BACT. ALKALESCENS IN INFECTION OF THE URINARY TRACT AND BACTERIOPHAGE THERAPY

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ANDREWES (1918) in a paper on the differentiation of true dysentery bacilli from allied organisms described and named three species or groups of species of bacilli which though strongly resembling the true dysentery bacilli were not considered by him as causal agents of dysentery; one of these was *Bacterium alkalescens*.

Andrewes described it as a Gram-negative non-motile bacillus which produced acid but no gas in glucose, maltose, mannitol and dulcitol. Lactose and saccharose are not fermented. Indole was formed by all strains examined by him and litmus milk became markedly alkaline after a week or ten days. The organism was not agglutinated by specific Shiga or Flexner-Y serum within the ordinary time limits of 4 to 5 hours at 55°C., but when the tubes were left at this temperature for 20 to 24 hours agglutination with Flexner serum occurred with some strains but always well below the titre of the serum. In no case was it agglutinated by the serum of the patient from whom it was isolated. Andrewes concluded that *Bact. alkalescens* 'can be rejected as having no connexion with dysentery'.

Many of the subsequent authors regard *Bact. alkalescens* as non-pathogenic. Park and Williams (1934) write of it as 'apparently non-pathogenic and of importance only because of the possibility of confusing it with the pathogenic varieties'. Gay (1935) states that it is 'distinctly non-pathogenic', and Havens (1935) as an organism 'whose pathogenicity has not yet been established'. Topley and Wilson (1936) write 'whether this organism is capable of giving rise to real dysentery is doubtful. Since, however, it has been isolated from the blood stream of a woman with puerperal fever (Smith and Fraser, 1928) and has been found in an institutional outbreak of food-poisoning (Welch and Mickle, 1934) its occasional pathogenicity for man must probably be accepted'. Bergey (1939) in the latest edition of the *Manual of Determinative Bacteriology* describes it as 'not pathogenic'.

Smith and Fraser (1928) were the first to assign a definite pathogenic rôle to *Bact. alkalescens*. They described a case of continued fever due to this organism. Since then there has been an increasing number of reported instances where *Bact. alkalescens* has caused disease in man. This evidence has been collected, reviewed and well summarized by Nabarro and Edward (1939) who also record a series of seventeen of their own cases where *Bact. alkalescens* was isolated from the fæces. In these it was associated with disease nearly always involving the intestinal tract. These authors conclude that infection with *Bact. alkalescens* is primarily intestinal giving rise to a mild form of acute dysentery or chronic colitis and that lesions produced elsewhere are to be regarded as complications. These workers give thirteen references in which *Bact. alkalescens* is reported to have caused pyelitis or other infection of the urinary tract. In these cases *Bact. alkalescens* was recovered in pure culture from the urine and in several, agglutinins in significant titre were demonstrated in the serum. In India, Boyd (1932) found *Bact. alkalescens* five times, three times in Poona and twice in Bangalore. Of its pathogenicity he states 'all five strains were recovered from the stools of normal individuals. There is, therefore, no suggestion of pathogenicity, a finding which accords with the opinion formed by Andrewes'.

From this brief survey of the literature it is obvious that there is no unanimity of opinion regarding the pathogenicity of *Bact. alkalescens*. It is for this reason that a brief account is given of a patient from whom this organism was isolated in pure culture several times from the urine and in whom there was sufficient evidence to regard it as the causative agent. There were

(*Continued from previous page*)

syringefuls of air and closing the tube while removing and re-applying the syringe by means of an adapter. The water aspirator pump, fixed to a water tap, may be used. Suction by mouth at the distal end of the outlet produces enough exhaustion of the bottle. Care is necessary in making a second attempt when saliva may be drawn into the bottle.

The General Scientific Engineering Co., 4/1, Harish Mukherji Road, Calcutta, supply two metal tubes and four adapters, complete set for a bottle, for Rs. 10. The metal is silver-plated brass.

Even glass tubes can be used in the place of the metal tubes. They are, however, inconvenient to fit into rubber tubes and of course are liable to break.

Incidentally, the writers now use routinely a 3 per cent solution of sodium citrate instead of 2.5 per cent. As before, one-tenth volume of the ultimate content of the bottle is taken (*e.g.*, 40 c.cm. for 400 c.cm.). The concentration in the citrated blood is 0.3 per cent instead of 0.25 per cent.

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in addition certain interesting features following bacteriophage therapy; and reference to these is included.

The patient, a Scot, aged 52 years, who had seen some 25 years of service in India had been suffering from symptoms typical of cystitis for about a month. There was no history of intestinal disturbance or of any previous urinary trouble. Except for a slight but definite enlargement of the prostate (probably physiological), nothing abnormal was found on physical examination. The urine was turbid and contained a large number of pus cells and on culture *Bact. alkalescens* was isolated in pure culture. During the first month of observation 51 samples of urine were examined and the organism was isolated from 45 of the samples. It was also isolated from each of the three samples of stools examined.

All strains gave identical biochemical reactions. They produced acid but no gas in glucose, maltose, mannitol and dulcitol. There was no change in lactose, saccharose and salicin. Indole was produced and litmus milk turned alkaline. Representative strains were tested with the patient's serum (blood drawn about five weeks after the onset of symptoms) and were agglutinated up to 1 in 500 dilution. This organism agglutinated with a polyvalent Flexner serum but only to 1/10th of the titre of the serum. A serum was raised against the strain isolated from the first specimen of urine and this serum agglutinated to titre (1 in 10,000) the strains isolated later.

An active and potent alkalescens phage was prepared. It caused complete clearing of a young broth culture in about one hour and the lysis was maintained for about 72 hours when a faint turbidity appeared. This bacteriophage was given to the patient in doses of 2 c.cm. in 2 ounces of water three times a day for a month. Bacteriophage active against *Bact. alkalescens* was not present in samples of stool and urine examined before the administration of alkalescens phage, but was recovered from the stool a day after and from urine two days after the administration of the phage by mouth. *Bact. alkalescens* was not found in any of the eight samples of stools examined during and after phage treatment.

The effect of bacteriophage therapy on the organisms in the urine was interesting. The first effect was to render the urine less turbid and fewer organisms were recovered and these were obviously phage-infected. The colonies on the plate were variously notched and some showed minute areas of phage clearings. This was followed by some days when the urine contained potent alkalescens phage and gave no growth of any organisms or when, in spite of the presence of active phage, a few isolated colonies were obtained. After about a week however of such findings the urine became markedly turbid and gave a heavy growth of *Bact. alkalescens*. Bacteriophage was present in the urine intermittently; it would be found regularly for two days (two samples examined each day), be absent for two or three days, and then be found again. An attempt was made to correlate this with the reaction of the urine, but no such correlation could be made.

A study was made of the strains of *Bact. alkalescens* isolated from the urine before and after the administration of alkalescens phage and their lysability by (1) the phage administered, (2) the phage recovered from the stool and (3) the urine, and (4) the phage contaminating the organism isolated after phage therapy. The strains (urine and stool) isolated before the administration of alkalescens phage were lysable by (1), (2), (3) and (4). The strains of *Bact. alkalescens* recovered from the urine after the administration of phage orally and when the phage had appeared in the urine were lysed by (1) and (2), the original phage, and by the phage recovered from the stool. These strains were resistant to the phage races (3) and (4), those found in the urine and those contaminating the organisms. These results show that the phage given to the patient contained more than one type and that only one type of alkalescens phage was able to get through to the urine or survive in the urine.

The alkalescens phage was given daily for a month without producing any effect either on the clinical symptoms or on the condition of the urine, which continued to contain pus cells and the organisms in large numbers. An autogenous vaccine was prepared with the strain originally isolated. The response to vaccine therapy was striking and the urine was clear and free from organisms 17 days after the commencement of vaccine therapy. The clinical condition improved considerably and the patient was completely cured.

Summary

1. Attention is drawn to the evidence implicating *Bact. alkalescens* as a pathogen of man.

2. A case is recorded in which *Bact. alkalescens* caused cystitis. This organism was isolated in pure culture from the urine on several occasions during the course of the disease and disappeared when the symptoms subsided. It was isolated also from samples of stool. Agglutinins for *Bact. alkalescens* were present in the patient's serum.

3. Alkalescens phage was given by mouth for a month. This led to the rapid disappearance of the organism from the stools, but had only a transient effect on the ordinary infection. Only one type of alkalescens phage was found in the urine, whereas the bacteriophage given by mouth contained two distinct types.

4. Bacteriophage therapy having failed to control the infection, autogenous vaccine was used with satisfactory results.

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BACTERIOPHAGES IN SOIL

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DURING the course of certain experiments designed to demonstrate 'antagonistic bacteria' for intestinal pathogenic bacteria of man, the interesting observation was made, that many samples of garden and field soil contain bacteriophages active against these organisms.

A 1 in 100 suspension in saline of soil when added in 1 c.cm. amounts to melted agar containing a thick suspension of one of the test bacteria and poured, after incubation, showed a number of bacteriophage colonies. *Bacterium typhosum, Bact. flexneri, Bact. shigæ* and *Vibrio choleræ* were used as the test organisms, and from twelve of the sixteen samples of soils examined bacteriophages active against some or all the four test organisms were isolated. In some plates as many as 120 bacteriophage colonies were present. The most frequently occurring bacteriophages were the dysentery-phages and next in order typhoidphages and choleraphages. These bacteriophages were present in samples of soil taken at different levels (down to 3 feet) below the surface.

These findings demonstrate how widely bacteriophages are distributed in nature.

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NOTES ON COMMON SKIN DISEASES

III. RINGWORM OF THE SCALP : FAVUS

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FAVUS is so distinct from other ringworms that we decided to treat it separately. It is a highly contagious disease and affects adults and children alike; it spreads by extension from the scalp to the body. In India, the disease is endemic in Kashmir, the Punjab, the North-West Frontier Province, and Rajputana, but does not usually occur in the eastern and southern parts of India. It is commonly found amongst the poor and is not a problem of the boarding schools.

The causative organism is a fungus of the genus *Achorion* and, of the various species, both *Achorion schönleini* and *A. actoni* have been reported from India.

Clinically, the disease has certain distinctive features. It begins as small yellow sulphur-coloured cup-shaped discs around the hair follicles. The concavity of the cup is upwards and the convexity is towards the surface of the scalp. When a disc is removed, it leaves an oozing ulcerated area on the scalp; the base of the ulcer is red and oozes a sero-purulent discharge. The yellow discs, or 'scutula' as they are called, gradually increase in size and coalesce with the adjacent ones. In an advanced case, the whole scalp appears to be covered with a thick yellow-coloured mud plaster. The lesions spread from the scalp to the body and form the same type of scutula among the lanugo hairs. A fully-developed case of favus presents no difficulty in the diagnosis and the patients emit a peculiar smell from the lesions like that of mouse urine.

If one of the discs or scutula is removed with a pair of forceps, some amount of force is required to pull it off and the hairs at the centre of the scutula come out with them from the root.

When a scutulum is dissolved with 40 per cent liquor potassii and examined under the microscope, it is found to consist of a network of mycelial threads in which are embedded epithelial debris and pus cells. In the hairs, the mycelia are arranged along the long axis and hence the hairs split longitudinally and do not break.

Prophylaxis.—The disease is highly contagious and complete segregation of the patient is necessary. Hats, turbans or any other head dress must be burnt and tight-fitting cotton caps given to wear until the patients are completely cured.

Treatment.—Epilation of the infected hair manually, or by *x*-rays, and then treatment of the scalp with mild antiseptics are essential features of the treatment. In favus, unless