The diagnosis and treatment of donovanosis (granuloma inguinale)

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Abstract

Donovanosis is a predominantly tropical cause of genital ulcer occurring chiefly in small endemic foci in all continents except Europe. Diagnosis requires the careful collection, staining and examination of smears or biopsies of characteristic genital and, occasionally, extragenital lesions for demonstration of the pathognomonic Donovan bodies (*Calymmatobacterium granulomatis*) within histiocytes. Successful isolation of *C. granulomatis* has rarely proved feasible, the last report being in 1962. Donovanosis has a characteristic histopathological picture which occasionally simulates epithelioma. The antibiotics reported as showing good activity in donovanosis are those with good activity against gram negative bacilli and whose lipid solubility ensures good intracellular penetration. They include streptomycin, choramphenicol, erythromycin, lincomycin, cotrimoxazole and the tetracyclines. More recently, good results have been reported with norfloxacin and thiamphenicol. The treatment of donovanosis in pregnant women and patients with AIDS poses special problems. Complications of donovanosis such as elephantiasis, stricture and pelvic abscess may require surgery. Contacts should be traced for examination but only treated if lesions are found.

Introduction

The diagnosis and treatment of donovanosis was last reviewed in this journal 40 years ago by Greenblatt and Barfield[1] who made many important contributions to the study of this neglected disease. Since that review, progress in our understanding of donovanosis has been painfully slow; no successful isolations of the causative organism, *Calymmatobacterium granulomatis,* have been reported in the past 30 years. Although the days when Greenblatt could estimate that there were 10 000 cases in the United States of America[2] are long gone, the disease remains prevalent in many of its other endemic areas and currently appears to be making a resurgence in South Africa.[3,4]

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Distribution

Donovanosis has an unusual geographical distribution, predominantly tropical, but concentrated in certain regions and, in others, apparently absent (fig 1). It is most well known in south-east India, where it was first described,[5] in New Guinea, the Caribbean and neighbouring parts of South America, particularly the Guianas and Brazil. Additional foci are found in Zambia, South Africa, Vietnam, Japan and among Australian aboriginals. The current status of donovanosis in China, Malaysia, Zimbabwe and West Africa is not known to the author although it has been reported in all these places in the past. It has all but disappeared now from the southern states of the USA. Knowledge of the special distribution of donovanosis assists with its recognition in endemic areas and may alert clinicians to the possibility of donovanosis in unusual cases of genital ulcer in patients giving a history of travel to these areas.

Clinical diagnosis

While the clinical features of donovanosis lesions are sufficiently characteristic to suggest the correct diagnosis in most cases, the plethora of variants,[6] atypical lesions[7,8] and presentations[9–16] that have been described should serve as a reminder that the accurate clinical diagnosis of donovanosis, as with other forms of genital ulcer, is fraught with pitfalls, even in the most experienced hands. In typical cases the patient will give a history of sexual contact (not infrequently with a prostitute) 3 to 40 days[17] prior to the appearance of the initial lesion. This is generally a small papule which may be preceded and accompanied by pruritus. Ulceration soon follows. The predominant sites for primary lesions are the distal penis for men and introitus for women. Many other sites may be involved either as a primary event or by secondary spread. The most important are the groins, the anus (especially in homosexuals[18]), the cervix (see below, *Intrapelvic donovanosis*) and various sites remote from the genitalia, the commonest of which are the neck and mouth.[19] In its most characteristic form, donovanosis is an infection

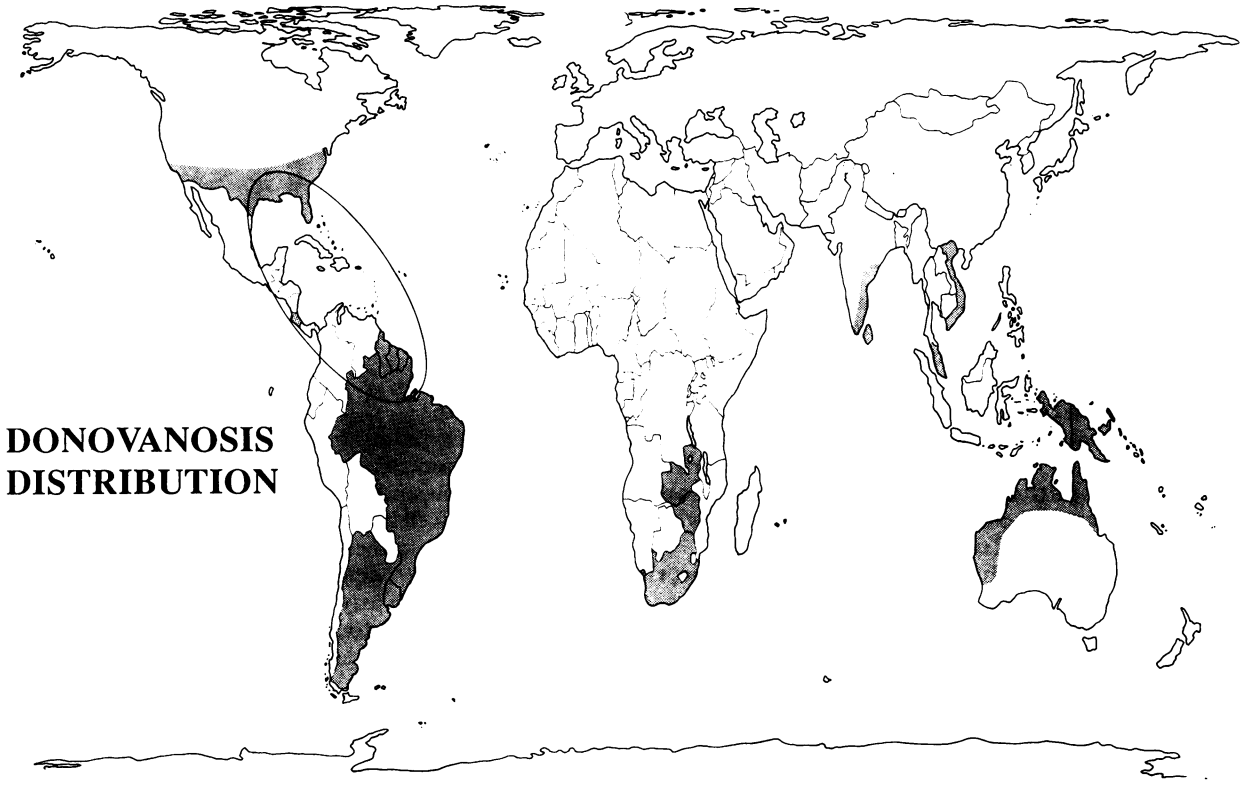

Fig 1 Principal areas from which donovanosis has been reported.

which produces slowly extending, relatively pain-free, velvety genital ulcers with a bright red colour (traditionally likened to raw beef). The lesions bleed easily. Induration is very variable but rarely prominent in young lesions. Systemic symptoms are notably absent except for cases with very extensive or intra-pelvic spread, secondary infection or the very rare cases with haematogenously disseminated disease.[20] Extension along skin folds and contact (kissing) lesions on apposed surfaces are characteristic. While inguinal ulceration is a common feature many observers have commented on the infrequent occurrence of lymph node enlargement in this disease. The explanation for these apparently contradictory observations appears to be that lymphatic spread to the inguinal glands occurs but enlargement or suppuration of these glands is infrequent. Instead, the infection tends to escape into the surrounding tissues, producing a periadenitis which may lead to the formation of an abscess (for which the term "pseudobubo", was coined by Greenblatt[21]) but more usually results in ulceration of the overlying skin. Lesions of donovanosis are frequently elevated above the level of the surrounding skin (fig 2), with a smooth rolled edge. A serpiginous outline is characteristic of larger lesions (fig 3). In some patients extensive scarring accompanies active disease. The rarity of these cicatricial lesions in Melanesians was noted in the classic original paper by Conyers and Daniels[22] and can be confirmed by the present author.

Differential diagnosis

Donovanosis has to be distinguished from other infectious and non-infectious causes of genital ulcer, bubo and genital elephantiasis. In practice the lesions which are most likely to cause confusion are primary and secondary syphilis,[23,24] ulcerated genital warts, squamous carcinoma[25] and chancroid.[26] Early lesions can pose difficulty because the differentiating characteristics are less well developed.[24] The problem of differentiating syphilis is compounded by the high proportion of donovanosis patients who acquire both infections together. For instance Vacca and MacMillan reported positive syphilis serology in 30% of a series of women with confirmed anogenital lesions due to donovanosis[27] and Lal and Nicholas reported

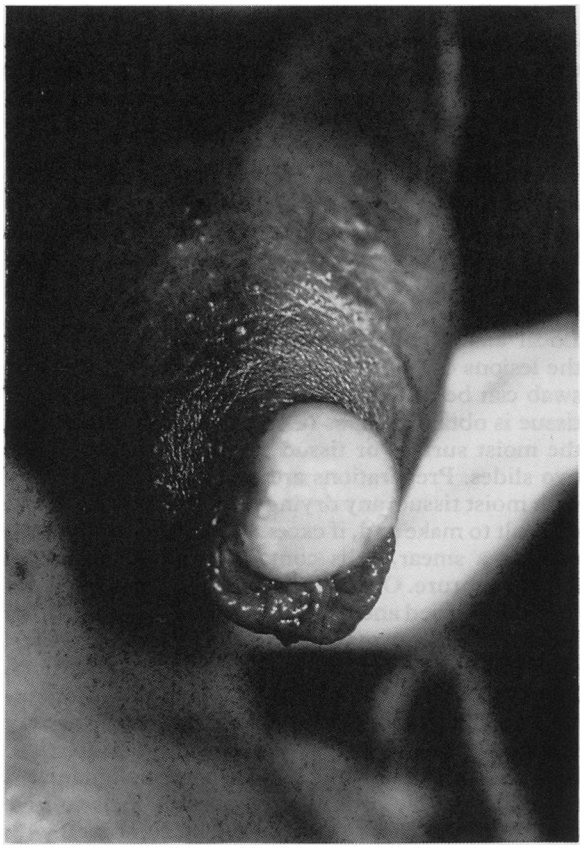

Fig 2 Early lesion of donovanosis in male.

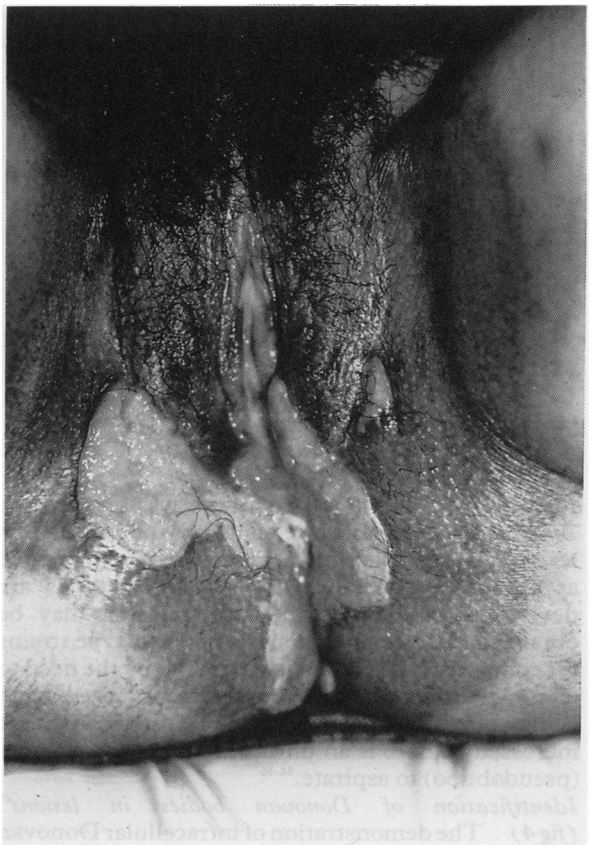

Fig 3 Advanced lesion of donovanosis in female.

concurrent syphilis in 45·5% of 165 cases of donovanosis.[28] Further, non-pathogenic spirochaetes are found with such frequency in donovanosis lesions that they led early researchers to conclude that donovanosis was caused by these organisms.[29] Recently attention has been drawn to a variant of chancroid with a strong resemblance to donovanosis[30 31] and dubbed "pseudogranuloma inguinale" by some writers.[32] All of these diseases have been reported to co-exist with donovanosis, in particular syphilis. However, the older literature is bedevilled by a lack of sufficiently specific diagnostic tests for lymphogranuloma venereum (LGV) and chancroid which make it impossible to be certain about the true aetiology of genital ulcers described in many papers. LGV is constantly confused with donovanosis in the literature because of the host of similar synonyms used for both, as well as similarities of clinical picture and geographical distribution. In particular, the confusing term "lymphogranuloma inguinale" has been employed by some authors to refer to donovanosis and by others to refer to LGV.[33] Clinically, LGV is best distinguished by the prominence of systemic symptoms in its early stages, and by its tendency to cause proctitis, lymphangitis and lymphadenitis with discharging sinuses. Skin ulceration occurs but, apart from the primary lesion, which is generally small and often passed unnoticed, it is a late secondary feature, rather than the main pathological event, as in donovanosis. Labial fenestration and the combination of ulceration with elephantiasis termed esthiomène have been described as diagnostic of LGV. This is incorrect; all these findings occur in donovanosis patients also.[34]

Confirming the diagnosis of donovanosis

Isolation of Calymmatobacterium granulomatis

This curious bacterium was named by Aragâo and Vianna in 1913[35] but not convincingly isolated until 1942 when Kathleen Anderson obtained pure growth, in the yolk sac of fertile chick eggs, of a capsulated Gram negative bacillus, with a close morphological resemblance to the bacteria seen in smears of donovanosis lesions.[36 37] These isolates failed to grow on conventional solid media. Antigen preparations provoked strong complement fixation reactions when tested with large numbers of sera from verified cases of donovanosis.[38] The bacteria were subsequently adapted to a number of liquid media.[39 40 41 42] In all, some 14 isolates have been

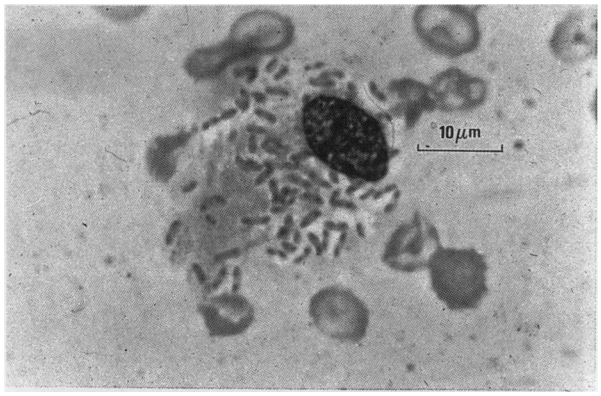

Fig 4 Donovan bodies in mononuclear cell (Giemsa, × 1000).

reported.[37 41 43–48] The last of these was reported in 1962[48] and the organism remains very poorly characterised. Isolation attempts cannot be recommended as a routine procedure until better methods are devised to characterise any isolates that may be obtained. Culture collections do not have type strains for comparison. Isolation is hampered by the need to eliminate the numerous contaminants present in genital ulcers. The chances of successful isolation are increased if there is an unruptured inguinal abscess (pseudobubo) to aspirate.[41 46]

Identification of Donovan bodies in lesions[49] (fig 4) The demonstration of intracellular Donovan bodies in material from lesions has remained the "gold standard" for the diagnosis of donovanosis ever since they were first described by Donovan in 1905.[50] The finding of Donovan bodies provides a simple, highly specific way of confirming the diagnosis. They can be demonstrated, in 60–80% of cases,[51] in either direct smears, or biopsy specimens. Good technique in making and staining the smear, careful searching and familiarity with the appearance of Donovan bodies are all important. Morphological details of Donovan bodies are easier to recognise in well-made smears than in tissue sections,[52 53] but, in patients with negative smears, the demonstration of Donovan bodies may only be possible after a careful examination of sections. More rarely they have been identified in inguinal pseudobubo aspirates,[49] cytology specimens,[54 55 56] and, in an isolated report of an atypical case, in peripheral blood monocytes.[57] The characteristics of the Donovan body are sufficiently individual to distinguish it from other microorganisms that parasitise macrophages in the skin (tables 1 and 2).

The closest resemblance is seen with the Frisch bacilli (*Klebsiella rhinoscleromatis*) of rhinoscleroma which produce lesions with a close histological similarity to donovanosis. Electron microscopic appearances of *C. granulomatis* have been described but are not specific.[39 58 59 60 61 62]

Techniques for the demonstration of Donovan bodies

Smear and biopsy An active area of ulceration should be selected and cleansed with saline or a disinfectant. The leading edge of an ulcer is usually chosen, although material from the base of the ulcer may also be satisfactory. Cells may be obtained by a variety of means. Direct impressions on a glass slide are not usually adequate because surface debris and other bacteria are liable to obscure the picture. It is best to detach a small piece of tissue. The infected tissue is usually friable and easily detached with forceps, a curette, scalpel blade or punch biopsy. Local anaesthetic may be necessary. Alternatively the lesions can be scraped with a scalpel or a cotton swab can be rolled over the surface of the lesion. If tissue is obtained, dabs or smears can be made from the moist surface or tissue can be crushed between two slides. Preparations are best made immediately with moist tissue; any drying renders the smear more difficult to make and, if excessive drying occurs while making a smear, cells containing Donovan bodies tend to rupture. Once the smear has been made it can then be air dried and heat fixed before staining. Other forms of fixation may shrink the Donovan bodies. Repeated smears are recommended by some authors. Biopsy is recommended for lesions in which organisms are likely to be scarce, that is, very early or very sclerotic lesions and those with heavy superinfection. Biopsy is mandatory in cases where malignancy is thought possible or antibiotic therapy fails to give improvement. Biopsy can always be combined with smears from the cut surface of the specimen. A wide variety of stains will demonstrate Donovan bodies. For smears, Giemsa, Leishman or Wright's stain are all satisfactory. Giemsa staining takes considerably longer unless newer rapid Giemsa techniques are used.[63] When Wright's stain is used, Dienst *et al* recommend extending the initial staining in undiluted solution to one and a half minutes.[64] For fixed, embedded tissue the least satisfactory results have been obtained with haematoloxylin and eosin, though Pund favoured Delafield's haematoloxylin with a small amount of eosin.[65] Most prefer Giemsa or silver stains. The use of semi-thin sections, although more expensive and time-consuming, demonstrates Donovan bodies with impressive clarity[59 66] and can be recommended for difficult cases. Good results have been reported recently with a slow Giemsa[67] and with thionine azure II basic fuchsin.[66]

Histological features of donovanosis[65 68–71]

(1) The large mononuclear cells containing Donovan bodies are described in table 1. These cells are scattered diffusely through the dermis. D'Aunoy and Von Haam have drawn attention to the presence of histiocytes containing Donovan bodies deep within areas of fibrosis in some cases.[72]

(2) The epidermis at the borders of ulcers commonly shows some degree of hyperplasia, ranging from

Table 1 Characteristics of Donovan bodies

Morphology of Donovan bodies: pleomorphic 1–2 × 0·5–0·7 μm. A capsule is often visible but the extent to which this takes up stain varies considerably from case to case and according to the technique used. Bipolar densities giving closed safety-pin appearance are often observed. No spore. Non-motile.

Staining properties: Gram negative, well seen with Giemsa, Leishman, Wright's or silver stains; poorly visualised with haematoxylin and eosin; not acid-fast.

Host cell: large mononuclear cells 20–90 μm in diameter scattered throughout the dense plasma cell infiltrate of the lesion. Nucleus often oval, eccentric and vesicular or pyknotic. Vacuolated cytoplasm containing clusters of Donovan bodies which are, occasionally, confined to the periphery of the phagosomes.

Other sites for Donovan bodies: occasional extracellular forms and organisms within polymorphonuclear neutrophils.

Table 2 Differential diagnosis of Donovan bodies

Condition	*Description of inclusions*
Rhinoscleroma	2–3 μm Frisch bacilli (*Klebsiella rhinoscleromatis*) in Mikulicz cells closely resemble Donovan bodies. Mikulicz cells, slightly larger and more abundant than the large histiocytes of donovanosis. In rhinoscleroma PAS +ve 20–40 μm Russell bodies also occur.
Leishmaniasis	Leishman-Donovan bodies (not to be confused with Donovan bodies*) are 2–4 μm non-encapsulated amastigotes of *leishmania* species showing a separate kinetoplast (paranucleus) within 20–30 μm macrophages. Nucleus and kinetoplast stain bright red with Giemsa.
Lymphogranuloma venereum	Chlamydial inclusion bodies identifiable by iodine, Giemsa or fluorescent antibody staining.
Histoplasmosis	Round or oval 2–4 μm inclusions with clear halo, not in vacuoles, occurring in epithelioid granulomas with foci of necrosis. Inclusions deeply basophilic with Gram or Giemsa and also take up PAS and methenamine silver.
Chronic lymphocytic cervicitis	Tingible body macrophages, heavy lymphocytic infiltrate.
Malakoplakia	Michaelis-Gutmann bodies, round, often lamellated, 5–15 μm in diameter, within von Hansemann cells (macrophages with eosinophilic granules). Inclusions are PAS positive, diastase resistant and stain positively with von Kossa and Perls' stains.

*The same Donovan discovered inclusion bodies in both diseases within a two year period. He initially wrote of what are now called Leishman-Donovan bodies of visceral leishmaniasis as "Donovan bodies", while further confusion was caused by later writers referring to Leishman-Donovan bodies in donovanosis instead of Donovan bodies.

a mild acanthosis to pseudoepitheliomatous hyperplasia with pearl formation sufficient to cause confusion with true malignancy on occasion.[73 74] The dangers of this are highlighted by Rajam and Rangiah who state, "Marked and irregular epithelial hyperplasia, simulating neoplasia histologically, in the genital lesion of a young person should alert the clinician that the condition may be granuloma venereum. The mistaken diagnosis of cancer in the penis based on histology alone in this part of the country where granuloma venereum is endemic has cost many a patient a cruel unjustifiable ablation of the most important member of his anatomy. We have records in many instances where such tragedies have happened".[75]

(3) The dermis shows a dense infiltrate of plasma cells. Polymorphonuclear neutrophils are usually scanty but may cluster near the epidermis in microabscesses. Lymphocytes are notably rare. The number of eosinophils varies. Endothelial cells are often swollen. Fibrosis and oedema are prominent in some patients.

Other diagnostic methods

Skin tests and complement fixation tests have been reported by a number of authors (tables 3 & 4).

Although sensitivity and specificity were encouraging they have not become established adjuncts to the diagnosis of donovanosis. The sensitivity of the complement fixation test is much lower in early stages of the illness; Goldberg *et al* reported a sensitivity of only 43% in seven patients with lesions of two weeks or less duration.[79] The specificity of the humoral responses first reported by Anderson[38] is rendered questionable by the findings of Rake and others who demonstrated that similar responses could be obtained in patients with other types of chronic ulcer or by substituting a *klebsiella* antigen for *calymmatobacterium* antigen.[84 85] More recently, studies from South Africa have shown that tissue sections from donovanosis lesions, after incubation with serum from patients with donovanosis, show positive immunofluorescence[86] and immuno-peroxidase reactions.[87]

Co-existing diseases

Of sexually transmitted diseases, syphilis is most often reported in conjunction with donovanosis (see above, *Differential Diagnosis*). In the older literature several fatal cases of donovanosis were shown to have concomitant tuberculosis.[88–90] There are a substantial number of reports of squamous carcinoma being

Table 3 Complement fixation studies in donovanosis

No of patients		*Controls*				
+	−	+	−	*Sensitivity (%)*	*Specificity (%)*	*Reference*
12	3	1	18	80	95	38
1	0	1	19	100	95	45
21	4	4	27	84	87	76
22	2	7	57	92	90	40, 77
50	8	12	78	86	87	78
136	15	0	158	90	100	79
27	1	0	5	96	100	80

Table 4 Skin tests in donovanosis

No of patients		*Controls*				
+	−	+	−	*Sensitivity (%)*	*Specificity (%)*	*Reference*
24	1			96		81
10	0	8	11	100	58	38
10	6			72		40, 77
17	2	2	18	89	90	82
40	0	7	21	100	75	83

found either alongside active donovanosis[91] or supervening on longstanding lesions,[92] or developing at sites of healed lesions.[93] Rajam and Rangiah found malignancy with or following 5 out of 2000 cases of donovanosis seen at their Venereal Diseases Department.[75] In the Caribbean, an unusually high incidence of squamous carcinoma of the vulva has been reported in pre-menopausal women who have had donovanosis.[94 95]

The treatment of donovanosis

Many questions remain about the ideal treatment of donovanosis. It is often stated that donovanosis has no tendency to spontaneous resolution but the extreme chronicity of the disease in some patients[96] shows that the balance between healing and progression can be fine; in addition there are reports of cases that relapsed only in pregnancy[97] and cases where spontaneous resolution has occurred.[98 99] In evaluating treatments for donovanosis it is important to see what proportion of patients have been confirmed by smear or biopsy and to examine the length of follow-up which needs to be 6–18 months if late relapses are to be detected. It is also useful to know how frequently follow-up smears have been performed while on treatment and how many days elapse before smears become negative and before lesions heal. Healing is considerably influenced by the extent of lesions and differences between groups of patients need to take this into account. The optimum duration of treatment for the individual case cannot be stated categorically. As a rule, small lesions can be cured with shorter courses of treatment. A common practice is to treat and review weekly until ulcers have healed over. Because relapse is relatively frequent extension of treatment for some time after lesions have healed has been advocated by Marmell.[100] On the other hand, it has also been noted that, if antibiotics are stopped before re-epithelialisation is complete, many lesions will go on to full healing. Relapses will sometimes respond to the first drug used but may require a change of therapy. Most patients are treated as outpatients but inpatient treatment is advisable for cases with extensive or complicated lesions and when it is thought that compliance with medication is likely to be poor. For the patient's comfort, and to minimise the characteristic pungent odour, lesions should be kept clean and dry. Beyond this local measures are of questionable value.

Early treatments

Donovanosis is of some interest historically as it was one of the few bacterial infections for which effective and specific therapy was available in the pre-antibiotic era. Large numbers of patients were successfully treated with intravenous potassium antimony tartrate (tartar emetic) and related trivalent antimonials. Relapses were fairly frequent and resistant cases could prove exceedingly difficult to manage. Antimonials remained the mainstay of treatment until the advent of streptomycin. The only other treatments which achieved any measure of success before antibiotics came in were surgical excision of lesions,[101] diathermic fulguration,[102] local treatment with podophyllin,[103] ultra-violet radiation[104] and radiotherapy.[105]

Antibiotics

Many antibiotics have been employed in the treat-

ment of donovanosis. Their efficacy has been assessed mostly in open trials. Direct comparisons have rarely been reported and none has been randomised. In vitro data on the sensitivities of *Calymmatobacterium granulomatis* to antibiotics are very scanty[44 106 107] and have not been reported since 1951. Thus treatment has to be empirical, taking into account the responsiveness of donovanosis in the area concerned to the antibiotics available. Donovanosis appears to respond best to lipid soluble antibiotics, such as chloramphenicol, erythromycin, lincomycin, quinolones and tetracyclines, which combine activity against gram negative bacilli with an ability to reach high intracellular to extracellular concentration ratios. Individual cases of resistance to most of these antibiotics have been reported and multiply resistant cases also occur.[80 108] (A detailed table of the results of all the trials cited in the following section is available from the author on request.)

Ampicillin[59 109–112]
Results with this drug were excellent in Vietnam[110] and in one other report[109] but very poor in other reports.[59 111 112] On the available evidence ampicillin cannot be recommended as first line treatment for donovanosis.

Chloramphenicol[80 113–122] *and thiamphenicol*[123]
Chloramphenicol is highly effective in donovanosis, treatment failures being very rare. The use of this drug for conditions that are generally not life-threatening is often condemned outright. It is possible, however, that the risks of aplastic anaemia from chloramphenicol are lower for some ethnic groups and that the risks in relation to those from cotrimoxazole and tetracyclines have been rather overemphasised.[124] It has been used as the standard treatment for donovanosis for many years in Papua New Guinea where no serious adverse effects have been reported (author's observations). A recent report has suggested that thiamphenicol is of comparable efficacy.[123] It has the advantage of once daily administration. Intracellular to extracellular concentration ratios are lower than for chloramphenicol[125] which may partly explain why serious marrow toxicity has not been reported with thiamphenicol.[126]

Cotrimoxazole[127–130]
Cotrimoxazole was introduced in India in 1962.[127] Good initial results were confirmed in a later large series.[128] Two failures with Septrin are reported by Pradinaud *et al*[98].

Macrolides and lincosamines
Published reports with erythromycin[131–135] are few in number but mostly report excellent results. Carbomycin,[136 137] a macrolide similar to erythromycin is now obsolete. Lincomycin[110 135] which has excellent intracellular penetration has been found useful but experience with it is very limited. Clindamycin which is now often preferred to lincomycin has not been evaluated in donovanosis.

Streptomycin[80 122 130 138–159] *and gentamicin*[80 160]
There is extensive experience with streptomycin in donovanosis. High doses (eg 4 g daily) were often employed and reported toxicity with short courses was low. It is now felt generally unsafe to exceed a daily dose of 2 g. Streptomycin has now generally been superseded by other drugs though it remains a candidate for combination therapy[130] and its use in India continued until fairly recently.[159] Relapse rates with streptomycin appear to be rather higher than with alternatives. Gentamicin has been rarely used in donovanosis.[80 160] Results are satisfactory but appear to have no special advantages over alternatives.

Tetracyclines[97 116 122 161–185]
Many antibiotics of this class have been employed and they are felt by many to be the treatment of choice for donovanosis.[186] The results are usually excellent although well-documented individual cases of resistance have been reported[96 187 188] and tetracycline appeared to be ineffective against donovanosis in Vietnam.[189] Experience with newer tetracyclines such as minocycline and doxycycline is much less extensive but available reports suggest they are of value.[171–173]

Other antibiotics
Success with small series or single patients has been reported with phosphomycin[190] and cycloserine.[191] Of particular interest are the excellent recent results obtained with norfloxacin in India.[192] Sulphonamides, with the exception of a couple of reports[193 194] have not been found useful in donovanosis other than as a component of cotrimoxazole. Drugs without effect in donovanosis are penicillin[195–197] and spectinomycin (when given as a single dose).[198] Penicillin has never been evaluated at full dosage. It has been shown to have some activity in vitro[107] and does have some value in clearing secondary contaminants.[196] The use of cephalosporins in donovanosis has not been reported, despite their activity against gram negative organisms.

Antibiotic combinations[130 135 173 199 200]
Antibiotics in combination have rarely been evaluated in donovanosis. The rationale for their use is sound, particularly in more serious cases or in pregnancy. Combinations that have been used include chloramphenicol and tetracycline,[199] and streptomycin with penicillin, tetracycline or chloramphenicol.[130 173 200] Streptomycin with tetracy-

cline showed no advantages in a comparison with cotrimoxazole.[130] Lincomycin with erythromycin gave good results in pregnant aboriginal women in Australia.[135]

Donovanosis in pregnancy

The lesions of donovanosis show a marked tendency to proliferate[201] or recur[97] in pregnancy, and diminished responsiveness to standard antibiotic therapy. The use of cotrimoxazole, tetracyclines, streptomycin, erythromycin estolate and chloramphenicol in pregnancy is of questionable safety. Ashdown *et al* have reported favourably with lincomycin and erythromycin.[135] The transplacental side-effects of doxycycline on teeth appear to be substantially less than those with tetracycline[202] though there is the additional concern of hepatotoxicity to pregnant women to consider.[203] In Papua New Guinea chloramphenicol has been used in many pregnant women with donovanosis without reported adverse effects (author's observations).

There are additional considerations in the treatment of donovanosis in pregnancy. There is good evidence that delivery through a cervix infected with untreated donovanosis predisposes to haematogenous dissemination of the disease,[204] not infrequently with fatal results.[205] If a cervical lesion of donovanosis is discovered during pregnancy it may be possible to administer treatment and effect healing before labour[137] but where the diagnosis is made late or there are doubts about the effectiveness of treatment, elective Caesarian should be considered.[206] The neonate too is at risk of acquiring donovanosis when exposed to untreated lesions of donovanosis though this is extremely rare.[207] It would be wise to treat any neonate so exposed with careful cleansing of the ears, umbilicus and genitalia and to a course of prophylactic antibodies.

Treatment of sequelae and complications

Surgery

Successful eradication of *C. granulomatis* with antibiotics can still leave many patients with substantial genital deformities. In women particularly, elephantiasis, strictures and fistulae may require surgery. Parkash *et al* have emphasised the considerable benefits that these patients may get from modern plastic surgical techniques.[208] Surgery on active lesions carries a distinct risk of spreading the infection[209–211] and so should await antibiotic treatment or, at least, be carried out with antibiotic cover. Extragenital lesions sometimes prove refractory to antibiotic treatment and antibiotics combined with surgical curettage may give the best results.[80] Robinson *et al* were successful in curing surgically 10 patients in whom all chemotherapy had failed.[101]

Intrapelvic donovanosis

The case fatality rates for donovanosis involving the cervix of 5·2% reported by Arnell and Potekin[212] and 14·3% reported by Pund and McInnes[205] indicate the great importance of recognising and giving adequate treatment to patients with this particular form of the disease. The close similarity of isolated cervical lesions of donovanosis to carcinoma has frequently resulted in delays in diagnosis.[213] Involvement by donovanosis of the uterus, tubes and ovaries can mimic pelvic inflammatory disease or pelvic malignancy. Reported clinical findings include tubo-ovarian abscess, frozen pelvis, hard masses and hydronephrosis.[214–216] Such lesions can resolve to a remarkable degree on antibiotic treatment alone and surgical exploration, while required for drainage of collections, carries the risk of disseminating the infection if unwittingly carried out without suitable antibiotic cover.[211]

Disseminated donovanosis

This life-threatening complication of donovanosis is strongly associated with pregnancy (see above, *Donovanosis in pregnancy*). It manifests most commonly as lytic bone lesions which may spread into and ulcerate the overlying skin. Lesions of lung, liver and spleen have also been recorded.[173 217 218] Antibiotic treatment should suffice though combination therapy may give better results.[173]

Secondary infection

In the older literature on donovanosis are many reports of chronic indolent lesions of the vulva suddenly changing course with rapid and extensive tissue destruction leading to the formation of a large cloaca, haemorrhage, abdominal perforation and death.[29 72 89] It is generally felt that this complication results from complicating fusospirochaetal infection.[72] Lesions displaying any tendency to behave in this way should be treated with vigorous extended antibiotic regimens, and, in cases with necrotising fasciitis, surgical debridement.

Donovanosis and AIDS

There is already evidence that donovanosis may behave differently in patients with AIDS. An early report describes donovanosis appearing with typical clinical lesions in two AIDS patients but failing to respond to extended courses of treatment with combinations of cotrimoxazole, tetracycline and thiamphenicol.[219] The explanation for these failures is likely to lie not so much in primary antibiotic resistance but in inability of antibiotics to clear the infection in the presence of immune deficiency. If immune suppression is an important factor in the observed association between haematogenous dissemination of donovanosis and pregnancy, then this rare complication of donovanosis may begin to appear more frequently as AIDS spreads to areas endemic for donovanosis. In South Africa it has been noted that patients with donovanosis often remain

sexually active[220] and that HIV-1 seropositivity is significantly associated with donovanosis.[221]

Contact tracing

Sexual partners of patients with donovanosis are frequently free of disease but the incidence of infection when sought with care can exceed 50%.[28] Clusters of patients contracting the disease from a common source have been described.[129 222] Clearly contact tracing should be attempted when possible. Blind treatment of contacts without lesions has not been advocated but counselling and follow-up should be offered.

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