thrown into sharp relief by the mobilization of our manpower for war. It would occasion little surprise if the quickening tempo of modern life were found to have a direct bearing on the problem presented by the increasing occurrence of the dyspepsias. No entirely convincing clue to this enigma has yet been offered, but it will be interesting to learn whether or not life in our Forces is adding significantly to the already high frequency of such disorders. Final judgment on this point must, of course, await the conclusion of the present conflict. We are in entire agreement with the leading article in the *British Medical Journal* of December 14, 1940, which stated that "the Army still marches on its stomach even though it travels in mechanized vehicles," and the dyspeptic passenger must be carefully scrutinized before taking part in the journey.

Summary and Conclusions

In Army medicine digestive disorders are presenting a large and increasing problem. Of 790 medical in-patients 246 (31.1%) were admitted to a military hospital on account of gastro-intestinal complaints.

The methods of investigation and treatment of dyspeptic patients in a large military hospital are outlined.

Of 246 cases of digestive disorder 135 (54.88%) were found to have duodenal ulcers, 23 (9.35%) had gastric ulcers, 60 (24.39%) gastritis, and 28 (11.30%) miscellaneous dyspepsias. Details are given of the clinical findings in these groups and of the ultimate disposal of the patients. A review of 353 similar cases admitted for radiological investigation to another military hospital yielded substantially similar results.

Many observers have shown that peptic ulcer is the major cause of sickness among the Forces. In our series 64.23% were proved to have peptic ulcer, cases with duodenal ulcers forming 85.4% of this group.

Complications such as haematemesis and perforation were conspicuous by their rarity.

In the vast majority of ulcer patients we were dealing with an exacerbation of an old-standing condition which was adequately dealt with in civil life by simple medical treatment, enabling the sufferer to continue as a useful member of the community. But the strain of Army life tends to induce recrudescence.

Patients with acute gastritis can often be adequately treated by their own medical officers, while men with either acute or chronic gastritis, if given a fresh start by a period of residence in hospital, generally do well and can safely be allowed to remain in the Army.

It is suggested that the quickening tempo of modern life is related to the increasing occurrence of the dyspepsias, especially peptic ulceration, and the question is raised whether or not Army life will add to the frequency of such disorders.

The point of highest military importance which emerges from this investigation is the large proportion of those with a definite history of peptic ulcer who on embodiment in the Army soon become a serious charge on the medical authorities.

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EXPERIENCES WITH SULPHANILAMIDE DERIVATIVES IN SOME TROPICAL CONDITIONS

BY

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A review by Buttle (1939) of the uses of sulphanilamide derivatives in tropical diseases prompts me to give my experiences with this drug not only in some purely tropical diseases, but also in some of world-wide distribution the clinical picture of which is influenced by the tropical background, and in the treatment of ordinary streptococcal invaders of pathological conditions essentially tropical in origin.

All the cases reviewed were treated in Trinidad, British West Indies, except where otherwise stated. The drugs used were sulphapyridine (M & B 693) and sulphanilamide (prontylin).

Diseases due to Filterable Viruses

(a) *Dengue*.—In a series of cases studied during an epidemic in Trinidad (Earle, 1939a) sulphapyridine had no apparent curative effect on the temperature, rash, or cervical gland enlargement (which is present in from 30 to 60% of cases—Castellani, 1939), arthralgia and myalgia, or state of malaise in the patient. Indeed, the epigastric pain and headache produced by the drug so exacerbated the patient's condition that its use had often to be abandoned. The danger of reducing the leucocytes in a condition in which there is already a leucopenia is a further disadvantage in the use of sulphapyridine.

Case 1.—A female English child aged 2, first seen on April 26, 1939, when she complained of generalized pain. Temperature 101° F.; a well-marked dengue rash was present. Sulphapyridine, 0.125 gramme (1/4 tablet) four-hourly, was given. An improvement was recorded on April 27, the temperature falling to 99° F.; but it subsequently rose again, giving the saddle-back type of curve (Megaw, 1937). Recovery was uninterrupted. Here, although at first sight it might be thought that the drug had had a curative effect, it was obvious that it had no influence on the course of the disease.

Case 2.—A female aged 17, English, seen on February 2, 1939, during the dengue epidemic, when she had generalized body pain, headache, and enlargement of the submaxillary and superficial cervical lymphatics. Temperature 103.8° F., pulse rate 126. A red flush over chest and face was seen. Sulphanilamide 2 grammes (4 tablets) was given at once, followed by 1 gramme four-hourly. The course was continued for five days. No alteration in the patient's condition occurred, and she took the usual time to recover.

Case 3.—A Scotsman aged 35, seen on February 12, 1939, when the usual clinical signs of dengue were apparent. 1 gramme of sulphapyridine was given four-hourly. The next day the pains had greatly increased and epigastric pain, nausea, and vomiting were present. The drug was suspended; the patient's condition improved after twenty-four hours, and he made an uninterrupted recovery.

(b) *Lymphopathia Venereum*.—The beneficial effects of sulphanilamide compounds in my practice have already been described (Earle, 1939b, 1939c, 1939d). Briefly, good results may be expected in early cases, before fistula formation. But even in later stages or when fistulae have formed some improvement may result. Lymphogranulomatous papillae of the vulva and rectum are reduced in size and indurated strictures of the rectum become softer and therefore amenable to dilatation.

Ulcerative Granuloma

The action of sulphanilamide alone on ulcerative granuloma, although favourably reported on by Ross (1939), has in my experience proved unsatisfactory. When combined with injections of foudadin (a complex salt of trivalent antimony with a pyrocatechin derivative) the results are much more encouraging (Earle, 1940-1). The treatment consists of a course of sulphapyridine, 3 grammes daily for five days, the course being repeated after an interval of three to four days. At the same time the standard course of foudadin, injected intramuscularly, is given. (Initial dose 1.5 c.cm., rising to 5 c.cm.; total dosage, 75 c.cm.) The injections are made every second day.

Tropical Pyomyositis

The action of sulphanilamide in this condition has already been described (Earle, 1939e). The standard dosage of the drug may be given, and good results are to be expected.

Tropical Ulcer

(a) *Typical Tropical Ulcer*.—Sulphanilamide is of value only in very early ulcers or pre-ulcerative papules of the idiopathic type (Earle, 1940a). It is of very limited value in old-standing ulcers.

(b) *Tropical Ulcer Associated with Popliteal Abscess*.—I group separately the case described below, as I have only once seen tropical ulcer associated with popliteal abscess in all the cases of this ulcer I have studied in Trinidad. This type of case is common among Chinese coolies at Ocean Island (Central Pacific) and among native Nauruans at Nauru. Possibly this form of tropical ulcer differs from the ordinary tropical ulcer in aetiology.

Case 4.—A male negro aged 14, first seen on June 22, 1939, when examination showed a tropical ulcer of the left foot associated with a popliteal abscess of the same side. Sulphapyridine, 2 grammes daily for five days, was given. On June 30 the popliteal abscess was almost healed; the course of sulphapyridine was repeated, and on July 11 both abscess and ulcer had healed. (Cod-liver oil was used as a local application in this case.)

Streptococcal Infection Implanted on to Fungous Diseases

In the Tropics certain fungous diseases appear to be readily infected by streptococci.

(a) *Intertriginous Ringworm*.—The infection caused by *Trichophyton (Epidermophyton) interdigitale* often leads to severe cellulitis or severe ulceration or maceration of the feet, due to a secondary streptococcal infection. I have found it advantageous to clear up the secondary infection with sulphanilamide before proceeding to a radical cure of the fungous condition.

Case 5.—A Chinese clerk aged 30, first seen on January 10, 1939, when he complained of pain and swelling of the left foot. On examination there was a well-marked ringworm of all the interdigital clefts, with cellulitis involving the whole foot. Sulphapyridine, 3 grammes daily for six days, was given, and magnesium sulphate and glycerin were applied to the open lesions. On January 19 the cellulitis had cleared up, and local treatment (Castellani's fuchsin paint) could be started.

Case 6.—An English storekeeper aged 40, seen on December 3, 1939, when he complained of severe ulceration of the interdigital clefts and soles of both feet, this condition supervening on "athlete's foot." Sulphapyridine, 4 grammes daily for four days, was given. The course was repeated twice, two-day intervals separating the courses. At the end of these courses the secondary infection had healed sufficiently for the fungous condition to be treated by x-ray therapy.

(b) *Fungous Infection of the External Ear*.—"Tropical ear," or "salt-water ear," appears to be an invasion of the

external auditory meatus by the *Pityrosporon* of Malassez, secondarily invaded by streptococci and staphylococci. If untreated, crops of painful furuncles may occur. I found it a useful precaution to give sulphanilamide in incipient "tropical ear" and also in later cases in which furuncles had already formed. In five cases, all in young children, sulphapyridine given in an appropriate dose at the first sign of soreness following sea-bathing prevented the onset of complications. In a sixth case multiple small abscesses supervening in an infected ear were cured in three days.

Complications of Yaws

One case of severe secondarily infected yaws favourably influenced by sulphapyridine is worthy of record.

Case 7.—A negro boy aged 3, found on May 23, 1939, to be suffering from infected and ulcerative yaws of legs. Sulphapyridine, 1 gramme daily for three days, together with bismuth injection, was given. On June 1 the gross secondary infection had cleared up. Bismuth injections were continued and neosalvarsan injections were added to the treatment.

Lymphangitis

(a) *Non-filarial*.—Lymphangitis of obscure origin is seen in Trinidad. It is not necessarily filarial, since filaria is rare in that island (see Health Reports of Trinidad and Tobago for the years 1937 and 1938). A typical example of non-filarial lymphangitis is appended.

Case 8.—A white Trinidadian overseer aged 48, seen on March 15, 1940, when he complained of fever, and pain and swelling of the right leg. He gave a history of a shrapnel wound in the right thigh during the 1914-18 war. Since his demobilization and return to Trinidad he had had recurring attacks of lymphangitis in the affected extremity, these being at times combined with erysipelas-like attacks. The temperature was 102° F., pulse rate 96. The right thigh and calf were swollen and painful. Irregular red areas, somewhat like erysipelas patches, were scattered over the skin of the calf. Thickened, red, inflamed lymphatics were seen in the thigh, and the crural lymph glands were swollen and tender. About four inches distal to Poupart's ligament there was a deep irregular scar, which caused great distortion of the adjacent tissues. The whole extremity was extremely tender. *Plasmodium vivax* but no microfilariae were found in the blood films. Sulphapyridine, 4 grammes daily (together with atebirin, 3 tablets daily), was given, and the fever and leg infection subsided in five days.

(b) *Filarial*.—In this condition—filarial lymphangitis—I have recently seen very favourable responses to sulphapyridine therapy in native Nauruans. As pointed out by Buttle (1939), this beneficial action is probably due to a curative effect on secondary streptococcal invaders.

Venomous Marine Animals

(a) *Portuguese Man-of-war (Physalia pelagica)*.—Stings of this animal may, in my experience, give rise to severe ulceration and necrosis of the affected parts. Cellulitis and ulceration due to secondary infection may respond to sulphanilamide, and I therefore consider it a wise precaution to give the drug prophylactically in all these stings.

Case 9.—A white Trinidadian aged 21, seen on November 2, 1939, immediately after leaving the sea. The chest, abdomen, back, and arms were covered with scores of lesions from the tentacles of a Portuguese man-of-war. Sulphapyridine, 2 grammes, was given at once, followed by 1 gramme four-hourly for two days. No complications occurred.

Case 10.—A Chinese aged 23, seen on July 6, 1939, when he displayed severe cellulitis of the right forearm following a sting by a Portuguese man-of-war. Sulphapyridine, 4 grammes daily, was given. Recovery occurred within a week.

(b) *Sea-urchins*.—Spines of the white sea-urchin (*Tripneustes esculentus*), known in Barbados as the "sea-egg," may give rise to suppuration if not completely

removed. The use of sulphapyridine in such cases has already been described (Earle, 1940b).

(c) *Catfish*.—The spines of the catfish of Trinidad may produce localized cellulitis, ulceration, or gangrene. Sulphanilamide should be given prophylactically if possible.

Case 11.—A negro aged 14, seen on January 7, 1939, when he showed a cellulitis of the right hand due to a prick from a catfish spine. He was given sulphapyridine, 3 grammes daily, for two days. Cure was reported on January 9.

(d) *Barracouda*.—Bites from this fish often suppurate, and should receive prompt sulphanilamide therapy.

Case 12.—A Venezuelan aged 40, seen on January 8, 1939, when he displayed an infected barracouda bite of three days' duration. The area bitten was surrounded by a zone of ulceration and cellulitis. Sulphanilamide, 1 gramme thrice daily, was given, and the wound was dressed with magnesium sulphate and glycerin. On January 11 marked improvement was noted, and cure was complete on January 18.

Venomous Arthropoda

(a) *Insecta*.—(i) Chigoe Disease.—Ulceration and cellulitis surrounding the gravid female chigoe (*Tunga penetrans*) may respond to sulphanilamide therapy. I have seen three such cases react satisfactorily in this manner.

(ii) *Culicoides* Bites.—Prophylactic treatment of bites of various *Culicoides*—*C. amazonius*, *C. furens*, *C. stellifer*, and *C. diabolicus* (Myers, 1935; Adamson, 1939)—which in Trinidad may be the starting-point of a tropical ulcer, has already been described (Earle, 1940a).

(b) *Arachnida*.—Several cases of encrusted scabies (gale norvégienne) have responded well to sulphanilamide therapy combined with local treatment with mitigal (dimethyl-diphenylene disulphide).

Case 13.—An East Indian labourer aged 20, seen on March 10, 1940, when he had encrusted and septic scabies of the palms, abdomen, penis, and scrotum. Sulphapyridine, 3 grammes daily, together with mitigal locally, was given. Cured in ten days.

(c) *Myriapoda*.—Severe cellulitis and ulceration which may follow bites of the centipede (? *Scolopendra gigantea*) have been controlled by sulphanilamide. Four successful cases have been noted, of which one is here described.

Case 14.—A negro labourer aged 30, seen on January 17, 1940, with severe cellulitis of the left hand following a centipede bite on the previous day. He was given sulphanilamide, 1 gramme thrice daily. The infection subsided in four days.

Beriberi

Bearing in mind the possible association of a bacterial exotoxin with vitamin B₁ deficiency in the production of beriberi (Low, 1936; Joyeux and Sicé, 1937), I tried the effect of sulphanilamide in a case of B₁ avitaminosis associated with cardiac lesions and oedema of the feet.

Case 15.—A female East Indian aged 25, first seen on January 4, 1939, when she complained of tingling and loss of sensation in the legs and feet, swelling of the feet, dyspnoea on slight exertion, and general weakness. The date of onset of the disease was uncertain. Examination showed a poorly built woman. The lips and conjunctivae were pale, teeth carious, and tongue furred. Firm oedema of both feet, dilatation of the right heart, and systolic murmurs were present. Pulse rate 96, tension low. Sensation of light touch was impaired in both feet and calves. Ankle-jerks were sluggish, knee-jerks were present. Ankylostome ova were observed in the stools. No malarial parasites were found in the blood. Anti-hookworm treatment was started at once. Vitamin B₁, 5,000 units daily, was injected intramuscularly for a week, and sulphanilamide was given orally for five days. On January 7 the patient had less dyspnoea and less oedema of the feet. A second course of sulphanilamide was given after three days' interval and vitamin B₁ every second day. The patient made an uninterrupted recovery.

It is of course useless to draw any conclusions from an isolated case history. However, in cases of infantile beriberi seen recently in the island of Nauru—the patients sometimes being desperately ill, showing head retraction, spasticity of the limbs, Kernig's sign, and mental confusion, in addition to liver enlargement and hydrocele—dramatic results often followed lumbar puncture and intrathecal and intramuscular injection of large doses of vitamin B₁ combined with sulphapyridine by mouth. The vitamin used alone appeared to produce far less satisfactory results. Confirmatory work is obviously necessary in this obscure condition.

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LABORATORY INFECTION WITH BRUCELLA ABORTUS

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The report by Huddleson and Munger (1940) of an epidemic of brucellosis in Michigan State College due to laboratory infection with *Brucella melitensis* raises in a dramatic way the problem of dissemination and the possible portals of infection in man of the pathogenic *Brucella* group.

Three Recent Cases

In this connexion the experience in my laboratory is perhaps worth recording, although in this case infection was due to the less virulent *Br. abortus*. Case 1 (H. N. G.) arose two years after experimental work had been in progress with a strain of *Br. abortus* originally isolated from a human case of undulant fever. The organism, after primary isolation in liver broth in an atmosphere of 10% CO₂, had been subcultured on plain media (agar or glycerin-agar) almost daily throughout this period, without any animal passage, and latterly grew rather better in air than in 10% CO₂. Careful precautions against accidental infection were taken, and the only direct exposure was in making frequent colonial counts from open agar plates, and in preparing and diluting small volumes of bacterial emulsions in saline from agar slopes. The attack of undulant fever did not arise after any unusual procedure or undue exposure, or after any known accidental contamination of the skin or laboratory benches. It followed a severe course, and though a trial of most of the therapeutic measures described was made, it subsided naturally after three months, immediately following the most severe pyrexial period of the illness. Sulphanilamide treatment was not, however, adequately carried out owing to sensitivity to the drug, which on one occasion produced an almost complete amblyopia lasting several hours. In the fourth week of convalescence a severe and protracted "myositis" of the lumbar muscles arose. There was no pyrexia, and the lesion was possibly allergic in nature.

Work was restarted with the same strain of organism two months after recovery, with more stringent precau-