# Lymphogranuloma venereum in Puerto Rico[1]

A BRIEF SURVEY OF ITS CLINICAL MANIFESTATIONS AND TREATMENT IN 45 CASES

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LYMPHOGRANULOMA VENEREUM, commonly known as lymphogranuloma inguinale, climatic bubo, and also Nicholas, Durand, Favre's disease, may be defined as a contagious disease, usually acquired venereally, which is caused by a filtrable virus. It is characterized by the appearance of a herpetiform primary sore and is followed by inflammation of the inguinal, inguino-femoral, and iliac lymph glands. Trousseau,[2] in 1865, described inguinal buboes with suppuration and discharge among young Creoles. In 1867 Bourguet[3] found the disease among Mexican troops, but not associated with syphilis. After this date several reports on climatic bubo and lymphogranuloma venereum appeared, and it has gradually become clear that both conditions are the same. Though the disease has been known for many years, only during the last twenty has it been thoroughly studied. The introduction of the intracutaneous test of Frei[4] and the transmission of the virus to monkeys, mice, guinea pigs, and chick embryos have laid a sound basis for the study of this condition.

Findlay[5] gives credit to Gay Prieto for the earliest recognition of a virus as the etiologic agent of lymphogranuloma venereum, the diameter of which, as measured by different observers, varied from 0.24 to 0.33 microns.

Landmarks in work on the virus have included Levaditi's transmission of the infection to the mouse brain, the demonstration of the virus in the pus of the inguinal bubo (Hellerström and Wassen, Cohen and Kleeberg, and others), and the demonstration by many workers of the presence of the virus in all the recognized lesions of the disease.

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1. Received for publication May 12, 1942.

2. C. Trousseau, cited by H. Stannus Stannus, in *A Sixth Venereal Disease* (London: Ballière, Tindall and Cox, 1933).

3. Bourguet, *ibid.*

4. W. Frei, "New Skin Reaction in Lymphogranuloma inguinale," *Klin.Wchnschr.*, IV (1925), 2148.

5. G. M. Findlay, cited by J. H. Stokes *et al*, in "Lymphogranuloma venereum," *Am.J.M. Sc.*, CXCVII (1939), 575.

The virus is active at room temperature for 24 to 48 hours, loses its virulence at a temperature of 46° C for 30 minutes, is killed in 10 minutes at 56° C, but is unaffected by freezing temperature for one day.[6]

The incidence of lymphogranuloma venereum varies in different places. Table I shows its prevalence in several parts of the world; Table II, its frequency in various government institutions of Puerto Rico. Most of the studies on the incidence of the disease have been carried out on "clinic cases and upon those who are sexually promiscuous, or actually engaged in prostitution . . . therefore sound conclusions on the distribution of the disease throughout the population may well be doubted."[7]

This disease can no longer be considered a tropical one, for it has been found in nearly all sections of the world. It was once thought that the colored race was more susceptible, yet recent investigations have revealed that neither sex nor race has any influence on its incidence or distribution. From the public health viewpoint, the disease constitutes a problem of growing importance. The facts that in the female the lesions often pass unrecognized and that the virus has been obtained from the intact vaginal mucosa of a patient with inguinal lymphoadenitis explains the futility of preventive measures, especially when no prophylactic immunization is available.

### CLINICAL MANIFESTATIONS

The primary lesion of the disease occurs in some part of the genitalia, most commonly at the coronal sulcus, and usually presents itself as an ulcer or a vesicle, circular in shape, oftentimes single, occasionally multiple, with clean edges and a whitish gray base. It is nonpruritic, painless, not tender to touch, and surrounded by a reddened zone with no induration. This lesion is often transitory, heals spontaneously, and may easily pass unnoticed; sometimes, though, it remains for many weeks. However, six to eight weeks after the initial sore, the patient begins to experience a slight soreness in one or both of the inguinal regions, accompanied by general malaise, fever, chilliness, headache, photophobia, nausea, and generalized bodyaches. In some cases these symptoms are absent. Gradually the lymphatic glands of the superior femoral group commence to enlarge; several other glands may be affected at the same time, feeling like discrete, tender, or nontender resilient

6. *Ibid.*
7. *Ibid.*



TABLE I[a]

*Incidence of Positive Frei Tests among Individuals in Several Parts of the World*

| *Author* | *Place* | *Total Number of Persons Tested* | *Percentage of Positive Frei Tests* | | | | |
|---|---|---|---|---|---|---|---|
| | | | *Individuals* | | | *Prostitutes* | |
| | | | *White* | *Colored* | *Total* | *White* | *Colored* |
| Gray *et al* | St. Louis, Missouri | 790 | 3.4 | 40 | 43.4 | 4.4 | 47.7 |
| De Wolf and Van Cleve | Cleveland, Ohio | 1,010 | ... | .. | 58 | ... | .... |
| Haim and Mathewson | San Francisco General Hospital | 788 | ... | .. | 2.7 | ... | .... |
| | San Francisco Marine Hospital | 700 | ... | .. | 8.9 | ... | .... |
| Tasaki and Kaminura | Harbin and Mukden, China | 995 | Japs<br>Koreans | .. | 12.8<br>23.4 | Chinese | 27.2 |
| Goldblatt | Cincinnati, Ohio | ... | ... | .. | 32 | ... | .... |
| Clyne | Fort Sam Houston, Texas | 1,158 | ... | .. | 4.1 | ... | .... |
| Simon and Bralez | St. Lazare Hospital, France | 412 | ... | .. | 4.1 | ... | .... |
| Hanschell | Seamen's Hospital, London | 17,900 | ... | .. | 0.7 | ... | .... |

[a] Prepared after Stokes *et al*, "Lymphogranuloma venereum," *Am.J.M.Sc.*, CXCVII (1939), 575.

TABLE 2

*Incidence of Positive Frei Tests in Government Institutions of Puerto Rico*

| *Place* | *Total Examined* | *Sex* | | *Race* | | *Positive Frei Tests* | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | *Sex* | | *Race* | |
| | | *Male* | *Female* | *White* | *Colored* | *Male* | *Female* | *White* | *Colored* |
| Insular Penitentiary for Men | 118 | 118 | . . . | 63 (53.4%) | 55 (46.6%) | 13 (11%) | . . . | 4 (31%) | 9 (69%) |
| Insular Penitentiary for Women | 96 | . . . | 96 | 27 (28.2%) | 69 (71.8%) | . . . | 11 (11.4%) | 3 (27.3%) | 8 (72.7%) |
| Bayamón District Hospital | 131 | 84 (64.1%) | 47 (35.9%) | 81 (61.8%) | 50 (38.2%) | 16 (19%) | 5 (10.8%) | 13 (61.9%) | 8 (38.1%) |



structures on palpation, with some resemblance to the syphilitic bubo. In the so-called "Form frustes" of the French there is no other development, and the involved glands gradually recede to normal.

In its acute form, however, the glands become matted together, assuming an oval configuration with the long axis parallel to the inguinal ligament. Multiple foci of fluctuation begin to appear, giving a characteristic feeling, on palpation, of minute depressions here and there. The overlying integument then becomes edematous and stretched and assumes its typical purplish color. By this time frank fluctuation has occurred; at times a large abscess is formed by the confluency of several smaller ones, and thereafter the disease runs a variable course.

In some untreated cases and in many, in spite of the treatment fistulization takes place. Multiple fistulae gradually form, from three to thirty or forty in number and likened to "the rose of a watering can . . . considered pathognomonic of the disease."[8] The fistuale are rather characteristic: "There is no ulceration about their mouths, their lips are simple and non-infiltrated, the skin is not undermined, and there is no granulation. The discharge exudes in small amounts and consists of a thick, opalescent, yellow white, or greenish viscid, gluey, tenacious pus which adheres to an instrument and is somewhat difficult to spread on a slide. The process lags for months and months before all the fistulae are closed."[9]

Other constitutional symptoms which may accompany the second stage of the disease, just described, are generalized adenopathy, visceral disturbances, splenomegaly, arthritis, erythema multiforme, erythema nodosum, lymphangitis of the dorsal vessels of the penis and, in many cases, deep iliac adenitis, which at times may be mistaken for an acute surgical abdominal condition.

In the female the primary lesion occurs most frequently in the fourchette, in the cervix, or in the posterior wall of the vagina, being unrecognized in almost all cases. The lymphatic vessels from these regions drain into the perirectal glands, which become thus involved in an acute and chronic inflammatory process marking the beginning of one of the most dreadful complications of the disease, namely, the anorectal syndrome.

After the second stage it is difficult to determine whether the

8. Stannus, *op. cit.*
9. *Ibid.*

patient will be the victim of one of the sequelae of lymphatic drainage obstruction, any one of which is likely, in most instances, to cripple him for life. Some of the most important conditions which develop after the secondary stage of adenitis are: (1) rectal stricture; (2) elephantiasis of the penis; (3) elephantiasis of the scrotum; (4) elephantiasis of vulva, or esthiom†ne; (5) elephantiasis of lower extremities; (6) recurrent tropical lymphangitis; (7) rectovaginal fistula; (8) rectovesical fistula; (9) regional enteritis with stricture.

This report is mainly concerned with two of the above-mentioned conditions, namely, recurrent tropical lymphangitis and the anorectal syndrome. The clinical manifestations of the former are too well known to deserve any lengthy discussion here; it suffices to mention that in all cases suffering from this condition one should always bear in mind that recurrent tropical lymphangitis may be secondary to destruction of the lymphatic glands by the virus of lymphogranuloma.

However, the anorectal syndrome is such an important medicosurgical problem that it deserves more thorough study. Victims of this dreadful complication have a history of chronic gastrointestinal disturbance, localized mainly in the large bowel. After a considerable period of time, following the second stage of adenitis, symptoms of colitis are apparent. Bowel movements become irregular; diarrhea alternates with constipation; tenesmus develops; the stools are poorly formed, fetid, liquid on many occasions, but later charged with mucus and blood and, lastly, with purulent material. The patient gradually loses ground, his appetite is no longer good, food ingested is not well tolerated, and anemia develops. The final stage then comes on—a stenosing stricture, with chronic constipation up to the point of obstipation; the patient dreads to defecate, for every bowel movement produces intense rectal pain. As time passes, the stricture closes more and more, until a final state of complete obstruction ensues.

Physical examination reveals a chronically ill, anemic, cachetic individual with a descending colon full of feces, spastic and tender to touch. At times energetic peristaltic waves are observed. One usually encounters local verrucous, or papillomatous, growths projecting through the external anal sphincter, a few hemorrhoids, a loss of tone of the anal sphincter, purulent bloody discharge, an ulcered, ragged, irregular anal and rectal mucosa, and a stenosing, circular, fibrotic, nonyielding contracting ring located about two or three inches from the anus, with tremendous fibrotic thickening of



the perirectal tissues. Sometimes the perirectal glands undergo suppuration and fistulous tracts are observed in the perineum similar to the ones described previously. In the male the anorectal syndrome is considered to be the outcome of unorthodox sexual contact.[10]

Regional involvement of the gastrointestinal tract has also been described.[11] This condition, however, has been confused with Chron's disease, and its etiology has not been realized until surgery has been undertaken.

### DIAGNOSIS

"The Frei intracutaneous test is the principal diagnostic resort at the present time."[12] Several antigens have been used: mouse brain, chick embryo, antigen prepared from the aspirated contents of the affected glands and from affected glands which have been macerated. There is a commercial preparation obtained from the intracerebral injection of mice, which the writers have tried with good results.[13] More recently an antigen prepared from the chick embryo chorioallantoic membrane has been made available.[14] However, the writers' experience with this last preparation is very limited and, in their opinion, human antigen gives more intense reaction in positive cases, being easily prepared from aspirated contents following the technique advocated by Frei.[15]

The skin test is as follows: after sterilization with alcohol of the upper inner portion of the forearm, 0.1 cc. of the commercial or prepared antigen is injected intracutaneously. If commercial antigen made from mouse brain is utilized, a control test is performed on the opposite forearm with a solution prepared by macerating normal mouse brain in saline solution. If antigen prepared from aspirated pus is used, the control is only plain saline solution. The test is then read in forty-eight hours. If positive, a definite papule measuring not less than 7 mm. in diameter is observed, surrounded by an erythematous, infiltrated circular zone. The control must show no reaction. The Frei test, if once positive, may remain so for many

10. A. A. Grace and G. W. Henry, "Mode of Acquisition of Anorectal Type of Lymphogranuloma venereum," *N.Y. State J.Med.*, XL (1940), 285.
11. W. E. Coutts, L. Opazo, and M. Montenegro, "Digestive Tract Infection by Virus of Lymphogranuloma inguinale," *Am.J.Dig.Dis.*, VII (1940), 287.
12. Stokes *et al*, *op. cit.*
13. Frei antigen prepared by the Lederle Laboratories, Inc., New York.
14. *Lygranum*, prepared by E. R. Squibb and Sons, New York.
15. W. Frei, "On the Skin Test in Lymphogranuloma inguinale," *Investigative Dermatology*, II (1939), 119.

years, in some cases, for life. However, instances in which it becomes negative have been reported.[16] In the presence of mixed infections, that is, lues, tuberculosis, and chancroids, the Frei test may be negative at first,[17] a fact which should be borne in mind.

The intracutaneous injection of Frei antigen, prepared from the aspirated contents of a bubo in a suspected case, into a known positive case is a method that has been also used to prove that a given case is one of lymphogranuloma venereum. Aspirated contents have been injected into rabbits, producing a localized reaction which may be used as a further diagnostic test.[18] The complement fixation reaction has also been utilized, but its reliability has not been fully established. Melczer and Sipos[19] found this last method reliable in 87.5 percent of instances, while other investigators have obtained negative results with it. In cases of doubt, biopsy can be practiced, though this last procedure invites secondary infection, a complication which by all means should be avoided.

Recently a new test has been reported.[20] It consists of an intradermal injection of spinal fluid from patients with the disease, concentrated by special methods. In positive cases a vesicle forms at the site of the injection twenty-four hours later. However, the writers have had no experience with this test.

During the adenitis stage a mild leukocytosis with mononucleosis is found. The red blood cells and hemoglobin are very little altered at first, but during the phase of the anorectal syndrome profound anemia is usually encountered. A hyperproteinemia, with a hyperglobulinemia, has been found in a high percentage of cases.[21] The serum lipoids, on the other hand, have been decreased. This hyperglobulinemia may explain the positive reactions to the Wassermann blood tests, as well as the increased sedimentation rate encountered in the disease.

## DIFFERENTIAL DIAGNOSIS

All the conditions producing enlargement of the inguinal glands must be considered. Infection in the lower extremities usually produces enlargement of the inferior inguinal glands. The same can be said for recurrent tropical lymphangitis, or filariasis. Infections secondary to anterior urethral, meatal, preputial, coronal, or penile lesions also affect those glands, affected by the virus of lymphogranuloma venereum. When the infection is luetic, the early stage of the bubo resembles that of lymphogranuloma venereum but as soon as fluctuation appears, clinical differentiation becomes easy. When adenitis is purulent, as in that secondary to chancroids, the extreme tenderness, local pain, and muscle spasm present an unequivocal picture. Involvement of the lymphnodes by leukemia, Hodgkin's disease, and lymphosarcoma can be ruled out by study of the blood smear or by biopsy, but it should always be borne in mind that a person may have had lymphogranuloma venereum and have later developed one of the above-mentioned conditions.

A positive reaction to the Frei test may divert one's attention from the real underlying condition, and it is in these cases that close observation is necessary. Generalized involvement of the lymphatic tissues and the lack of development of small abscesses and poradenitis will make one suspect some disease other than lymphogranuloma venereum. The authors have seen this happen in two cases. Once in a while, and in their experience, tuberculosis of the inguinal glands is found, but only in children.

Dilatations of the lymphatic channels of the femoral regions are sometimes mistaken for enlarged glands. Careful examination establishes the diagnosis. However, granuloma inguinale is very often mistaken for lymphogranuloma venereum, though the clinical characteristics of the two diseases are so different that a diagnosis should offer no difficulty.

16. Stannus, *op. cit.*
17. *Ibid.*
18. G. M. Findlay, "Experiments on the Transmission of the Virus of Climatic Bubo to Animals," *Tr.Roy.Soc.Trop.Med. and Hyg.*, XXVII (1933), 35.
19. N. Melczer and K. Sipos, cited by Stokes *et al*, *op. cit.*
20. C. Ottolina, "Vesicular Test," *Am.J.Trop.Med.*, XXI (1941), 597.
21. M. E. Howard, A. J. Elisemann, and M. J. Strauss, "Alterations in Serum Proteins in Lymphopathia venerea," *Am.J.Syph.*, XXIII (1939), 83.



## TREATMENT

*Adenitis stage.* Several remedies have been tried in the past and the results as reported were variable: arsenicals, antimony preparations, Frei antigen administered intravenously, hypodermically, and intracutaneously, mercurial preparations, surgical extirpation of affected glands, gold salts, and X-ray therapy. Recently, results of using newer chemotherapeutic drugs have been published; however, the action of any drug or group of drugs is difficult to evaluate. Many cases of this disease do recover spontaneously; simple aspirations bring rapid recovery in some, but in a few the disease continues its course no matter what treatment is tried.

In the writers' experience neoprontosil has given gratifying results. This drug can be given for a long time without any untoward reactions, since its toxicity is lower than that of other similar compounds, making it more suitable for the ambulatory patient. For the adult patient three tablets of five grains each, every four hours, is the customary dosis, the treatment to be continued for a reasonable period of time. During such medication careful watch must be kept for toxic reaction and for the appearance of blood disturbances. If definite fluctuation is present, aspiration is performed with a 20 or 22 gauge needle. Every case has responded favorably to this technique, and not a single instance of suppuration has occurred in the few cases treated.

*Anorectal syndrome.* On the other hand, the treatment of the anorectal syndrome is extremely disappointing. The writers have tried almost every remedy advocated, with very little success. A low-residue diet and mineral oil are usually prescribed, with rectal dilatations avoiding trauma as much as possible. However, perforations may occur in such treatment, especially in the cul-de-sac and, for this reason, the obliteration of the latter before dilatations are attempted has been advocated.[22]

Recently the writers have been trying diathermy, as advocated by Martz and Foote.[23] A cervical metal dilator is introduced through the stricture and connected to the diathermy machine; from 900 to 1,800 miliamperes are administered for twenty minutes, the treatment being repeated twice a week. Although no change has ever been noticed radiologically in the caliber of the stricture, the patients receiving this treatment have felt better subjectively.

Surgery is sometimes indicated, but in the writers' opinion it should be deferred as long as possible.

## PRESENTATION OF MATERIAL

Among the last 1,500 admissions to the Outpatient Department of the University Hospital of the School of Tropical Medicine there were encountered forty-seven cases of lymphogranuloma venereum, showing an incidence percentage of 3.1. The highest number of cases, twenty-five, occurred among persons between twenty and twenty-nine years of age, or during the age span of greatest sexual activity. The proportion of males to females was thirty to seventeen, or almost two to one, which can be explained to some extent by the facts that inguinal adenitis occurs more frequently in males and that, as a rule, they seek medical care sooner. In females, primarily because of variation in the location of the lesion, the disease is usually unrecognized during its early stages.

Primary sores were found in only four instances, all males; they consisted of a small lenticular, indolent, noninfiltrated, superficial ulceration in the region of the corona.

Inguinal adenitis was observed in twenty-seven cases. In nineteen the left inguinal glands were affected; in six the right; and in only two were both sides involved. Generally the glands affected were the superior group, though the deep iliac also seemed involved in the process.

The most common symptoms described by the patients were: fever, twenty-one cases; chills, seventeen; localized pain, eleven; headache, ten; loss of weight, eight; anorexia, four; dizziness, two; body pains, one; visual disturbances, one. Nearly all patients with adenitis were ambulatory cases. Though some prostration was noticeable in a few, the great majority were able to continue their daily routine. Ophthalmoscopic examination was performed by a specialist in only three cases; in all of them the macula was thought to be of a deeper color than normal. Localized pain varied greatly, depending on the nervous make-up of the individual. Most patients complained little of pain or tenderness on palpation—a very important point, in the authors' opinion, for differential diagnosis. In all cases the glands involved assumed a typical pattern. The skin overlying them had become adherent to the surrounding structures and violaceous in color. When the head ached, the pain was severe in most instances, but it was generally relieved by acetylsalicylic acid.

Kahn test of the blood was positive in twenty-five cases with inguinal adenitis. Sixteen of these patients, however, gave a history of previous antiluetic treatment. In four of the positive cases without previous history of antiluetic treatment, the serum globulin values were 4.1, 3.7, 4.4, and 2.67, expressed in grams per 100 cc. of blood. In two of these cases, therefore, the serum globulin had been definitely increased, which may possibly account for the positive Kahn tests.

Their hemoglobin varied between 50 and 100 percent. In two cases

22. H. J. Warthen, "Operative Treatment (Obliteration of Cul-de-sac and Colostomy) for Benign Rectal Stricture; Preliminary Report," *Arch.Surg.*, XXXVIII (1939), 617.

23. H. Martz and M. N. Foote, "Stricture of Rectum Secondary to Lymphogranuloma venereum; Treatment with Diathermy," *J.A.M.A.*, CXIV (1940), 1041; "Lymphogranuloma Strictures of Rectum; Treatment by Diathermy," *Rev.Gastroent.*, VII (1940), 144.

TABLE 3

*Treatment by Sulphonamides*

| Hospital Number | Age | Sex | Race | Duration Before Treatment | Inguinal Adenopathy | Laboratory Data | | Treatment with Neoprontosil | Number of Aspirations | Number of Days of Treatment Necessary To Obtain a Clinical Cure | Remarks |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Frei | Wass. | | | | |
| 9731 | 23 | M | W | 30 | Left | + | 0 | + | 0 | 9 | |
| A733 | 22 | M | C | 21 | Left | + | 0 | 0 | 0 | | Did not return |
| A860 | 17 | M | C | 14 | Right | + | + | + | 0 | 28 | |
| 10008 | 18 | M | W | 14 | Left | + | + | 0 | 0 | | Did not return |
| 9972 | 19 | F | W | 21 | Right | + | + | 0 | 0 | | Did not return |
| 9928 | 14 | M | W | 21 | Left | + | 0 | + | 1 | 17 | |
| 10208 | 22 | M | C | 30 | Left | + | + | + | 2 | 7 | |
| 10204 | 29 | M | W | 30 | Left | + | 0 | + | 4 | 61 | |
| 10103 | 14 | M | W | 25 | Left | + | + | + | 2 | 25 | |
| 10080 | 16 | M | W | 60 | Left | + | 0 | + | 0 | 28 | Glands excised |
| 10053 | 18 | M | M | 9 | Left | + | 0 | 0 | 0 | 15 | Spontaneous cure |
| A830 | 21 | M | C | 7 | Right | + | + | 0 | 0 | | Did not return |
| A879 | 22 | M | C | 30 | Left | + | + | + | 1 | 5 | |
| A264 | 28 | M | W | 30 | Left | + | 0 | + | 0 | 44 | |
| A281 | 28 | M | W | 60 | Left | + | 0 | + | 0 | 69 | |
| 9970 | 26 | M | W | 14 | Right | + | + | 0 | 0 | 63[a] | Spontaneous cure |
| A444 | 25 | M | W | 30 | Right | + | + | + | 0 | 37 | Frei antigen |
| 8454 | 18 | M | W | 30 | Left | + | 0 | 0 | 0 | 120 | Fuadin and anthiomaline used |
| A48 | 23 | M | C | 270 | Left | + | 0 | + | 0 | 41 | |
| A55 | 22 | M | W | 16 | Left | + | 0 | + | 0 | 12 | |
| A110 | 25 | M | C | 60 | Left | + | 0 | + | 0 | 46 | |
| A849 | 33 | M | W | 60 | Right & left | + | 0 | + | 0 | 23 | |
| 9927 | 27 | M | M | 21 | Right | + | + | 0 | 0 | 32[a] | Spontaneous cure |
| A489 | 21 | M | W | 30 | Right | + | + | + | + | | Toxic reaction; drug stopped |
| A145 | 41 | M | W | 20 | Left | + | 0 | 0 | 0 | 33[a] | Spontaneous cure |

[a] From beginning of illness to disappearance of glands.



it ranged from 50 to 59 percent; in five, from 70 to 79; in fourteen, between 80 and 89; in nine, between 90 and 99; and in four, over 100. These values demonstrated that, generally speaking, there is very little anemia early in the disease.

The red blood cell counts showed values corresponding to the above. In twenty-three of the cases, the counts were between four and five million cells per cmm. In only six were the values between 2,500,000 and 4,000,000 cells per cmm. White blood cells varied anywhere from 4,000 to 12,000 per cmm. though in seven instances the count was reported higher than 10,000. The greatest number of cases, seven, had a count between 6,000 and 6,500 per cmm., and in only one instance was this higher than 12,000.

The total serum proteins were determined in thirteen cases, and the values obtained varied as follows: in two cases, between 6.5 and 6.99 grams percent; in four, between 7.00 and 7.99; in five, between 7.50 and 7.99; and in two, between 8.00 and 8.49 grams percent. In one case the total proteins were 6.49 grams percent.

The globulin fraction of the serum proteins varied between 1 and 1.49 grams percent in two cases; 2.50 and 2.99 in three; 3.5 and 3.99 in two and four, respectively, and 4.91 in three. In three different patients it was 2.49, 3.49, and 4.99 grams percent, respectively. The globulin fraction was therefore increased definitely in only four cases. These last findings were contrary to those of other observers who found a hyperglobulinemia.[24]

## TREATMENT OF CASES PRESENTED

*Adenitis stage.* In discussing the treatment of the adenitis stage of lymphogranuloma venereum, one must bear in mind that spontaneous cure can and does occur and that it is therefore very difficult to determine whether or not a particular treatment has any beneficial effect.

Since the introduction of the sulphonamides enthusiastic reports have appeared describing dramatic cures by their use. The writers have preferred to use neoprontosil because of the reasons already stated. Table III shows the results obtained with this treatment in twenty-five cases of inguinal adenitis.

Adenitis disappeared spontaneously in four patients; average time of treatment was 35.7 days. The case requiring the longest period of treatment received Frei antigen intravenously, fuadin, and an-

24. Howard, Elisemann, and Strauss, *op. cit.*

thiomaline before enlargement of the glands disappeared. In six cases aspiration was performed, together with the administration of neoprontosil, since it was found necessary to aspirate the contents of those glands that had undergone fluctuation. In only one case did the neoprontosil have to be discontinued because of toxic reaction; all other cases tolerated the drug remarkably well. Four patients did not return for further observation.

The newer sulphonamides have not been tried by the writers, for they feel that the results to date have been unusually gratifying and that, if bettered in some respects, the improvement would be at the expense of increased toxicity.

*Rectal stricture stage.* In thirteen of the forty-five cases rectal stricture was one manifestation of the disease, the proportion of males to females being ten to three. There were seven white and six colored patients, and the age distribution was as follows: two between twenty and twenty-four years; three between twenty-five and twenty-nine; five between thirty-five and thirty-nine; and two between fifty-five and fifty-nine. One patient was thirty-two years old. None of them gave a history of previous inguinal adenitis; unorthodox sexual contact was denied in every instance.

The most important symptoms complained of were: diarrhea, constipation, painful defecation, reduced size of stools, suppuration per rectum, weakness, and anemia. A history of antiluetic treatment was given by five.

Hemoglobin values varied from 30 percent (Sahli) to 99 percent; in eight patients it was between 50 and 79 percent. The red blood cells varied between 2,500,000 to 3,990,000 per cmm. The white blood cells were generally found within normal limits, varying between 4,000 to 8,500 per cmm. in nine of the cases.

Determination of the total blood proteins was performed in only one case, and this was found normal, 7.1 grams percent. The globulin fraction was, however, increased to 4 grams percent.

Protoscopic examination generally revealed a lack of tonus of the anal sphincter, a fibrotic, nonyielding stenosing ring about two to three inches from the anus, a ragged hyperplastic mucosa, and occasionally protruding warty growths. X-ray studies of the colon showed rectal strictures of various sizes, in one instance involving almost the whole of the sigmoid.

Table IV shows the results obtained in treating eleven of the cases with rectal stricture. Improvement was obtained in seven, although this was mostly subjective, that is, the patient asserted that the



TABLE 4

*Treatment of Rectal Stricture*

| *Unit History Number* | *Age* | *Sex* | *Race* | *Duration of Symptoms* | *Frei Test* | *Wass. Test* | *Neoprontosil* | | | | | *Diathermy* | *Improved* | *Not Improved* | *Remarks* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | *Used* | *Duration of Treatment* | *Daily Dose (In grains)* | *Toxic Reaction* | *Dilatation* | | | | |
| 9939 | 26 | F | W | 8 mos. | X | O | X | 163 days | 40 | X | X | X | X | .. | Bleeding and suppuration continued. |
| A152 | 37 | F | C | 4–5 yrs. | X | O | X | 43 " | 40 | O | O | X | .. | X | Stopped coming after the 4th diathermy R. |
| A173 | 25 | F | W | 3 yrs. | X | O | O | ... | .. | O | O | O | .. | X | Only 2 visits. |
| 10209 | 22 | F | W | 6 mos. | X | X | X | 99 " | 40 | X | O | X | X | .. | Only 2 diathermy R. |
| 9881 | 34 | F | W | ... | X | X | X | 120 " | 40 | O | X | X | .. | X | Stopped coming; then returned. |
| A509 | 34 | F | C | 10 yrs. | X | O | O | ... | .. | O | O | O | .. | .. | Permanent colostomy performed. |
| A828 | 34 | F | W | 8 yrs. | X | O | O | ... | .. | O | O | X | .. | X | 29 diathermy treatments. |
| 9545 | 59 | F | C | ... | X | X | X | 365 " | .. | O | X | X | .. | X | 15 diathermy treatments; extensive stricture. |
| A1125 | 22 | F | .. | 3 yrs. | X | X | X | 13 " | 40 | O | O | X | .. | X | 10 diathermy treatments; neoprontosil later. |
| 8345 | 35 | M | C | 5–6 yrs. | X | O | X | 2 yrs. | 40 | O | X | X | X | .. | Frei antigen used at first; developed T.B. |
| 8553 | 25 | F | C | 6 yrs. | X | O | X | 2 yrs. | 40 | O | X | .. | .. | X | |

bowel movements were better formed, less painful, and contained diminishing amounts of mucus and pus. Objective improvement was really insignificant, for the size of the stricture, determined by digital examination and by barium enemas, was only slightly decreased.

A combination of treatments usually followed; the case with the permanent colostomy was operated upon at another hospital. Four patients stopped coming to the clinic, and their cases could not be followed up.

## DISCUSSION

From past personal experience in the treatment of the anorectal syndrome in lymphogranuloma venereum, the writers find it difficult to arrive at any definite conclusions. Although conservative treatment was always advised, they believe that neoprontosil by itself had no influence whatever on the stricture, though definite improvement of the mucosa was generally obtained, the amount of bleeding and suppuration being greatly diminished or totally eliminated. Dilatations were followed by very little improvement.

The same can be said about diathermy; however, no final conclusions will be reached until the cases have been more intensively treated. Martz and Foote[25] report dramatic results after five or six treatments. So far, none of the cases under our observation has shown such improvement.

In five cases of colitis, all females, the Frei test was found positive. Rectosigmoidoscopic examination revealed in every instance diffuse acute, or subacute, inflammation of the mucosa and abundant mucoid discharge. Neoprontosil proved very effective for this condition.

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25. Martz and Foote, *op. cit.*



## SUMMARY AND CONCLUSIONS

1. Lymphogranuloma venereum seems to occupy a prominent place among venereal diseases in Puerto Rico, though no exact figures are yet available as to its incidence.
2. Clinical manifestations of the disease are presented and discussed herein.
3. Rectal stricture is perhaps the most common and dangerous sequela of the disease in Puerto Rico.
4. Though neoprontosil has been used with gratifying results in the treatment of the adenitis stage of the disease, no conclusions can yet be established, since it is well known that spontaneous recovery frequently occurs.
5. Neoprontosil and diathermy seem to have very little beneficial effects on the rectal stricture.