

# SYSTEMIC DONOVANIASIS\*

BY

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Donovaniasis (granuloma inguinale or granuloma venereum) is primarily and predominantly a localized disease of the skin and mucous membranes of the genital and inguinal regions of the body. The causative organism of the disease was first discovered by Donovan (1905) by the microscopic examination of the exudate from the oral lesion of a patient under his care who also suffered from genital lesions.

The disease spreads usually in three ways :

- (1) by direct contiguity of tissues along the corium of the skin or mucous membranes,
- (2) by auto-inoculation of adjacent or opposing surfaces,
- (3) by mediate transmission through infected clothes or fingers.

Greenblatt (1943) claimed that the disease may spread through the lymphatics and explained the occurrence of elephantiasis in the external genitalia, and the involvement of the pelvic organs and tissues from a lesion of the cervix on the hypothesis of a lymphatic spread of the infection. Although the external genitalia and its environs are most commonly affected in the female, granuloma of the cervix, either as a primary lesion or as a secondary spread from the vulva and vagina, does occur more frequently than is usually recognized or reported. The lesion in the cervix may simulate cancer clinically and even histologically, and hence is frequently liable to be mistaken for the latter by the unwary gynaecologist.

It has long been recognized that extra-genital lesions invariably occur secondary to genital disease and usually by auto-inoculation. Next to the involvement of the genito-inguino-anal regions, the oro-pharyngeal cavity and neck are most frequently the sites of the disease. In over 2,000 cases of Donovaniasis seen by us, extra-genital lesions

occurred in 6 per cent. which is, interestingly enough, the same as the percentage reported by Greenblatt and others (1938).

Systemic haematogenous disseminated lesions of the disease have only been infrequently reported in the literature. Infection in the liver and lung was reported by Vogel (1928). Thierfelder and Thierfelder-Thillot (1924) referred to the occurrence of polyarthritides deformans in granuloma venereum. Thierfelder (1925) described a patient with involvement of joints and skull. Hoffmann (1920) reported a case showing abscesses of the bones, liver, lungs, and peritoneum at autopsy. Kuhn (1906) described a patient with involvement of the bones, liver, and spleen. Becker (1939) mentioned a case of granuloma venereum in which involvement of the ribs and intestinal tract was found at autopsy.

It would appear that most of the earlier observations on the subject are based on autopsy findings.

## Clinical Reports from the Literature

During the past 10 years a number of well-documented case reports of systemic Donovaniasis have appeared exclusively in the American medical literature. An attempt is made here to review in some detail the case reports that have appeared in recent years.

(I) *Paggi and Hull* (1944) reported the occurrence of metastatic osteolytic lesions of granuloma venereum in the clavicle, rib, and scapula of a young Negro female suffering from a primary lesion of Donovaniasis in the cervix uteri. Donovan organisms were demonstrated in the cervix uteri and in the aspirated material obtained from abscesses overlying the affected bones.

(II) *Lyford, Scott, and Johnson* (1944) reported three cases of systemic Donovaniasis.

(1) *A 20-year-old Negro female* came under their observation with lesions of Donovaniasis in the vulva, vagina, and cervix uteri with a tender mass in the left lower quadrant of the abdomen. Biopsy revealed

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Donovan bodies in the large mononuclear cells. She underwent radical vulvectomy and fulguration of the ulcers of the cervix and vagina, and during the succeeding 4 months of her stay in the hospital developed painful swellings of the knees, elbows, fingers, wrist and ankles, and ulceration of the 3rd toe preceded by migratory pain in all the joints. She had an irregular, hectic temperature, was anaemic, and lost weight. Another exploratory operation was performed on her right elbow joint and the tissue removed showed Donovan organisms. The continuous tissue culture of material from the right elbow and left 3rd toe showed organisms resembling *Donovania granulomatis* which grew for several weeks. The patient showed temporary improvement with sulphadiazine and was discharged from the hospital, but 2 months later was admitted again with multiple swellings of the joints, skull, and long bones. Radiographs showed a diffuse lysis of all the small bones of both hands, and both feet, and areas of lysis in the left fibula, both tibiae, skull, both ulnae, right clavicle, and right acromion. No organisms grew in the tissue cultures of the blood. The patient's condition gradually went downhill with continuous, irregular temperature. The swelling of the joints ruptured giving rise to multiple granulomatous ulcers. She was reported to have died ultimately.

(2) A 21-year-old Negro woman was admitted with pain in the lower abdomen of 4 months' duration and tender swelling in both groins, which ulcerated later. There was no evidence of any active or old genital lesion. The biopsy of the inguinal masses revealed granulation tissue containing plasma cells and macrophages with typical Donovan bodies. Frei and Itô tests were negative. During a period of 7 months she had received 38 injections of Fouadin. She developed pain in the lumbar region and left hip. Radiographs revealed destructive changes in the bodies of the 4th and 5th lumbar vertebrae and in the left hip. There were palpable tender nodes in the neck, both axillae, and groins. The tuberculin skin test was positive. Tests for syphilis were negative. There was a slight reversal of the albumin/globulin ratio in the serum. The white blood count was normal. When applied again the Frei skin test was positive. The bone removed from the lumbar vertebrae after an exploratory laparotomy showed only granulation tissue, but no Donovan organisms were demonstrated either in stained smear or tissue culture. The inguinal sinus tracts were found to communicate with the left hip and lumbar vertebrae. The granulation tissue of the sinuses revealed Donovan organisms. At the time of reporting the patient was still under treatment.

(3) A 16-year-old Negro girl with a history of repeated episodes of pyogenic infection in different parts of the body during a period of 7 years, was seen by these authors with bilateral ulcerating masses of the labiae and circular erosions of the skin of the left forearm. No Donovan organisms were observed in the smears from the genital lesions. The Frei test and serological tests for syphilis were positive. She was treated with sulpha drugs, potassium iodide, and a few injections of Mapharsen and bismuth. Two months later the left first metacarpal bone was excised for osteomyelitis following the non-healing of a paronychia of the left thumb. The lesion failed to heal and radiographs showed destructive changes in the carpal bones and the distal end of the left radius. An amputation at the mid-forearm was performed as the radiographs showed further destruction

of the upper part of the forearm bones, and the patient finally sustained a total amputation of the entire arm through the surgical neck of the humerus. The wound healed and the tissue removed from the left hand and arm showed granulation tissue with plasma cells and macrophages containing Donovan bodies.

The data put forward for the diagnosis of Donovaniasis of vertebrae and hip in Case 2 and for the extensive ascending infection of the left arm bones, starting with a metacarpal lesion, are rather unconvincing. In Case 2, the tracking nature of the inguinal lesions with positive Frei and tuberculin tests and negative findings for Donovan bodies in the tissues removed from the vertebrae and hip, together with the lymphadenopathy of the neck, axillae etc., rather favour a diagnosis of either lymphogranuloma venereum or tuberculosis of the bones with a superimposed infection of the sinuses of the groin with granuloma venereum. While the granulation tissue of the inguinal sinuses was positive for Donovan bodies, that of the lumbar vertebrae was negative in Case 2. The reverse finding was reported from Case 3, in which the genital lesions were negative and the bone lesions were positive to Donovan bodies.

(III) *Sheldon, Thebaut, Heyman, and Wall* (1945).

A male Negro had an ulcer on the left leg, which was followed by a large lytic defect in the tibia, osteoporosis of the tibial condyles and distal end of the femur, and an area of lysis in the anterior end of the 7th rib on the left side. These authors claim to have isolated Donovan bodies by cultivation of the granulation tissue from the leg.

(IV) *Palik and Schenken* (1945).

A 21-year-old Negro woman with primary granuloma of the cervix developed multiple metastatic lytic lesions in several bones, clavicle, rib, and scapula. Smears from all the lesions were reported to have contained Donovan organisms.

(V) *Rhinehart and Bauer* (1947) reported a fatal case of disseminated Donovaniasis of the bones secondary to primary lesions in the cervix uteri and vaginal vault.

A 33-year-old Negro woman was admitted with a foul, bloody discharge from the vagina, pain in the left hip, low fever, and rapid pulse. Physical examination revealed a soft ulcerating growth of the cervix extending to the vaginal vault and communicating through a sinus track with a large mass in the left pelvis. By cystoscopic and proctoscopic examinations it was found that the mass in the left pelvis was pressing on the bladder, left ureter, and rectum. Intravenous urography demonstrated a non-functioning left kidney. This was removed and a psoas abscess was disclosed behind the kidney. A biopsy of the cervical and vaginal lesions revealed the characteristic, specific granulation tissue, consisting of many macrophages filled with *Donovania granulomatis*. Six weeks after nephrectomy the patient developed multiple painful swellings over the forehead and over almost all the long bones of the body. Radiographic examination of the bones disclosed the presence of osteolytic lesions in both tibiae, both fibulae, both ulnae, the upper end of the left radius, the shaft of the proximal phalanx of right ring finger, both frontal bones, and the left astragalus. The bone defects

were multiple, irregular, osteolytic lesions of the cortex with no evidence of sequestrum or surrounding osteoplasia. Aspiration of the bone lesions revealed the large cells of granuloma venereum containing Donovan bodies. Despite treatment with tartar emetic and Fouadin the patient was found dead lying in a pool of blood that had escaped from the vagina. Autopsy, in addition to confirming the *ante-mortem* findings, revealed extensive caseous tuberculosis of the abdominal, para-aortic, and tracheo-bronchial lymph nodes.

(VI) *Packer, Turner, and Dulaney* (1948) reported a case of Donovaniasis in the vagina and cervix with bone metastasis.

A 19-year-old Negro girl was admitted with a history of having passed some fleshy discharge from the vagina and there was evidence of pneumonia of the upper lobe of right lung. A tentative diagnosis of abortion complete or incomplete was made. With rest and sulpha therapy she recovered from the illness, but was readmitted 7 months after her discharge from the hospital, complaining of pain in the left hip, right lower quadrant of the abdomen, haematuria with dysuria, and passing of bloody vaginal discharge. On admission she was emaciated and weak and her temperature was 102.4° F. with increased pulse and respiration rates.

Physical examination revealed a tender, nodular, friable infiltration of the cervix uteri, with woody induration of the anterior vaginal wall, and marked tenderness of the lower abdominal quadrants, that prevented a successful bimanual examination. There was moderate secondary anaemia, leucocytosis, and increased sedimentation rate. During her stay in the hospital she had an operation for a peri-rectal abscess. Thereafter she soon developed pain and swellings over the right knee, the knuckle of the left hand, and the left knee. The latter swellings progressed to form fluctuating abscesses beneath the skin which were incised. The other swellings subsided. Radiological examination of the swollen areas revealed bone destruction under each swelling. The medial surface of the condyle of the left tibia, the distal end of the shaft of the 2nd metacarpal bone of the left hand, and the navicular bone of the right hand showed areas of destruction associated with a certain amount of periosteal proliferation and sclerosis. A cystoscopic examination revealed a granulomatous lesion of the floor and left wall of the bladder, and obstruction to the left ureter, with hydro-ureter and hydronephrosis on that side. A tentative clinical diagnosis was made of malignant disease of cervix uteri spreading to involve the bladder and pelvis, and secondary metastases in the bones. But biopsy and contact smear of the cervical lesion revealed macrophages containing Donovan organisms. Likewise the incised lesions of the left hand and right knee were positive for Donovan organisms. The blood culture employing tryptose-peptone-egg-yolk agar showed organisms morphologically resembling Donovan bodies. The response to intravenous injections of tartar emetic was reported to have been dramatic. The lesions of the cervix and bones healed and the general constitutional reactions subsided.

(VII) *Lipp and Bibby* (1950).

A 20-year-old Negro woman suffered from genital, extra-genital, and skeletal disease.

### Case Report

The case of systemic Donovaniasis reported below is the first of its kind encountered by the authors in a practice of 25 years, during which over 2,500 cases of Donovaniasis of the genitalia, groin, and oro-pharyngeal regions of the body have been examined and treated at the V.D. Department of the Government General Hospital, Madras.

A married woman aged 22 presented herself for examination at the V.D. Department of the Government General Hospital, Madras, on October 30, 1953, complaining of pain in the right hip of 4 months' duration, and along the right lower limb of 3 months' duration, and a white discharge per vaginam of 3 months' duration.

*Previous History.*—The patient had three children, the last child being 10 months' old. During the 10 months following the delivery of the last baby, the patient had menstruated only once some 4 months previously. There was no history of abortion or miscarriage. The patient had had regular sexual relations with her husband after the last confinement.

*Clinical Examination.*—The patient was a rather weak, pale-looking woman, suffering from pain in the right lower limb which caused her to limp. Multiple, circular granulomatous ulcers were noticed on the inner aspect of the labiae and around the perineum. Inguinal lymph nodes were palpable but not tender. On introducing the vaginal speculum there was brisk bleeding, even before the cervix uteri could be visualized. This was thought to be coming from the external os and further examination was deferred.

*Diagnosis.*—In view of the history of amenorrhoea of 4 months' duration and the bloody discharge from the vagina a diagnosis of incomplete abortion was made. The patient was immediately referred to the Hospital for Women and Children as an emergency, and was kept there for 5 weeks, where it would appear that a diagnosis of "cancer cervix uteri with ulcerating syphilides of the vulva" was made.

*Therapy.*—The patient was given 4.8 mega units PAM for the latter condition. The vulval ulcers having failed to respond to anti-syphilitic treatment, the patient was referred back to the V.D. Department for opinion.

*Clinical Condition on Second Admission to the V.D. Department.*—The patient looked profoundly ill and pale (temperature 100.4°, pulse 110 per minute, respiration 26 per minute). There was marked oedema of both feet and legs. The right hip was kept flexed and any attempt at extension of the limb caused great pain. On the antero-medial aspect of the middle of the right leg a localized painful and tender swelling was observed. A similar tender swelling was noticed over the inner 3rd of the right clavicle. The abdomen on the right side was rather resistant to palpation although there was no actual tenderness. The liver was enlarged two fingers breadth below the costal margin and the edge of the liver was regular.

*Local Examination of Genitalia.*—Multiple, unhealed, granulomatous ulcers were observed in both labiae and perineum (Fig. 1). The vestibule and urinary meatus were normal. Examination with a vaginal speculum revealed a nodular, easily friable, and bleeding infiltration of the cervix uteri, obscuring the external os and extending to the anterior vault and right lateral fornix of the vagina. The non-cooperative attitude of the patient prevented a proper bimanual examination to determine the condition of the uterus and its adnexae.



FIG. 1.—Multiple granulomatous ulcers of both labiae and perineum. Positive for Donovan organisms.

*Laboratory Investigations.*—Tissue spreads from the vulval and cervical lesions revealed typical capsulated Donovan organisms in the cytoplasm of large mononuclear cells, along with polymorphonuclear leucocytes and lymphocytes and plasma cells. The aspirated material from the pre-tibial lump of the right leg also showed capsulated Donovan organisms.

Dark-field and serological tests for syphilis negative.

Frei test negative for lymphogranuloma venereum.

Blood count: red blood corpuscles 2.4 m./c.mm., haemoglobin 35 per cent., white blood corpuscles 19,000 per c.mm., with 93 per cent. polymorphonuclear leucocytes.

Erythrocyte sedimentation rate 133 mm./45 min. Blood chemistry: sugar 66.7 mg. per cent., blood urea 75 mg. per cent., total proteins 7.8 g. per cent., albumin 3 g. per cent., globulin 4.8 g. per cent.

Gel test: immediate positive.

Urine: pus cells, red blood corpuscles, and suspicious Donovan organisms, along with other banal bacterial flora, and a trace of albumin.

Stools: plenty of round worm ova.

Liver function tests: within normal limits.

Radiological examination of the skeleton revealed:

- (1) localized area of bone destruction on the right tibia under the subcutaneous lump.
- (2) area of rarefaction at inner end of right clavicle.
- (3) mass obscuring sacro-iliac articulation of right side (Fig. 2).

X-ray screening of lung: no abnormality.

Biopsy of cervical lesion revealed the characteristic, specific granulation tissue containing many macrophages in which Donovan organisms were faintly demonstrable.

Biopsy of liver was performed on December 16, 1953, and the sections were stained by various procedures. These sections revealed moderate fatty change in liver cells, with marked peri-portal cellular infiltration with commencing fibrosis. Scattered in the liver-parenchyma were multiple foci of suppurative inflammation—micro-abscesses—with destruction of the liver cells. In one or two areas the section showed cirrhotic changes in the portal area with sclerotic thickening of the vessels; but the most striking aspect of the histological picture was



FIG. 2.—Radiograph of irregular mass anterior to and completely obscuring right sacro-iliac articulation.

the presence of clusters of Donovan organisms in the cytoplasm of the liver cells, with the characteristic pleomorphism of coccoid, coccobacillary, safety-pin, and capsulated types, the last predominating. The organisms were best observed in sections stained with Dieterle's silver and Giemsa by the slow method (Figs 3, 4, 5, opposite).

A contact smear taken from the biopsied liver tissue showed scattered extra-cellular capsulated Donovan bodies besides a few scattered liver cells containing the same organisms in their cytoplasm.

Sternal puncture: no Donovan organisms.

Thick blood smears: negative for Donovan organisms.

*Diagnosis.*—Systemic metastatic Donovaniasis in the liver and bones, secondary to a primary lesion in the cervix uteri.

*Progress.*—From December 8 to 16, 1953, while the patient was subjected to these diagnostic procedures, her general condition was getting worse with hectic temperature and rapid pulse. The oedema of the feet and legs was visibly increasing. On December 15, 1953, she was given a blood transfusion of 150 ml.

*Specific Treatment.*—Parenteral streptomycin 1 g. twice daily was started on December 16, 1953. Vitamin C and yeast tablets were administered orally. During the course of treatment it was noticed that she was occasionally wetting the bed. As the patient was very ill and uncooperative she was not subjected to any further examination to determine the cause of the wetting.

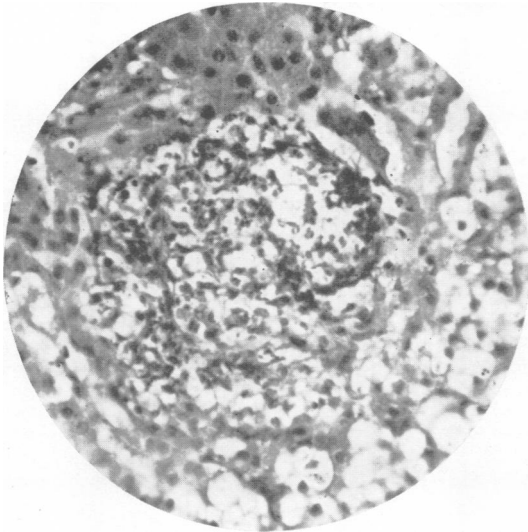


FIG. 3.—Photomicrograph of section of liver showing focus of suppurative inflammation, micro-abscess amidst liver parenchyma. Haematoxylin and eosin.  $\times 320$ .

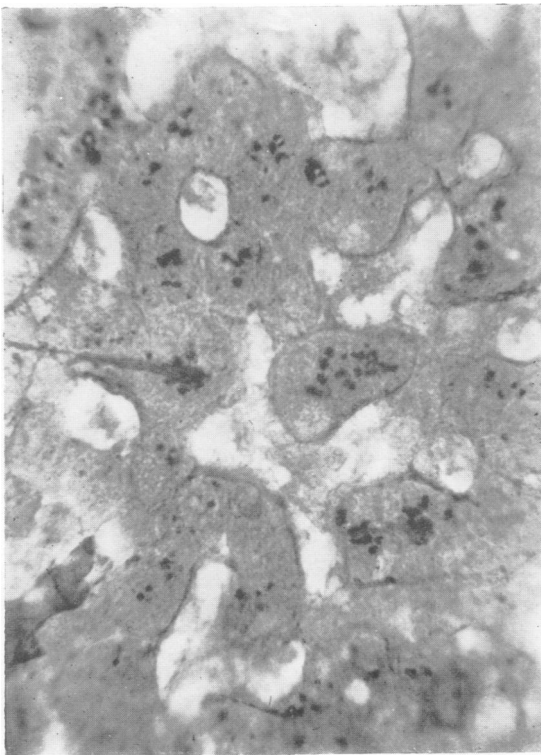


FIG. 4.—Photomicrograph of liver biopsy, showing liver parenchyma cells containing Donovan organisms in varying numbers. The sinusoids are dilated. Dieterle stain.  $\times 720$ .

It had been intended that portion of the liver biopsy should be transplanted into a human volunteer, but the entire first biopsy was despatched for histological examination. Hence a second biopsy was performed on December 18, 48 hrs after starting specific therapy. After demonstrating Donovan organisms in the contact smear from the biopsied material, the latter was divided into two equal parts, one portion was directly implanted into the groin of a male volunteer and the other half was minced, emulsified, and injected subcutaneously into the forearm of a female volunteer. Up to the date of despatching this paper for publication neither volunteer has taken the infection.

Routine examination of the cerebrospinal fluid showed no significant changes. A second transfusion of 350 ml. blood was given on December 24, 1953. On December 26, 1953, after 20 g. streptomycin had been given the lesions of Donovaniasis were still positive for Donovan organisms, and the general constitutional condition with hectic pyrexia, oedema etc., persisted without perceptible improvement. The patient was now given 16 g. terramycin from December 27, 1953, to January 5, 1954. After the second blood transfusion and the administration of oral terramycin there was a temporary improve-

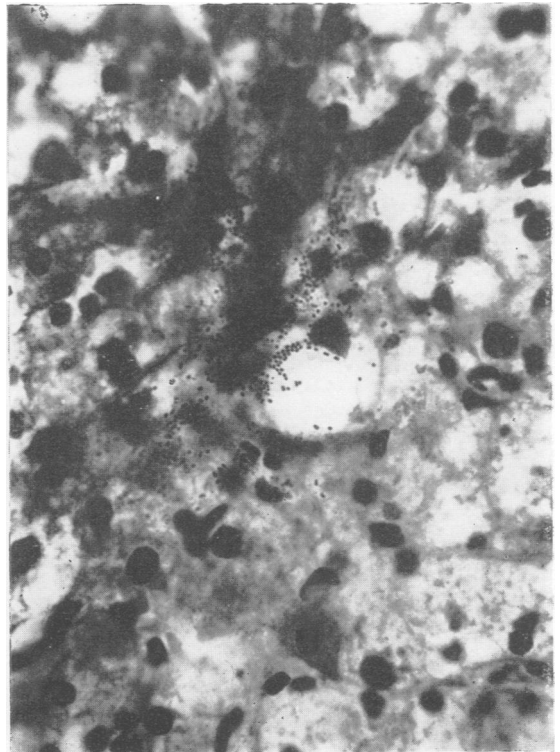


FIG. 5.—Photomicrograph of liver biopsy. One liver cell at the centre appears to be blown out into a cyst containing a number of capsulated forms. The nucleus of this cell is pushed towards the periphery. The organisms are found scattered throughout the field. Giemsa.  $\times 720$ .

ment and the temperature fell to normal for about 6 days. On January 1, 1954, the ESR registered a dramatic fall to 9 mm./1 hr. On January 5, 1954, the blood count showed red blood corpuscles 2·8 m./c.mm., white blood corpuscles 11,000 per c.mm., with 69 per cent. of polymorphonuclear leucocytes. As terramycin was scarce, specific treatment was continued with strepto-penicillin, two injections daily from January 6 to 14, 1954, and January 21 to 29, 1954. On January 13, 1954, 350 ml. blood was transfused and a third liver biopsy was performed. When the patient became a little cooperative, examination on January 2, 1954, had revealed a vesico-vaginal fistula on the right fornix of the vagina through which urine was dribbling. The vulval lesions showed signs of healing. The infiltration of the cervix uteri was firm, small, and less prone to bleed on manipulation. The flexion contracture at the right hip and the pain along the right lower extremity disappeared, and the patient was able to move the limb freely. The liver was just palpable. The patient was slowly recovering except for low, continued fever and slight dribbling of urine through the vesico-vaginal fistula. After intravenous urography on January 16, 1954, the radiologist reported :

Marked hydronephrosis with hydro-ureter on the right side and a non-functioning left kidney. ? Mass in the right sacro-iliac region.

On January 21, 1954, a cystoscopic examination was carried out by a surgical colleague, who made the following report :

A large growth fills the trigone of the bladder and overlaps the ureteric orifice on both sides. The patient has a vesico-vaginal fistula which admits a probe easily. This fistulous tract was present on the right side and communicated with the vagina through the right fornix. The cervix is ulcerated and bleeds readily on examination. The growth seems to have extended from the right fornix and anterior lip of the cervix uteri to the trigone of the bladder. A portion of the growth was removed for pathological study. The ureteral catheter could not be passed as the orifices were overlapped by the growth.

A contact smear from the biopsied material from the bladder showed mononuclear cells, polymorphonuclear leucocytes, and plasma cells, with degenerating, faintly-staining Donovan organisms. The third liver biopsy, performed on January 13, 1954, after the patient had received 36 g. streptomycin with 6·4 mega units penicillin and 16 g. terramycin, surprisingly showed Donovan organisms in the liver cells, although the cervical, vulval, and tibial lesions of the disease were healing satisfactorily and showed no Donovan organisms. The number of organisms per cell were fewer in number than that found before treatment; they were pyknotic and deeply stained. The liver cords were markedly distorted in areas where there was necrosis of the parenchymatous cells—presumably in the regions of micro-abscesses found in the biopsy done before treatment (Fig. 3). There was a varying degree of fatty change of the liver cells. The lobular structure appeared much obscured, and the central vein could be located only occasionally. There was no trace of any residual inflammatory cellular

reaction. Vascularization with commencing fibrosis was a conspicuous feature in the areas of disintegration, while fibrosis with bile duct proliferation was pronounced in the peri-portal triangles. Bile stasis was not seen. These changes were widespread and irregularly distributed. The biopsy from the bladder lesion revealed ulceration with dense granulation tissue, in which a few Donovan organisms, ill-defined, deeply-stained, and pyknotic, were observed in the macrophages. No bladder epithelium was seen in the section.

The blood urea which had been 75 mg. per cent. on December 10, 1953, rose to 90 mg. per cent. on December 21, 1953, and came down to 30 mg. per cent. on January 1, 1954. The fall in the blood urea is not easy to reconcile with the report of the intravenous urography and the chromo-cystoscopy. On January 16, 1954, the blood count showed improvement: red blood corpuscles 3·15m/c.mm., haemoglobin 60 per cent., white blood corpuscles 10,600 per c.mm., 72 per cent. polymorphonuclear leucocytes. But the ESR which fell to 9 mm./hr. on January 1, 1954, increased to 140 mm./hr. on January 19, 1954.

*Recovery.*—With the third blood transfusion and continued antibiotic therapy, in addition to general supportive treatment, the patient recovered steadily though slowly from the serious constitutional upset. Incidentally, she passed fourteen round worms as a result of administration of an anthelmintic.

The total antibiotic therapy which she had received was 52 g. streptomycin, 12·8 mega units penicillin, and 16 g. terramycin in 6 weeks from December 12, 1953, to January 29, 1954.

The low hectic temperature with occasional exacerbation and short remissions, which had continued from December 12, 1953, to January 27, 1954, finally subsided and has since remained normal (Fig. 6, opposite).

The lesions of the cervix uteri healed completely leaving a deformed, anteriorly displaced, cervical stump. The vesico-vaginal fistula had apparently closed; no dribbling of urine was noticed after January 29, 1954, and the patient subsequently passed urine freely. It is remarkable that at no time did she complain of any vesical symptoms of frequency, strangury, haematuria, etc., although the sensitive trigone was the site of the granulomatous lesion. The vulval and tibial lesions healed completely although the last x ray, taken on February 10, 1954, showed a more extensive corticolysis of the antero-medial aspect of the tibia. It is expected that it may take a few months for the defect to be filled up by new bone. The swelling of the inner third of the right clavicle subsided long before the other lesions. The mass seen in front of the right sacro-iliac articulation was less evident in the x ray on February 10, 1954, and what appeared to be destruction and widening of the joint space was noted in its place. The liver was no longer palpable. Oedema of the lower extremities had completely subsided. The patient had shown an increase in weight from 72 to 90 lb.

On February 10, 1954, the blood count was much improved: red blood corpuscles 3·5m./c.mm., haemoglobin 65 per cent., white blood corpuscles 8,800 per c.mm. with 59 per cent. polymorphonuclear leucocytes,

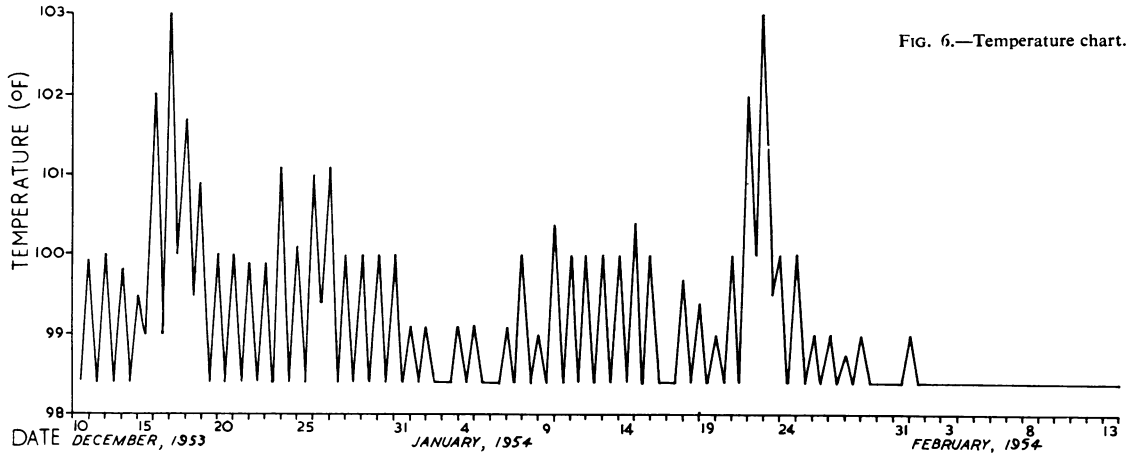


FIG. 6.—Temperature chart.

Blood urea 20 mg. per cent.

The ESR on February 10, 1954, was still high, however, showing 80 mm./hr.

The patient was anxious to go home and was discharged on February 11, 1954, with instructions to report again in 6 weeks.

### Discussion

The features of systemic Donovaniasis as described in the literature and in the case reported here are as follows :

(1) The victims of systemic Donovaniasis are all comparatively young women with ages ranging from 16 to 33 years (except in Case 3 of Sheldon and others, 1945).

(2) The site of the primary lesion of Donovaniasis in cases of systemic dissemination is the cervix uteri.

(3) The lesion of Donovaniasis in the cervix uteri is liable to be mistaken for cancer especially where it is associated with destructive changes in the bones.

(4) It is strongly recommended that a contact smear from the surface, or particles of granulation tissue from a lesion, of the cervix or vagina suspected of malignancy, be obtained and stained with Leishman stain, for the demonstration of Donovan organisms. The authors consider that this simple laboratory procedure has a higher diagnostic rating than the examination of biopsy sections, and should be routine in places where, as in Madras, Donovaniasis is endemic.

(5) Systemic dissemination may occur after an abortion, or some operative procedure such as vulvectomy, fulguration of the cervix, nephrectomy,

etc., as in some of the cases reported. In the present case there is a strong presumption that an abortion had occurred 5 months before the signs and symptoms of systemic dissemination became manifest. The occurrence of pregnancy in women with cervical Donovaniasis carries a certain unpredictable hazard of spread of the infection not only to the internal genitalia, bladder, and pelvic tissue, but also throughout the blood stream.

(6) The spread of the disease from the cervix to the internal genitalia, bladder, and pelvic tissue through the lymphatics seemed to have preceded the onset of general dissemination through the blood stream.

(7) The destructive lesions of the bones and joints, which were the most frequent type of metastatic involvement, can only be explained by a haematogenous transmission.

(8) Systemic Donovaniasis is associated with a severe constitutional toxæmia, characterized by long-continued spiking temperature, progressive anaemia, and loss of weight, and may prove fatal as in some of the cases reviewed in this paper.

(9) The involvement of the liver in systemic Donovaniasis is liable to be overlooked because of the more obvious skeletal manifestations. Liver biopsy in the patient presented by us revealed a more or less pure culture of clusters of Donovan organisms in the liver cells without contamination by the other banal organisms which are a constant feature of the surface lesions of the disease. We were unable to find in the literature any instance in which the microorganisms of Donovaniasis were demonstrated in the *liver cells of a living patient*. Most of the previous

reports of visceral involvement were based on autopsy findings. Culture of the Donovan organisms in our study could not be undertaken because of lack of laboratory facilities.

(10) Although our patient has apparently recovered, and the surface and skeletal lesions have healed, the persistence of organisms in the liver even after adequate therapy is a disturbing feature, and may require post-treatment observation for some time. The notorious tendency of the disease to recur after initial healing is well known. Apart from the possibility of recurrence of the disease, the long-term effect on the liver in which peri-portal cellular infiltration, micro-abscesses with destruction of liver cells, and fatty infiltration were the principal histological features, will have to be watched for the onset of any evidence of cirrhosis of the organ.

(11) The failure of experimental transmission to human volunteers, both by the transplantation of the whole liver tissue and by the injection of the minced emulsified liver, containing myriads of organisms in almost pure culture, has a certain analogy to the reported failure to reproduce the disease in human beings by the inoculation of cultured organisms from chick embryo. It is suggested that some unknown factor seems essential for successful transmission of infection. The paucity of partner infections in the naturally acquired disease may be explained on this hypothesis. In the case reported above the husband showed no anamnestic or clinical evidence of the disease, although he had regular sexual relations with the patient.

#### Summary

A brief review of systemic Donovaniasis is attempted, and a case is presented in which the initial involvement of the cervix uteri was subsequently followed by involvement of the bladder

resulting in vesico-vaginal fistula, and metastases in the bones and liver. It is claimed that this is the first instance in which the organisms of the disease were demonstrated in the liver cells of a living patient.

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