exposed to the same adverse conditions: nine soldiers developed symptoms within a few hours of a five-mile march in heavy rain, and other groups attributed their illness to a chilling consequent upon the over-zealous opening of windows in the sleeping quarters.

Stuart-Harris suggested that meteorological factors might determine the onset of an influenzal outbreak. We therefore obtained details from local Air Force stations of the conditions prevailing during January and February, 1949. No dramatic changes of temperature were associated with the onset or the peak of either epidemic, but rain fell on each day of the week preceding the peaks of both epidemics.

Discussion

These two outbreaks differ from those commonly reported in this country (Stuart-Harris, 1945) in that recruits and seasoned men were equally affected when living under comparable conditions. This finding suggests that the community had no recent experience of the infective agent. The new antigenic strain of virus which we reported had rarely been experienced in this country and would have been expected to provoke an equal incidence among recruits and trained men. We did not prove, however, that this strain was responsible for the epidemic as a whole. Furthermore, the American workers claim that the incidence of Virus A influenza of the usual antigenic types is not determined by the duration of residence in the community. This implies that Virus A influenza may not be an endemic disease. The behaviour of future epidemics in this country may be of interest in this connexion, but no definite conclusions can be drawn from the limited evidence which we have presented.

Differences of environment rather than of host susceptibility determined the variability of the American outbreaks, and overcrowding was responsible for the higher infection rate in certain groups. Our experience is similar, but exposure to cold seemed to play a greater part than cross-infection.

Summary

The incidence of influenza (Virus A) among troops in the Highland District of Scotland during January and February, 1949, is reported.

Epidemics were confined to two training centres. The form of these two outbreaks and the factors affecting the incidence and spread of infection are discussed.

Clinical features, laboratory investigations, and treatment are also described.

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The Ministry of Health states that gifts of blood to the National Blood Transfusion Service for hospitals in England and Wales during the quarter ending September 30, 1949, were the highest since the war. They totalled 116,021, as against 95,301 in the comparable quarter last year. New donors enrolled in the quarter numbered 37,219. Also a post-war record was the total strength of the donor panels—376,502, or 9,335 more than a year ago. For the Welsh Blood Transfusion Region alone the figures for the quarter (with those for the comparable quarter in 1948 in parentheses) were: Donations, 4,005 (3,022); new donors 1,617 (866); strength of donor panel, 12,417 (11,421).

AUREOMYCIN IN TREATMENT OF PERITONITIS

BY

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AND

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Recent observations have shown that the mortality encountered in peritonitis secondary to appendicitis, perforated peptic ulcer, and penetrating wounds of the abdomen has been reduced 60% by the post-operative use of variable combinations of sulphonamides, penicillin, and streptomycin (Altemeier, 1949; Pulaski, Voorhees, and Seeley, 1949). In spite of the better prognosis thus afforded, the case fatality is still between 5 and 10%. Consequently the search for more effective antibiotics to add to the surgeon's armamentarium continues. The new antibiotics chloramphenicol ("chloromycetin") and "aureomycin" have been used successfully in the treatment of generalized peritonitis incident to intestinal perforation complicating typhoid fever (Woodward, Smadel, and Ley, 1949), and in appendicitis and in carcinoma of the urinary bladder (Yeager, Ingram, and Holbrook, 1949).

During the course of recent investigations by the United States Army Medical Research Unit in Malaya several cases of generalized peritonitis were treated with the two new drugs. Those which received chloramphenicol are discussed in another article (Smadel, Bailey, and Lewthwaite, to be published). The present report summarizes the observations made on five patients treated with aureomycin who were suffering from peritonitis secondary to perforating lesions of the gastro-intestinal tract.

Clinical Observations

Three cases in the present group had acute appendicitis which resulted in rupture and peritonitis. Two of these three had generalized abdominal disease when in hospital. The third case was observed throughout the course of the illness but refused to grant permission for operation until after rupture had occurred; the fourth case developed peritonitis following perforation of a peptic ulcer; while the last of the group suffered perforation of the intestine late in the course of typhoid fever. Exploratory laparotomy and appropriate surgical procedures were done as soon as possible in the first four cases. The individual with the perforated typhoidal ulcer was treated with aureomycin alone without benefit of surgery.

Aureomycin ("duomycin")* was administered in the form of gelatin-coated capsules. Treatment was started one to three days after signs of peritonitis had appeared—that is, one to twenty-four hours after surgery was performed in those cases operated on. In general, an initial oral dose of 3 g. of aureomycin was given, followed by 0.25 g. every two hours for two days and then by 0.25 g. every four hours for the succeeding three to five days. Water in small amounts was administered along with the capsules during the acute phase of the disease.

Routine clinical and laboratory observations were made on the patients. Bacteriological studies were limited and no attempt was made to identify the bacterial flora of

*Aureomycin (duomycin) was supplied by Lederle Laboratories Division, American Cyanamid Company.

FIG. 1.—Clinical response of patient with peritonitis secondary to ruptured appendix (Case 1). Aureomycin therapy was instituted following appendicectomy.

peritoneal exudate obtained at the time of operation. The diagnosis of typhoid fever for Case 5 was established by the cultivation of *Salmonella typhosa* from the faeces after he had recovered from peritonitis.

At the time of operation each of the three cases of appendicitis had a perforated gangrenous appendix with faecal contamination of the peritoneum. Recovery was rapid in these three following appendicectomy and the institution of aureomycin therapy. The toxic signs and symptoms began to subside within one day and the patients were afebrile within four to five days. Convalescence was uneventful in Case 2. Cases 1 and 3 suffered recurrent infection. Case 1, whose record is summarized graphically in Fig. 1, developed an infected haematoma in the abdominal incision, which responded promptly when superficial drainage was effected on the 14th day. Case 3 developed a tender mass in the right iliac fossa 13 days after antibiotic therapy was discontinued. A second laparotomy revealed a localized abscess, and at this time abdominal drainage was carried out. Aureomycin was not given after the second operation, and it is worthy of note that the febrile period in this instance was two days longer than after the first surgical intervention.

Case 4 had an antecedent history suggestive of peptic ulcer. Perforation of the ulcer, as evidenced by sudden onset of abdominal pain with subsequent distension and frank signs of peritonitis, undoubtedly occurred three days before entry into the hospital. Laparotomy performed shortly after admission revealed a perforating lesion in the anterior pyloric region with a considerable amount of purulent exudate in the peritoneal cavity. The perforation was closed by suture. Aureomycin therapy was begun about six hours post-operatively. Gastric drainage was maintained by a Ry'e's tube, which was left in place. Following aspiration of the contents of the stomach, aureomycin, which had been removed from the capsules and suspended in a small amount of water, was administered by means of the tube. The record of Case 4 is summarized graphically in Fig. 2. Twenty-four hours after operation the abdomen was no longer rigid, and by the sixth day the temperature had returned to normal. Convalescence was uneventful, and the patient was discharged on the 16th day.

Case 5 was admitted to hospital *in extremis* on the 21st day of an illness diagnosed clinically as typhoid fever. Signs of intestinal perforation and generalized peritonitis of three

FIG. 2.—Clinical response of patient with generalized peritonitis secondary to perforated pyloric ulcer (Case 4). Aureomycin therapy was begun promptly after closure of the perforation.

days' duration were present. Laboratory confirmation of the diagnosis of typhoid infection was established late in the disease. Surgical intervention was considered to be inadvisable, as the patient's condition was so poor that it was thought he would not survive an operation. Aureomycin therapy, administered by a gastric tube, was begun three hours after admission. Supportive treatment was given in the form of parenteral fluids and intubation of the stomach and rectum. There was daily improvement in the patient's condition until by the sixth day of hospital treatment abdominal distension had disappeared and bowel movements occurred with normal frequency. Throughout this period and for an additional two weeks the temperature ranged between 99 and 102° F. (37.2 and 38.9° C.). However, after the first week in hospital, the patient was free of signs or symptoms suggesting peritonitis. Repeated cultures of blood, urine, and faeces were negative until the sixth week of observation, at which time two samples of faeces yielded *Salm. typhosa*. Aureomycin therapy had a profound effect on the peritonitis present at the time of admission, but the typhoid infection, which was the basic disease, was apparently unaffected. Aureomycin is known to have little, if any, effect on typhoid fever (Bryer, Schoenbach, Chandler, Bliss, and Long, 1948; Knight, McDermott, and Ruiz-Sanchez, 1949; Woodward, Smadel, and Ley, 1949).

Data on the five cases are presented in the accompanying Table.

Details of Cases

Case No.	Cause of Peritonitis	Duration of Peritonitis before Antibiotic Therapy (days)	Aureomycin Therapy		Duration of Fever After Antibiotic Started (days)	Result	Days in Hospital
			Total Drug (g.)	Duration (days)			
1	Perforated gangrenous appendix	1	20.5	7.5	6	Recovery	38
2	"	2	19.2	7.5	5	"	26
3	"	1	19.5	5.0	4	" (abscess RLQ)	34
4	Perforated pyloric ulcer	3	25.5	6.5	5	Recovery	16
5	Perforated typhoid ulcer (not operated)	3	30.5	7.0	21	"	56*

* See text.

Summary

Five cases of generalized peritonitis secondary to perforating lesions of the gastro-intestinal tract were benefited by treatment with aureomycin. Four of these received the drug post-operatively; the fifth recovered without surgical intervention.

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EPITHELIOMA AND PAPILLOMA ARISING ON RECENTLY IRRADIATED SKIN

REPORT OF THREE CASES

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[WITH PHOTOGRAVURE PLATE]

Hyperkeratosis and epitheliomatous degeneration are well recognized as late complications of chronic radiodermatitis following treatment. Typically they develop on a basis of obvious skin damage such as atrophy, telangiectasia, epidermal thickening, etc., though they may at times be caused by repeated irradiation over several years without obvious skin reaction. The latent interval is usually several or many years; MacKee and Cipollaro (1937) state that x-ray epithelioma has been seen as early as two years after excessive irradiation. The same authors (1946) refer to epithelioma shown to occur within a year after the healing of a third-degree reaction—that is, an “acute necrosis” involving the true skin (dermis).

The following cases, occurring a very few months after x-ray reactions of only moderate severity (second degree, with shedding of epidermis only), therefore seem to be worthy of record.

Case 1

Mr. A., aged 65, had carcinoma of the larynx involving the left cord and anterior commissure. Biopsy from the cord had shown a Grade 3 squamous epithelioma (Plate, Fig. 1). No secondary nodes were felt.

Treatment was given by x rays at 200 kV, H.V.L.=1.5 mm. Cu, filter of 1 mm. Cu and 1 mm. Al, 40 cm. F.S.D.; output (for 8 by 6 cm. field, including backscatter) 60 r per minute. Two principal parallel fields were used, with the aid of a wax mould which served the double purpose of acting as a “beam director” and filling in the air gaps. From December 28, 1946, to January 21, 1947, these two fields were treated daily to a total of 3,450 r incident dose on each (initial dose of 300 r, then 9×350 r)—24 days overall; treatment was continued from January 23 to 28 by an 8 by 6 cm. field from the back, to 1,200 r incident (3×400 r). Total treatment time was therefore 31 days, the estimated tumour dose was 4,600 r, and the skin dose at the sides of the neck approximately the same. The skin reaction proceeded to a deep erythema with dry desquamation and a few small moist patches. Healing was rapid and uneventful.

Seven weeks after the end of treatment there was no trace of the primary lesion, the site of which was marked by a pale scar; the case notes record “little skin change” in the neck. In June, 19 weeks after treatment, “a little atrophy and pigmentation in the treated region” was noted; in the middle of the field on the right side was a skin nodule 7 mm. across, which according to the patient (an intelligent observer) had been present five weeks. A month later it had grown to 9 mm.; the accompanying photograph (Fig. A) shows its appearance at that time. It was therefore excised and sectioned; the histological report stated: “The section shows the structure of a simple squamous papilloma, which has been completely removed” (Fig. 2). The patient has remained well to date, after 26 months.

FIG. A.—Case 1. External lesion in July, 1947: simple squamous papilloma.

Case 2

Mr. B., aged 72; carcinoma of hypopharynx (right arytenoid region), with a hard fixed secondary mass of nodes 4 by 2.5 cm. below the angle of the jaw on the right side. A “needle biopsy” (Ellis and Hermitte, 1947) from the nodes showed “several portions of a Grade 2 squamous epithelioma, in a mixture of blood and acute inflammatory exudate” (Fig. 3).

Treatment.—The same factors were employed as in Case 1. Two parallel fields were used, each 10 by 8 cm. to include primary and nodes. Between February 14 and March 19, 1947, 3,000 r was given to each field, by treatment on alternate days (12×200 r, then 2×300 r), both fields being irradiated at each session; the overall time was 33 days. The skin dose was estimated to be 3,900 r, and the dose at the primary about the same. The skin reaction was an erythema of moderate depth. Primary and nodes regressed to a considerable extent, but 11 weeks after the end of treatment a nodule 1.5 cm. across was noted within the treated field on the left side. This was excised, and the section report stated: “Grade 1 squamous epithelioma which appears to be primary skin growth. Completely removed” (Fig. 4). One year after treatment the patient died from the effects of the primary lesion.

Case 3

Mr. C., aged 76; secondary nodes in neck, primary uncertain. There was a large hard fixed mass of nodes below the angle of the jaw on the right, 6 by 3.5 cm. Needle biopsy showed “rather undifferentiated malignant cells, probably anaplastic squamous carcinoma” (Fig. 5).