it causes peripheral vascular dilatation. Probably the latter action of the drug, a certain amount of leucocytosis, and that part of it excreted through the skin, were the chief sources of improvement in the local condition. The amount of the drug administered orally, acting in the above way, would naturally be infinitesimal, owing to the very slow absorption. Some authorities, among them being Greig and Curjel, consider that the condition is only benefited by large doses of antimony tartrate (1 to 3 grains intravenously). This may be where the disease is extensive and advanced. Other authors have reported cases of failure. The case of the Cantonese woman already referred to was a failure, but it was hardly a fair test case, as the disease was far advanced, involving the clitoris, vagina, the fourchette, both labia minora, and the right labium major. It was impossible to give intravenous injections, owing to the smallness and inaccessibility of the veins, while the intramuscular injections of antimony tartrate, in saline or distilled water (grain $\frac{1}{4}$), caused several local abscesses, and had to be discontinued. Daniels stated to me that any improvement in such an advanced female case is very improbable.

Fortunately, the case here recorded was definitely localized, and neither advanced nor extensive; also, the progress of spread was extremely slow. It was an ideal case for the administration of the drug by the intramuscular route. The results were so satisfactory, and the cure so quickly attained by this method, that the report of the case may be the means of encouraging some others to use the same treatment. No doubt early cases—before the disease has got a firm hold, and where the ulcer is not extensive—will prove most amenable to the action of the drug intramuscularly.

With advanced and extensive cases it would be useless to treat them otherwise than by larger doses, by the intravenous route, over a more extended period, and in hospital, where the action of the drug and the condition of the patient can be observed carefully from day to day.

SEVEN CASES OF ESSENTIAL PENTOSURIA.

BY

P. J. CAMMIDGE, AND H. A. H. HOWARD,
M.D.LOND., B.Sc.LOND.

ALIMENTARY PENTOSURIA is not a very rare condition, particularly in summer when fruits containing arabinose are often eaten in considerable quantities, but essential or spontaneous pentosuria, which is not dependent upon the ingestion of pentose-containing foods, is exceedingly uncommon, some forty cases only being on record. Up to the present no example of the condition has been reported in this country, the published cases having all occurred in America or Germany. Last year we had the remarkable experience of meeting with seven cases, five of which were encountered in one month and the other two a few weeks later. Five of the cases proved to be examples of simple essential pentosuria, inactive arabinose being the only sugar present in the urine, in the other two small quantities of dextrose and pseudo-laevulose were found in addition. One of the patients with pure pentosuria had been treated for diabetes for twenty-six years, two had been dieted along orthodox lines for the same complaint without any improvement for several months, a fourth was referred to one of us as a case of lactosuria, presumably because the sugar in the urine did not ferment with yeast, and in the fifth the presence of sugar had been discovered accidentally, although its nature was not determined, previous to an operation. The remaining cases had been rejected for life insurance owing to the presence of glycosuria.

The majority of the cases of essential pentosuria hitherto described have been Germans, or of German or Russian descent, and a striking proportion have been Jews. Three of our cases were Jews, two were of Greek descent, but the others were purely English in birth and ancestry. A striking feature of the condition is its tendency to occur in several collaterals of a family, and some pentosurians have been members of diabetic families. Two of our patients, those of Greek descent, were father and son, but no history of glycosuria in any other member of the family could be obtained. Two of the Jews (Cases 4 and 6) were also related, being uncle and nephew. In this instance there was a family history of glycosuria, the father of the elder patient having been treated by the late Dr. Pavy for many years for diabetes, although he eventually died at the age of 67 from Bright's disease; a niece of the same patient and cousin of the other, consulted one of us and was found to be passing about 50 grams of sugar a day, the whole of which however was dextrose. The family histories of the other cases were free from diabetes or glycosuria, so far as could be ascertained. Six of the patients were males and one was a female. Their ages ranged from 19 to 75 years. These details, with the actual amount of sugar passed and the other more important results of the analyses of the urines, are shown in the following table (Table I). The data for Case 5 are incomplete, as only an odd specimen of the urine could be obtained for examination. The dextrose and pseudo-laevulose were estimated by the methods described by one of us in 1917¹ and the pentose by a modification of Jolles's process carried out as follows:

One hundred c.cm. of the urine are mixed with 150 c.cm. of hydrochloric acid (12 per cent.), and heated in a flask fitted with a reflux condenser for a quarter of an hour in a water-bath. The contents of the flask are subjected to steam distillation and 500 c.cm. of the distillate collected. Of this 100 c.cm. are neutralized with sodium hydrate (20 per cent.), using methyl orange as the indicator, and then made faintly acid by adding one or two drops of half normal acid. A measured quantity of normal sodium hydrogen sulphite is introduced, and the mixture left to stand for two hours. The excess of sulphite is then titrated with tenth normal iodine solution, using starch as the indicator. From the amount of sulphite consumed the percentage of pentose present can be calculated, each cubic centimetre of sulphite corresponding to 0.07595 gram of pentose.

Arabinose does not reduce copper salts as readily as dextrose, and, as the percentage of the sugar excreted is