case of a patient who took large doses of phenolphthalein, aloin, and podophyllum for 20 years and developed ileocolitis in many respects similar to that in Case 1. Heilbrun's patient and one other (Jewell and Kline, 1954) showed radiological evidence of improvement of the colon when the purges were reduced or stopped. However, it is most unlikely that the severe colitis in Case 1 would have healed even if it had been possible to stop the purges. Further, aloin was taken by Case 3 for 40 years without colitis arising; and, again, the two patients reported by Schwartz and Relman (1953) also took irritant purges with resultant severe loss of potassium but did not develop signs of colitis. In Case 2, when the purge was reduced the proctosigmoiditis disappeared, and here it is conceivable that the purge was the cause of the bowel changes.

Summary

Three cases are described in which chronic purgation caused excessive loss of sodium, potassium, and water in the faeces and gave rise to electrolyte-deficiency states. These disturbances were studied by chemical and radioisotope methods.

The manner in which these losses were brought about is discussed and the inadequate knowledge of the action of common purges on the intestine noted. The evidence in these cases suggested that "irritant" purges may exert an action on the small intestine.

This work was done in collaboration with Dr. M. Lubran, who was responsible for the laboratory investigations and who is publishing elsewhere (Lubran, 1959) an account of the methods used, with results in normal controls. We are grateful to Mr. J. Scholefield for referring these patients to us and for his help and co-operation in the studies undertaken in Case 1. We also thank Miss E. R. Harrison, lately senior dietitian at the hospital, for the diet histories; and Miss S. M. Robinson for help with the charts.

REFERENCES

- Aitchison, J. D. (1958). *Lancet*, 2, 75.
 Annis, D., and Alexander, M. K. (1952). *Ibid.*, 2, 603.
 Blick, P., Berardi, J. B., and Wozasek, O. (1942). *Amer. J. dig. Dis.*, 9, 292.
 Bloch, M. B. (1937). *Arch. int. Pharmacodyn.*, 56, 244.
 Bodansky, M., and Bodansky, O. (1952). *Biochemistry of Disease*, 2nd ed., p. 352. Macmillan, New York.
 Caldwell, G. H., and Crane, A. W. (1929). *Radiology*, 13, 403.
 Coghill, N. F., Lubran, M., McAllen, P. M., Edwards, F., and Richenberg, C. S. (1956). *Gastroenterologia (Basel)*, 86, 724.
 Cooke, W. T., and Brooke, B. N. (1955). *Quart. J. Med.*, 24, 1.
 Edelman, I. S., Olney, J. M., James, A. H., Brooks, L., and Moore, F. D. (1952). *Science*, 115, 447.
 Forbes, G. B., and Perley, A. (1951). *J. clin. Invest.*, 30, 558.
 French, J. M. (1955). *Proc. Nutr. Soc.*, 14, 33.
 — Gaddie, R., and Smith, N. (1956). *Lancet*, 1, 551.
 Goodman, L. S., and Gilman, A. (1955). *The Pharmacological Basis of Therapeutics*, 2nd ed., p. 1049. Macmillan, New York.
 Grollman, A., and Slaughter, D. (1947). In A. R. Cushny's *Pharmacology and Therapeutics*, 13th ed., p. 236. Churchill, London.
 Gruber, C. M., Richardson, L. K., and Bryan, W. T. K. (1932). *J. Pharmacol. exp. Ther.*, 45, 77.
 Heilbrun, N. (1943). *Radiology*, 41, 486.
 Houghton, B. J., and Pears, M. A. (1958). *Brit. med. J.*, 1, 1328.
 Jewell, F. C., and Kline, J. R. (1954). *Radiology*, 62, 368.
 van de Kamer, J. H., ten Bokkel Huinink, H., and Weyers, H. A. (1949). *J. biol. Chem.*, 177, 347.
 Lenz, E. (1932). *Schweiz. med. Wschr.*, 13, 256.
 Lubran, M. (1959). *J. clin. Path.* In press.
 McAllen, P. M. (1955). *Brit. Heart J.*, 17, 5.
 Magnus, R. (1909). *Ther. Mh.*, 23, 654.
 Mårtensson, J. (1953). *Nord. Med.*, 49, 56.
 Meyer-Betz and Gebhardt (1912). *Verh. Kongr. inn. Med.*, 29, 308.
 Miller, H., and Wilson, G. M. (1953). *Clin. Sci.*, 12, 97.
 Padtberg, J. H. (1910). *Pflügers Arch. ges. Physiol.*, 134, 627.
 Parsons, F. M., Powell, F. J. N., and Pyrah, L. N. (1952). *Lancet*, 2, 599.
 Schwartz, W. B., and Relman, A. S. (1953). *J. clin. Invest.*, 32, 258.

PLEUROPNEUMONIA-LIKE ORGANISMS IN GENITAL INFECTIONS*

BY

E. KLIENEBERGER-NOBEL, D.Sc., Ph.D.

Lister Institute of Preventive Medicine, London

In his monograph on non-gonococcal urethritis Harkness (1950, p. 1) says of the pleuropneumonia-like organisms (P.P.L.O.) that "their frequent association with certain types of abacterial urethritis forms presumptive evidence of their pathogenicity." The aim of the work reported here was to collect further evidence on the significance of P.P.L.O. in pathological genital conditions and particularly in non-gonococcal urethritis (N.G.U.) in men.

It should be emphasized that N.G.U. is not a single syndrome. It is only negatively defined, for the term is applied to all cases of urethritis in which gonococci cannot be demonstrated. Harkness describes more than a dozen different kinds of urethritis in the male, including urethritis ab ingestis, traumatic urethritis, urethritis due to focal infection, protozoa, or bacteria, and infection due to a virus or to P.P.L.O., these last being probably transferred by sexual contact.

Material and Methods

Persons Investigated.—Specimens from patients at the London and St. Mary's hospitals were examined for the presence of genital P.P.L.O. by electron microscopy and by cultural methods. The electron micrographs often showed particles which might have been elements of a P.P.L.O. culture. However, P.P.L.O. elements are not defined by a special size, shape, or structure, and unless aggregated by natural growth or occurring in large numbers they cannot be reliably diagnosed morphologically. Furthermore, the cultural results could not be correlated with the electron microscopical picture. Therefore these studies were discontinued, and only the cultural method was used. Male patients suffering from N.G.U. and other congenital conditions, female patients from the venereal clinics with various complaints, and a group each of pregnant women and gynaecological patients were examined. A number of sexual consorts were included among the V.D. patients.

Methods of Culture.—The following medium was used: boiled blood, heart infusion, peptone agar (Klieneberger-Nobel, 1954), with the addition of 0.5% of "oxid" yeast extract, using a filtered 10% stock solution (Edward, 1954); 20 µg. of desoxyribonucleic acid (D.N.A. per ml. (Edward and Fitzgerald, 1952); 20% inactivated pooled human serum (Klieneberger-Nobel, 1956); thallium acetate to a final concentration of 1 in 4,000 (Edward, 1954); 50 units of penicillin per ml. (Edward, 1954); 20% of a staphylococcus broth culture filtrate (Klieneberger-Nobel, 1956). This medium is very soft, a state well known to enhance the growth of P.P.L.O. Strains were also cultivated on the same medium without penicillin and thallium acetate, to determine their characteristic colony growth in the absence of these inhibitors. They were then established, by incubation while shaking, in a tryptic-digest horse-

*This work was carried out under the aegis of the Medical Research Council Working Party on Non-Specific Urethritis with the aid of a grant from the U.S. Public Health Service.

meat broth containing yeast extract, D.N.A., human serum, and penicillin in the concentrations given above. Human genital strains grow in this liquid medium with a characteristic slight turbidity within 24 hours. The broth cultures were stored at -20 to -30°C. ; they remained viable for many months.

Procedure

In male patients discharge or scrapings were taken from the anterior urethra with a small platinum loop after cleaning the meatus with 70% alcohol. Specimens from the vagina, cervix, or urethra of female patients were also collected with a platinum loop. In cases of Reiter's disease synovial fluids and urethral discharges were examined. A number of blood samples from female patients in the venereal clinics were also cultured for P.P.L.O.

One of the difficulties of the examination of controls is the absence of any substantial amount of material that can be obtained for culture by scraping—a procedure that in any event may be impracticable, especially with the young male. The sensitivity of urine culture in revealing P.P.L.O. was established (a) by proving that human genital P.P.L.O. remained viable in urine, and (b) by parallel tests of discharge and urine in men attending a V.D. clinic.

To test the suitability of urine as a specimen for P.P.L.O. culture six human strains were suspended in filtered sterile urine. In six hours at room temperature ($18-22^{\circ}\text{C.}$) the number of viable organisms fell to an average of 80% of the inoculum, which was approximately 100,000 organisms/ml. After 24 hours at this temperature approximately 50% of the organisms remained viable. In all of 14 strains viable organisms remained after 12 hours' incubation at 37°C. and in five of these more than 50% of the organisms were alive after this time. Accordingly, the sediments from patients' urines were invariably seeded on to nutrient medium within three hours of voiding.

The comparative examination of the yields of P.P.L.O. from urine and discharge was made in 66 male patients chosen at random.* P.P.L.O. were cultured from 18 of these. Both urine and discharge were positive in 11, only the urine in 4, and only the urethral discharge yielded P.P.L.O. in 3. Since approximately the same number of positive cultures were obtained from the urines as from the discharges we felt that urine was a satisfactory material for the detection of urogenital P.P.L.O. in the male, particularly as it had the advantage that specimens could easily be obtained, even from small boys.

About 30 ml. of each specimen of urine was centrifuged and the sediments were plated. The discharges and scrapings were inoculated on to fresh culture plates without delay. The synovial fluids were distributed on to solid and into liquid media. Subcultures to solid medium were made from the latter on three consecutive days. Specimens of blood were dispensed into liquid medium and similarly treated. The plates were incubated for seven days and were inspected by hand lens ($\times 6$) and microscopically ($\times 56$) by transmitted light.

Strains Isolated

Ninety-eight strains were isolated. All of those (40) so examined grew equally well aerobically and anaerobically. On the medium described they developed into

*These cases are not included in the tables.

microscopically visible colonies (about $200\ \mu$ in diameter) within 48 hours, provided the growth was not very dense. After three to five days the isolated colonies were about $500\ \mu$ in diameter. They grew larger with further incubation, and after seven days were readily visible to the naked eye and frequently were brownish yellow in colour. On the isolation medium the colonies have a slightly raised dark centre, under which the growth has penetrated into the agar, and a flat thin peripheral zone often marked with fine radiating lines. The edge is usually coarsely and irregularly broken, but sometimes entire. A few strains produce colonies with a fine structure consisting of translucent areas separated by darker lines giving the appearance of openwork lace, and resembling colonies of the L form of bacteria. All these colonies grow on the simpler stock medium with an entire edge.

In shaken broth culture at 37°C. the growth as a rule is slightly and uniformly turbid, but with a few strains it is finely granular. There is no growth at room temperature. Many strains grow on media enriched with horse serum, but some failed to grow unless human serum was used for enrichment.

There was no danger of confusing the P.P.L.O. with bacterial L-form colonies, with which they have certain properties in common (Klieneberger-Nobel, 1956), for in the few instances where P.P.L.O. colonies resembled L colonies they were distinguishable by their greater delicacy of structure. When coarser colonies, resembling those of the stable L forms of bacteria, were present, they all proved to be the so-called transformation forms induced by penicillin, and reverted to bacterial forms when cultivated on media not containing penicillin. No true L forms were seen in any of the primary cultures of the material.

The number of colonies from the discharges or urine sediments varied. Sometimes only a few were found. In most cases a considerable number, varying from many hundreds to many millions, developed. Bacterial colonies were found only rarely on the primary plates owing to the antibiotic and bacteriostatic contained in the medium.

A case was never diagnosed as P.P.L.O.-positive unless subculture on solid medium without penicillin and thallium acetate was established and the strain grew characteristically in liquid media as well.

Though workers sometimes feel able to distinguish between different species of P.P.L.O. by colony type and morphology, most of them conclude sooner or later that no dependable distinction can be made, because these characteristics vary with minute changes in the consistency and water content of the medium, and the density of growth. Strains may vary in colony type and exhibit differences of morphology in different sectors of the same plate. Some workers have used fermentation reactions, haemolysis, and growth inhibition by antisera for purposes of differentiation. In our hands none of these methods has proved to be reliable.

Two of the most constant characteristics we elicited from the strains were antibiotic sensitivity and antigenic structure.

Forty-eight of the strains were tested for antibiotic sensitivity by W. A. Blyth (to be published). All strains were resistant to penicillin, sulphonamides, erythromycin, and oleandomycin. The tetracycline group of antibiotics inhibited growth at concentrations of approximately $1\ \mu\text{g./ml.}$ of medium, whereas

streptomycin, chloramphenicol, spiramycin, and neomycin were less active, requiring 8–16 μ g. for inhibition of growth.

Of our 98 strains, 56 were tested serologically by a complement-fixation method (D. H. Card, to be published); all of them cross-reacted to high titre with antisera to human genital P.P.L.O. and were serologically distinct from human mouth P.P.L.O. and also from animal and saprophytic strains. It was concluded that they formed a single serological group. It is noteworthy that all except one of Nicol and Edward's (1953) 91 human genital strains fell into one serological group. Huijsmans-Evers and Ruys (1956) found serological and cultural differences among the P.P.L.O. strains they isolated from the human genital tract, and they classified them into three groups, but the majority fell into one group.

Cultural Results in Men

Of 100 urines from apparently healthy adult males, three were positive for P.P.L.O. (Table I). One of them proved to have N.G.U. The second one was consistently positive in a series of tests; he had no symptoms during

TABLE I.—Incidence of P.P.L.O. in the Urine of the Male (Control Groups)

Age	No. Tested	P.P.L.O.-positive
Adults	100	3*
13 years or less	47	None

* One developed N.G.U.

this period, but had had attacks of prostatitis. No inquiry was made into the third case. Of 47 urines from boys under the age of 13 from the medical wards of the London and St. Mary's hospitals, none were positive. Clearly P.P.L.O. are rare in the genital tract of healthy men. Boys under the age of puberty who have had no sexual intercourse are free from P.P.L.O.

Of 201 discharges and scrapings from male patients from the venereal clinics, 52 (25.5%) were P.P.L.O.-positive (Table II). We divided the 201 cases on clinical grounds into the six groups shown in Table II. The highest number of positive results (48%) was obtained in the recently acquired N.G.U. group. In the

TABLE II.—Incidence of P.P.L.O. in Urethral Discharges and Scrapings of Male Venereal Patients

Group	No. of Cases	P.P.L.O.-positive	
		No.	%
Recently acquired N.G.U. ..	65	31	48
Untreated gonorrhoea	49	15	30.6
Miscellaneous conditions* ..	43	4	9.3
Reiter's disease	20	2	10
Chronic N.G.U.	17	0	
Cured	7	0	
Total	201	52	25.5

* Epididymitis, chronic and low-grade prostatitis, penile sore and warts, and nine symptomless cases.

gonorrhoea group there were 30% positive P.P.L.O. cultures. The percentages in the groups of miscellaneous cases and Reiter's disease were much lower—namely, 9.3 and 10 respectively.

Six synovial fluids and all but two of 14 urethral discharges from cases of Reiter's disease were negative. The case histories of the two patients carrying P.P.L.O. are consistent with the assumption that the P.P.L.O. infection was superimposed on the Reiter's disease.

P.P.L.O. were not found in persons with chronic and cured N.G.U. However, the numbers tested are too small to be conclusive.

Cultural Results in Women

Two groups of women were examined—those attending the venereal disease clinics and those with other conditions such as pregnancy or gynaecological troubles. Of a total of 59 patients from the venereal clinics, 56% yielded a P.P.L.O. culture from the cervix, vagina, or urethra, or from a combination of these (Table III). In

TABLE III.—Incidence of P.P.L.O. in Female Venereal Patients

	No. of Cases	P.P.L.O.-positive	
		No.	%
Gonorrhoea, untreated	15	13	87
" treated	9	8	89
Cervicitis and/or vaginitis and/or urethritis	11	9	82
Trichomonal vaginitis	6	2	33
Salpingitis	1	1	
Warts, ulcers	3	None	
No symptoms at examination ..	14	"	
Total	59	33	56

untreated gonorrhoea (15 cases), in penicillin-treated gonorrhoea (9 cases), and in cases of cervicitis, vaginitis, or urethritis, or in a combination of these (11 cases), the proportions of P.P.L.O. cultures obtained were extremely high (87%, 89%, 82%). One case of salpingitis was positive. The six patients with trichomonal vaginitis were free from gonococci at the time of examination; two had P.P.L.O. in their discharge. Fourteen women who were completely free from symptoms and genital abnormalities (some of whom had been treated, possibly with a tetracycline) were P.P.L.O.-negative. Thus the incidence of P.P.L.O. in women suffering from venereal disease is generally very high. However, in an attempted

TABLE IV.—Incidence of P.P.L.O. in Obstetric and Gynaecological Patients

	No. of Cases	P.P.L.O.-positive	
		No.	%
Pregnant women	51	12	23.5
Gynaecological patients	58	10	17.3

isolation of P.P.L.O. from specimens of blood from 59 other female patients attending a V.D. clinic no positive cultures were obtained.

Of 51 pregnant women, 12 yielded cultures of P.P.L.O. from cervical specimens (23.5%), and 10 positive cultures were obtained from 58 gynaecological patients (Table IV). Thus approximately 20% of obstetric and gynaecological patients attending the London Hospital carry P.P.L.O. It was noted that several had trichomonal vaginitis or thrush.

Cultural Results in Consorts

Seven pairs of consorts were tested. In three pairs the male partner was suffering from recently acquired N.G.U., and P.P.L.O. were cultured from both partners. In the fourth pair of consorts the male partner had gonorrhoea, and P.P.L.O. were cultured from his discharge; his female partner also carried P.P.L.O. and developed abacterial cervicitis after penicillin treatment of gonorrhoea. In the three remaining pairs of consorts cultures for P.P.L.O. from both partners were negative. In one of the men a calculus was found which accounted for his purulent and haemorrhagic discharge. In the second pair the male partner had so little discharge that

treatment was thought to be unnecessary. In the third negative pair the male partner had chronic N.G.U. and low-grade prostatitis.

Discussion

Quite apart from N.G.U. there is evidence that P.P.L.O. can sometimes produce severe infections in humans. Stokes (1955) describes four cases in women. In one of them P.P.L.O. were isolated from the blood. Carlson, Spector, and Douglas (1951) reported two patients with Henoch-Schönlein purpura from whose blood P.P.L.O. were isolated on various occasions, and Gotthardson and Melén (1953) two patients with salpingo-oophoritis and with tubo-ovarian abscesses from which pure cultures of P.P.L.O. were cultivated. Dr. W. A. Gillespie, of Bristol Royal Infirmary (personal communication), isolated from a tubal abscess in a girl of 13 a pure culture of P.P.L.O. which in our hands proved to be of the same serological type as our genital strains.

We have shown that P.P.L.O. are found in almost 50% of men with recently acquired N.G.U. of short duration. In many of these positive cases the discharge contained pus cells but no visible organisms; in other cases bacteria were present, perhaps indicating a double infection. P.P.L.O. were also frequently present in men with gonorrhoea (30% positive); here the incidence was lower than in recently acquired N.G.U. Presumably, here also we are dealing with a double infection.

In striking contrast to this, almost all the healthy men of high hygienic standard and all the boys below the age of puberty were free from genital P.P.L.O.

We have confirmed the findings of Harkness and Henderson-Begg (1948), who found 50% positive in acute N.G.U. and no P.P.L.O. in 65 healthy controls (50 men and 15 women). Huijsmans-Evers and Ruys (1956) also report 50% of their N.G.U. cases positive. Nicol and Edward's (1953) interpretation of their own results is non-committal, but their incidence of positive cultures among various classes of people—though lower in N.G.U. patients—is not strikingly different from ours. Their highest percentage of positive cultures, like ours, is in men with N.G.U. (26%). However, their group comprises all N.G.U. cases; the incidence of P.P.L.O. in recently acquired infections only may well have been higher. Nicol and Edward's lowest number of positives (11%) were found in a group of 90 police candidates without genital abnormalities, which they regarded as a control group of healthy men. It is, however, possible that if these men had been kept under observation before and after the examination some would have been found to have genital disease. This possibility is enhanced by the fact that two men gave a past history of N.G.U. and that a third was found at a later examination "to have developed signs of recurrence of this infection."

Freundt (1956) has published results which are in striking contrast to ours and to those of most other workers. He cultured P.P.L.O. more often from men with no genital abnormality than from those with N.G.U., acute gonorrhoea, or epididymitis. However, his results cannot be compared with ours, as he took his specimens from the external surface of the meatus and from the prepuce, whereas we cleaned the meatus and took samples with a platinum loop inserted 1 in. (2.5 cm.) into the anterior urethra. Moreover, he has not typed his strains.

A high percentage of P.P.L.O.-positive cases was reported by Shepard (1956, 1957). He described a new type of P.P.L.O. colony designated T type (T for tiny). We found no T-type colonies on our plates. His illustrations suggest that he has interpreted decaying cells from the discharge and scrapings as colonies, and has confused small bacteria and debris with P.P.L.O. elements in his stained preparations. He himself emphasizes that subculture was very difficult and was successful in only a few cases. In our experience, diagnosis of P.P.L.O. from pathological specimens was not possible by direct microscopical or electron microscopical examination.

The high percentage of positive cultures which we obtained in recently acquired N.G.U. in the male is very striking, particularly when the difficulties of diagnosis and the unreliability of the patients' statements are taken into account and when it is realized that proper controls are almost invariably negative. We conclude that the human genital P.P.L.O. are of significance in a considerable proportion of the cases diagnosed as N.G.U.

In agreement with most other authors we found that women carry P.P.L.O. much more frequently than men. This applies in particular to the women attending the V.D. clinics. In both untreated and penicillin-treated gonorrhoea the incidence of P.P.L.O.-positive cases was almost 90%. Like Nicol and Edward (1953) we also found P.P.L.O. in cases of trichomonal vaginitis. In cases of cervicitis, vaginitis, and urethritis the incidence was as high as 82%. Attention should also be drawn to the fact that P.P.L.O. could not be cultured in 14 women without symptoms at the time of examination and in two patients with genital ulcers and one with genital warts. This agrees with Harkness's results in 15 women without symptoms. P.P.L.O. were found in approximately 20% of gynaecological patients and pregnant women in the Whitechapel area. Compared with the percentage of positives in women with gonorrhoea, cured gonorrhoea, cervicitis, vaginitis, and urethritis this is a low figure.

Reiter's disease and N.G.U. are sometimes considered to have a common aetiology, and P.P.L.O. have been suspected as the most common cause of both conditions. Our cultural investigations offer no positive evidence for this hypothesis. P.P.L.O. were not found in any of the synovial fluids from patients with Reiter's disease which we examined, and only rarely from the urethral discharges in our cases of this condition.

Examination of blood from female patients in V.D. clinics has so far yielded negative results. Probably the occurrence of P.P.L.O. in the blood is rare, particularly in afebrile patients.

Conclusions

Genital strains of P.P.L.O. are (1) associated with recently acquired urethritis in a high proportion of men suffering from non-gonococcal urethritis; (2) associated with cervicitis, vaginitis, and urethritis in women; (3) likely to be transferred by sexual intercourse; (4) often associated with gonococcal infection and trichomonal infestation; and (5) absent in boys under the age of puberty and rare in healthy men and women.

I am indebted to my colleagues, Dr. G. Csonka, of St. Mary's Hospital, and Drs. J. K. Oates and R. D. Catterall.

of the Whitechapel Clinic, for the clinical detail of the cases studied, and for help with the collection of specimens.

REFERENCES

- Carlson, H. J., Spector, S., and Douglas, H. J. (1951). *Amer. J. Dis. Child.*, **81**, 193.
 Edward, D. G. ff. (1954). *J. gen. Microbiol.*, **10**, 27.
 — and Fitzgerald, W. A. (1952). *Vet. Rec.*, **64**, 395.
 Freundt, E. A. (1956). *Brit. J. vener. Dis.*, **32**, 188.
 Gotthardson, A., and Melén, B. (1953). *Acta path. microbiol. scand.*, **33**, 291.
 Harkness, A. H. (1950). *Non-gonococcal Urethritis*. Livingstone, Edinburgh.
 — and Henderson-Begg, A. (1948). *Brit. J. vener. Dis.*, **24**, 50.
 Huijsmans-Evers, A. G. M., and Ruys, A. C. (1956). *Antonie v. Leeuwenhoek*, **22**, 377.
 Klieneberger-Nobel, E. (1954). *Biol. Rev.*, **29**, 154.
 — (1956). *Zbl. Bakt., I. Abt. Orig.*, **165**, 329.
 Nicol, C. S., and Edward, D. G. ff. (1953). *Brit. J. vener. Dis.*, **29**, 141.
 Shepard, M. C. (1956). *J. Bact.*, **71**, 362.
 — (1957). *Ibid.*, **73**, 162.
 Stokes, E. J. (1955). *Lancet*, **1**, 276.

ACHALASIA OF CARDIA, CARCINOMA OF OESOPHAGUS, AND HYPERTROPHIC PULMONARY OSTEOARTHROPATHY

BY

M. A. PEYMAN, M.A., D.M., M.R.C.P.*

Late Senior Medical Registrar, Charing Cross Hospital, London

It is generally considered that carcinoma of the oesophagus is an unusual complication of achalasia of the cardia. A case of achalasia is described below in which carcinoma of the middle third of the oesophagus developed together with hypertrophic pulmonary osteoarthropathy.

Case Report

A man aged 26 first attended the out-patient department of Charing Cross Hospital in 1931 with a history of difficulty in swallowing for the previous six months. No abnormalities were found on physical examination. A diagnosis of achalasia of the cardia was made, and he was given a mercury bougie to use regularly.

During the next 23 years he remained well and did not attend the out-patient department again until November 16, 1954, when he stated that the bougie had broken about two months previously. Since then he had developed increasingly severe dysphagia, especially for solid food, and he had lost about 14 lb. (6.4 kg.) in weight. During this period he had also experienced pain and swelling in the ankles, knees, wrists, and finger-joints. He was adamant that daily use of the bougie in the past had ensured normal swallowing.

Examination showed a thin ill-looking man with marked clubbing of the fingers and toes as well as some swelling and tenderness and slight limitation of movements of the ankles, knees, wrists, and finger-joints. The chest showed generalized emphysema and bronchospasm. There were no palpable lymph nodes and examination of the other systems was essentially negative.

A fortnight later (December 2, 1954) he was admitted to hospital for further investigation. The following results were obtained: Hb, 12.4 g./100 ml.; red cells, 4,900,000/c.mm.; white cells, 16,900/c.mm. (polymorphs 68%); E.S.R., 27 mm. in one hour; serum uric acid, 3 mg./100 ml.; serum

W.R., negative. A chest x-ray examination showed generalized emphysema with pleural thickening in the region of the oesophagus on the right side. The oesophagus was filled with food up to the level of the thoracic inlet and bulged to the right of the midline. A barium swallow showed that the oesophagus was dilated and tortuous, with evidence of oesophagitis. It was concluded that this appearance was due to achalasia of the cardia. Thin barium passed into the stomach without undue delay, but a mercury bougie could not be manoeuvred below the lower third of the oesophagus even after the inhalation of octyl nitrite. There appeared to be a filling defect in the middle third of the oesophagus (Fig. 1). A series of x-ray films of the limbs showed evidence of new bone formation in the subperiosteal regions of the bones of the hands and feet as well as of the lower parts of the radius, ulna, tibia, and fibula. The changes were those of hypertrophic pulmonary osteoarthropathy (Fig. 2).

During the next two weeks the patient received daily oesophageal lavages. At the end of this period screening examination of the chest showed that, although the oesophagus was still dilated and tortuous, a bougie could be passed through the cardia. The patient was using a bougie daily and finding that swallowing was becoming easier. On January 4, 1955, after a further fortnight of oesophageal lavages, oesophagoscopy revealed a large friable papilliferous growth involving the middle third of the oesophagus. A subsequent thoracotomy showed that the growth had spread into both hilar regions and was involving the pleura as well as becoming firmly attached to the aorta and vertebral bodies. No metastases were seen. The oesophagus was dilated and

FIG. 1.—Barium swallow showing dilated oesophagus with appearance of filling defect in middle third of oesophagus.

FIG. 2.—Radiograph showing new bone formation at lower ends of radius and ulna.

*Now at New England Center Hospital, Boston, Massachusetts, U.S.A.