reduction product of androsterone, which is very insoluble in body fluids, no fewer than thirteen successive implantations of the same set of 6-mg. tablets were made into successive sets of castrated rats for ten-day periods. The total time of each tablet in the animals was thus 130 days—about four calendar months. At the end of this time the tablets were reduced almost to nothing, but the remaining material was still physiologically active. The total weight of accessory organs produced in these experiments was incomparably greater than can be obtained by the injection of 10 mg. of the hormone in oil solution.

Tablet administration has the obvious advantage that there is no necessary fluctuation in the amount of material absorbed, such as must result from even frequent injection. Once absorption has begun it will continue week after week, or even month after month with substances of suitable solubility, declining steadily as the tablet decreases in surface area, but free from minor irregularities. There is no obvious local reaction in experimental animals following the subcutaneous implantation of tablets of oestrone, testosterone, or testosterone propionate. The evidence that neither testosterone nor oestrone is inactivated by long incubation at body temperature in the subcutaneous fascia is conclusive, and it would seem that where very prolonged effects are required a clinical trial of the technique is warranted.

Progesterone

The effectiveness of progesterone does not seem to be so much altered by conditions of administration, though possibly this is because the rabbit, the usual test animal, seems to make more economical use of injected gonadal hormones than does the rat (Deanesly and Parkes, 1937). So far as our preliminary experiments show, tablet administration of progesterone gives no increase of response in short duration experiments as compared with daily injections, possibly because absorption is extremely slow, but it is already obvious that a very prolonged effect from a single administration could be obtained by the tablet technique. In view of the difficulty of esterifying progesterone the technique may be of practical value.

Other Substances

Problems of absorption are not peculiar to gonadal hormones. It is well known that the effectiveness of gonadotropic extracts is raised by increasing the subdivision of the dose. Addition of a precipitant such as zinc sulphate to the solution also greatly increases effectiveness, presumably by retarding absorption (Maxwell, 1934). Unfortunately their high water solubility and their lability in contact with water at body temperature make gonadotropic preparations unsuitable for tablet administration. The observations of Bates and Riddle (1936) on the influence of route of administration on the effectiveness of prolactin, and those of Ch'en and van Dyke (1936) on increasing the action of thyrotropic extracts by the addition of merthiolate, are also relevant.

There are a number of well-known examples of the same principles applying to other hormones, notably the work leading up to the production of protamine insulin. In general it may be said of many of the hormones concerned in producing chronic effects that purification and isolation make the active substance so readily absorbed by the animal that in practical use high effectiveness can only be obtained by frequent injections or by retarding absorption in one of the ways described above.

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OTITIS EXTERNA: "HOT-WEATHER EAR"

AN INVESTIGATION OF 100 CASES AND A METHOD OF TREATMENT

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The scope of this contribution is limited to inflammation of the external auditory meatus apparently caused by hot humid climatic conditions and associated with an infection with *B. pyocyaneus* in pure culture. At the aural clinic of the Royal Air Force Hospital, Aden, a series of 100 cases was investigated, a line of treatment evolved on a simple practical basis, and search made for a common causative factor.

Occurrence

Infections of the external auditory meatus with *B. pyocyaneus* (*Pseudomonas pyocyanea*) among the troops in Egypt were described during the great war, and more recently have been reported from the Seychelles, Canton, Ascension, and East Africa (Hermitte, 1932), America (Greaves, 1936), and Australia (Bettington, 1934). Inflammations of the meatus are common in the troops generally,* and are often ascribed to a fungus infection. The conditions appear to be very similar and equally resistant to treatment, but as none of the cases which were bacteriologically examined in this series was found to have a fungus infection or any organism other than *B. pyocyaneus* and *Corynebacterium ceruminis diphtheriae*, no attempt is being made here to discuss any other infection.

It has not been possible to assess the incidence of the trouble in Aden. Many cases are treated as out-patients elsewhere than at the Royal Air Force Hospital, but all types seem to be affected, and it is by no means confined to the troops. A record of the monthly total of new cases was kept (see Chart), and it was noted that the majority were affected during the May-June and August-September

* This subject is dealt with in a joint discussion on the effect of aural conditions on fitness for active service, *Proc. roy. Soc. Med.*, 1937, **30**, 1523.

periods, more particularly the former. At these times—the beginning and the end of the south-west monsoon—the temperature and the relative humidity increase, and there is scarcely any appreciable "cooling off" during the night. "Prickly heat" is also very common at this

Chart showing in graphic form the new cases of otitis externa occurring monthly.

period; both conditions, however, improve under the fresher weather during July and August, and during the cool season they almost entirely disappear.

Aetiology

It has been thought desirable to investigate two popular theories—that of causation by bathing, and that of irritation by sand or interference. Of the 100 cases only forty-six had bathed in the sea within approximately one month previous to the onset of symptoms. Of these, thirty-five were regular bathers, the remainder taking only an occasional swim. Twenty-one used wool plugs in the ears while bathing, and twelve admitted to cleaning the ears with wool wound on match-sticks after bathing. The average number of bathes per week among the regular swimmers was 2.85. Figures were unfortunately not available for the total number of bathers at various times throughout the year, but as a matter of observation it is certain that there is no marked increase during the hot periods.

There are only one or two small private bathing pools of fresh water in Aden, so practically all bathing is in the sea. While it is admitted that the number of cases is small for the purpose of forming a definite judgment, these figures appear to discredit the sea-bathing theory. Fresh-water shower-baths were taken, on an average of two a day, by ninety-five of the patients, and ordinary slipper-baths by forty. The water used for this purpose is supplied from deep artesian wells and is also used for drinking. It is analysed regularly at the Royal Air Force Laboratory, and no evidence of faecal contamination has been evinced. Only twenty-five of the patients could fairly be considered to have been more exposed than other residents to sand in Aden, where the amount is not great: one or two minor sand-storms may occur in July, August, or September. It was observed that a few individuals had served for some years in India or Iraq and had been unaffected by real sand-storms, while at a time when personnel were encamped locally in bad drift sand the incidence of the condition did not increase. None of the cases had any gross disease of the ear, nose, or throat on examination, other than the meatitis.

The origin of the organism is still in doubt. Faecal contamination has been suspected, but there is hardly any water-borne sanitation in Aden at present, and, as has been noted, there is no evidence of a contaminated water

supply. It is, however, a fairly ubiquitous organism, and it appears that certain factors promote its growth and render it pathogenic. No suggestion can be given as to the reason why *B. pyocyaneus* in particular should be the infecting organism. It is believed that the chief of these factors are moisture and maceration of the epithelium, especially if devitalized by trauma. It is well known that these cases present a moist appearance clinically, and that the corollary in treatment is to keep the ear dry. Also it is shown that most cases are infected when the humidity of the climate is greatest.

As a ship surgeon, outward bound, I first met the condition in the Red Sea and to a lesser extent in the Java Sea, while cases improved in the cooler climates. This view has been confirmed by naval and ship surgeons passing through Aden, who also note that it is more common among stokers, some of whom report for treatment automatically, as the result of past experience in the tropics, when they arrive in the Red Sea. There is no evidence that all these cases are associated with *B. pyocyaneus* infection. For these reasons the term "hot-weather ear" has been maintained—a term used by Lieut.-Colonel Palmer, R.A.M.C., when he described it as a clinical entity (Palmer, 1934)—because this appears to be the strongest aetiological factor.

Clinical Aspects

Otitis externa has been described as clinically divided into two categories—the dry and the moist. This division has not appeared to be at all satisfactory, and for the purpose of description and treatment it has been found desirable to enlarge upon it. The classification adopted here is as follows: (1) acute; (2) subacute; (3) chronic; and (4) relapsing. The first two conditions and usually also the third are "moist," whilst the fourth is "dry." There is, however, considerable overlapping between these classes.

1. *Acute*.—The patient usually complains of acute pain in the ear, often of a throbbing character, that has developed after a variable period during which he will have noticed increasing discomfort and usually some discharge from the ear. Pyrexia of 101° to 103° F. and pre- and post-auricular lymphadenitis often occur. Occasionally there is a slight degree of trismus, and mastication is painful. On examination the auricle may be slightly oedematous, and any movement of it becomes acutely painful. The meatus is occluded by swelling of the epithelial walls, which appear white and sodden, and a white curdy covering is often observed externally. The tympanum is not visible by ordinary auriscope examination, and there is moderate diminution of hearing. If the meatus is examined under an anaesthetic the inner part is seen to be covered with sodden white epithelial debris, removal of which shows an inflamed, red, and very angry-looking meatus; but only rarely is there a definite boil to be seen. The tympanum is usually only affected to a slight degree; the normal light reflex is diminished, and the external surface is most frequently granular in appearance. Sometimes there is moderate injection in the region of the malleus, but never any bulging or pulsation. In most cases the tympanum is normal and mobile. As the condition progresses under treatment there comes a point of relief from the acute symptoms which is sometimes associated with the liberation of thin sero-purulent fluid and resolution of the acute phase temporarily. Observation and incision have failed to locate definite pus during this stage.

2. *Subacute*.—The majority of cases are first seen in this stage, and a large number can be prevented from

becoming acute. The complaint is of an aching ear, often associated with discharge from the meatus, which causes a yellow stain on the pillow-slip overnight. Slight adenitis may be present, and the auricle is tender on movement but not acutely painful. Hearing is only slightly diminished, but most distressing symptoms are caused in the hot humid atmosphere, and sleep is lost at night. Concentration at work is very difficult, and the condition may well be described as extremely aggravating. On examination the meatal walls are considerably swollen and "soggy," with plaques of white cheesy debris partly adherent and partly lying in the lumen. The tympanum can usually be seen through a narrow space and is generally normal. One very characteristic pitfall is a curtain of debris immediately lateral to the tympanum, usually incomplete, which very closely resembles a perforated tympanum with acute meningitis, the whole being bathed in purulent exudate. It is only when this has been removed that a normal tympanum is found to exist, and the differentiation of these conditions is largely a matter of familiarity with the appearances on auriscopy. For this reason the bright magnified view obtainable with an electric auriscope makes this the most useful method of examination. Removal of the sodden debris leaves excoriations which bleed very readily, and the ear then becomes more painful. Only those pieces which appear already detached can be removed without causing further trauma. There is in addition a thick purulent exudate, which lines the meatus and is very tenacious and difficult to remove efficiently. Most particularly is this true of the antero-inferior recess of the meatus immediately lateral to the tympanum. In long-standing cases this pus has been observed to assume a yellowish-green coloration with great regularity.

3. *Chronic*.—In this stage without treatment the condition in unfavourable circumstances readily relapses into the subacute phase. With treatment, however, and efficient careful removal of debris, the meatus assumes a slightly thickened red appearance, while scaly flakes of dead epithelium form on the walls. The tympanum is normal, but there is most frequently a sodden "subacute" area in the recess medial to the elevated floor of the meatus which is extremely difficult to eradicate. The chief symptom of this stage is most profound and distressing irritation, whilst the condition is aggravated by the rubbing and shaking of the auricle which this irritation provokes. There is a variable amount of discharge, which is of very thick greenish-yellow pus. Hearing is almost normal.

4. *Relapsing*.—In this stage the ear is to all intents and purposes normal both to the patient and on inspection. For a week or two after the chronic stage has been cleared after-treatment is necessary, as under very humid conditions the ear sometimes "feels wet again." If this is ignored recurrence is likely. In some cases this feeling persists during the hot season, and more acute symptoms can then be precipitated by the injudicious use of glycerinated ear-drops and wool plugs in the meatus (see below), designed to keep out irritating particles of foreign materials such as sand and dust. Cases under this heading are regarded as potential infections and are given prophylactic advice and treatment.

Bacteriology

Meatal swabs were taken from thirteen typical cases in varying stages. The reports upon each were of Gram-negative, non-sporing, motile bacilli with no evidence of fungus. Eight produced pyocyanine on culture and gave the sugar reactions of *B. pyocyaneus*. All contained

Corynebacterium ceruminis diphtheriae. A typical report of one of these cases in detail was:

A greenish-yellow pus, almost cheesy in consistency. Direct smears and hanging drop: numerous squamous epithelial cells. Actively motile coliform bacilli in large numbers, which were isolated in pure culture.

Characteristics of Gram-negative bacillus isolated:—Motility: + + +. Agar: Moist grey spreading growth. MacConkey: Moist grey spreading growth. Fluid MacConkey: No change. Glucose: Acid only. Lactose, saccharose, mannite, maltose, dulcitol: Minute bubbles of gas with no acid change, using Andrade's indicator. Peptone: No indole formed in five days; filmy grey pellicle. Litmus milk: Digested in twenty-four hours; no clot formation; greenish tinge developing to an intense blue-green by the fifth day. Glucose broth: Brownish wrinkled pellicle, Voges-Proskauer reaction negative.

Conclusions: The organism appears to be a true *B. pyocyaneus* in which, perhaps owing to oxygenation in the external ear, pyoxanthose, a yellow pigment, is in excess of pyocyanine.

In many cases there was intense blue pigment production in most of the above media. Of the five remaining cases in which the full sugar reactions were not examined the reports were:

Actively motile, Gram-negative bacillus, giving the following reactions:—Glucose: Acid. Lactose: No change. Mannite: No change. Litmus milk: Slight acidity.

The cases which were examined were selected at random, and presented lesions typical of the condition. It has already been pointed out that the pigmentation of the pus in the later stages and the definite yellow staining of the pillow-slips due to discharge from the meatus are fairly well-marked clinical signs.

Treatment

In standardizing treatment cases were classified into the clinical groups described, and the routine was strictly followed according to the group.

ACUTE CASES

These cases, consisting of those with "boil" formation or obstructed meatus with excessive tenderness, were most frequently admitted into hospital, where treatment could be more intense, especially if pyrexia was present. With this group no effort was made to clean out the meatus; to attempt it is sheer brutality, as the pain is exquisite. The meatus is very gently syringed with boric lotion, as hot as the patient will tolerate. After this the meatus is allowed to drain by posture for a few minutes. The ear is next filled with warm 1 per cent. carboglycerin drops and a hot boric foment is applied, large enough to include the pre- and post-auricular glands. This treatment is carried out four-hourly, and is combined with initial purging by 4 grains of calomel in split dosage followed by salts. At first there was considerable diffidence in syringing with really hot lotion, lest vestibular disturbances should be caused. However, this does not appear to occur in these cases; most probably because the lotion does not freely reach the depths of the meatus. The relief is great and almost immediate, whilst the removal of small portions of debris makes the application of the carboglycerin more effective. The latter has been used only in 1 per cent. solution, and as such the analgesic effect has proved satisfactory when combined with the hot syringing and fomentation. The question of incision in these cases is interesting. In some earlier cases the pain was so acute that the meatus was examined under an anaesthetic. Sodium evipan was used, but no actual

boil could be found. Once or twice the most turgid and inflamed region was incised without the liberation of definite pus. Despite the relief this procedure gives it is considered that incision is contraindicated. Even if a definite boil is seen, which is unusual, it seems better to allow it to burst under the conservative treatment described; the pain is relieved speedily by both methods, and convalescence is not hastened by incision. Except for these early cases no occasion to incise the meatus has arisen during the last two years.

SUBACUTE CASES

These are cases in which there is partial occlusion of the meatus that is sufficiently painless to permit the introduction of instruments. In this group the object of treatment is to tide over and shorten the gap between acute occlusion and the relative patency of the chronic infection. The meatus is gently cleaned by direct application of dry sterile cotton-wool on malleable wool-carriers, under direct vision with reflected light. The electric auriscope is used only for inspection in this stage. When moderately clear of debris the meatus is packed firmly, but not tightly, with sterile half-inch ribbon gauze soaked in 1 per cent. carboglycerin, being retained in position by an external wool plug. This procedure is repeated every twenty-four hours. The steady light pressure lessens the swelling, the glycerin loosens the dead epithelium, and the carbolic acts as a mild antiseptic and analgesic. This stage as a rule lasts only two or three days and leaves a clean but inflamed meatus, while debris persists in the recess near the drumhead.

CHRONIC CASES

This group comprises cases in which the condition has been present for some time; those recovering from an acute attack; and those in which the meatus is patent, pus is formed, and epithelial maceration is the rule. In this stage, in which the greatest difficulty has been experienced in ensuring successful and speedy recovery, various forms of treatment were tried and the basic principles of dryness and thoroughness were soon confirmed. Both present difficulties: the dry infected meatus produced the most aggravating irritation and distress to the patient, whilst excessive zeal in removing every piece of debris caused excoriations very easily and rendered the ear sore and difficult to treat.

The routine finally adopted has been as follows. First the ear is cleared of obvious gross debris: a day or two on the treatment described for subacute cases has been found most successful for this purpose. The meatus is then dried with either ether or boric and spirit drops. After mopping with dry sterile wool the patient inclines his head right over, to bring the affected ear uppermost, and is warned to keep his eyes tightly closed. A small quantity of boro-iodine powder is tapped well into the meatus and insufflated with a Siegle's speculum into all parts of the meatus. Care is taken to avoid blowing the powder into the operator's eyes. The meatus is then quickly packed with the powder until it is full, the whole being lightly tamped home. Without delay the meatus is now plugged with a firm pledget of wool.

The dressing is left undisturbed for forty-eight hours. It causes slight discomfort for the first hour or two, but in no case has this been intolerable. At the conclusion of this period the ear is very gently syringed to clear away the remains of the powder, the greater quantity of which has usually been dissolved, and the meatus is filled with boro-spirit drops for a few moments, after-

wards being drained by posture. It is sometimes necessary to detach dried pieces of dead epithelium with forceps, and occasionally small casts of the meatus are removed in this way; otherwise the use of instruments is avoided at this stage, and the meatus is not kept plugged with wool. Boro-spirit drops are applied twice daily for two days, and the treatment is repeated if it is then found necessary. As a rule only two such applications of boro-iodine powder have been indicated, although repetition has occasionally been necessary after about ten days.

Essential points are the drying of the meatus, speed in the application of the boro-iodine powder as the iodine evaporates rapidly in hot climates, and the subsequent avoidance of any form of plug in the meatus. The reason for the last-named is that the cartilaginous portion of the meatus contains sweat glands (Powell, 1934), and any plugging distal to these must cause increased humidity in the meatus and maceration of the epithelium, conditions which predispose to recurrence. With the use of only a thin film of powder it has been found that the iodine evaporates so quickly in a climate such as that of Aden that the filling of the meatus as described is regarded as essential. In no case has this caused any trouble: within a few hours the powder appears to be dissolved by the moisture of the plugged meatus.

After-treatment

Most cases are now discharged from the clinic with a bottle of boro-spirit drops, a small quantity of which they are advised to insert into the meatus last thing at night. Patients are instructed to dry the ears carefully after bathing, especially after taking a shower-bath, by gentle shaking with a towel inserted in the auricle on the tip of the little finger and with the head inclined over on the side. The insertion of wool plugs is strongly discouraged for the reasons mentioned above, although the question of using "a plug of cotton-wool soaked in olive oil during bathing" frequently arises. Unsterile oil and dirty wool are often used, and the plug is sometimes forgotten. It is of doubtful efficiency, and is needless if the ear is carefully dried.

Preparation of Boro-iodine Powder

The method described by Scott Stevenson was taken as a guide (Scott Stevenson, 1935) and modified to suit the climate of Aden. The following description has been prepared by the dispenser at the Royal Air Force Hospital, Aden:

"For the preparation of iodized boric powder sublimed iodine is used in a strength of 1 per cent. in acid. boric. pulv.; the iodine is first broken down with a few drops of alcohol 90 per cent. The boric acid is added in powder form in small quantities as quickly as possible, using a non-porous glass mortar and keeping the mixture moving all the time. As soon as the iodine appears to be evenly distributed the powder is transferred to a wide-mouthed dark glass-stoppered bottle, without waiting for complete drying. Evaporation of the iodine is very rapid; if any delay occurs all the iodine is lost, and the use of a glass-stoppered bottle instead of cork is necessary to preserve the iodine content."

Other Methods of Treatment

In many papers dealing with this and allied conditions there appear a variety of treatments, a number of which have been tried here in the hope of finding one more satisfactory than the others. At first diligent mopping of

the meatus with hydrogen peroxide, then drying with ether, and applying a solution of silver nitrate in spiritus aetheris nitrosi was tried. Then spirit and biniodide of mercury, 1 in 4,000, was substituted for the ether. Argyrol (2 per cent.), mercurochrome (1 per cent.), and liquid iodex packs were given exhaustive trials, with disappointing results. Zinc ionization promised well; a course of five treatments each of 1/2 mA for one-half hour, a stronger current being uncomfortable, produced good results at first, but recurrences were numerous. Vaccine therapy was not tried, although recommended by some observers (Hermitte, 1932), because it was felt that a simpler and more practical method of treatment could be evolved which could be practised efficiently at out-stations. Phenyl mercuric nitrate (Greaves, 1936) was not used in this series.

Finally one case arose in which all efforts to obtain a cure appeared futile; the condition just continued to relapse. First one side would improve and the other commence to discharge, then the state would reverse. This man spent fifty-seven days in hospital, in addition to receiving 107 days of out-patient treatment. The organism was a typical *B. pyocyaneus*, and all the methods of treatment described were tried with no avail. In the end the meatuses were treated with boro-iodine powder on the lines now described, and after one application on each side the condition cleared up completely. He has since passed through the whole hot season without recurrence, and only occasionally applies a few boro-spirit drops at night-time. The routine treatment was then evolved and adopted, with results which have been very satisfying, although not always as spectacular as in this one case.

Results

Since the treatment described was adopted as a routine and applied to the later sixty-six of this series of cases the average number of daily attendances has been 8.27 per case (maximum, 24; minimum, 2). Previously, under the other forms of treatment, this was considerably greater, and in the earlier thirty-four cases of this series the average was 22.6, or, excluding the exceptional case to which reference has been made, 18.1, with a maximum of 72 and a minimum of 3. Admissions to hospital have totalled five from the earlier thirty-four cases (16.6 per cent.) and three from the sixty-six later cases (4.54 per cent.)

Published results of vaccine therapy are good after periods of weekly injections extending over some five or six weeks (maximum, 12; minimum, 3). The vaccines used were autogenous, but the suggestion is made that a stock vaccine might prove equally efficacious (Hermitte, 1932).

Phenyl mercuric nitrate, used 1 in 1,250 in 95 per cent. alcohol, is claimed to have a spectacular effect on the acute stage and to shorten the course and hasten recovery in the chronic and long-standing cases (Greaves, 1936).

Summary

1. A series of 100 cases of otitis externa occurring chiefly during the hot humid seasons of Aden was investigated, and a representative number of cases were found to be infected with *B. pyocyaneus* in pure culture.

2. The influence of sea-bathing and a sandy atmosphere as aetiological factors is discussed and discredited; whilst the seasonal incidence is held to justify the term "hot-weather ear."

3. A routine method of treatment with facility of application is described, based upon boro-iodine therapy. The use of cotton-wool plugs in the meatus is discouraged. Prophylaxis and after-treatment are described.

4. The results of this form of treatment as applied to sixty-six cases are given, and are compared as far as possible with those of some recently published methods.

I wish to acknowledge my indebtedness to Squadron Leader Lee-Potter, M.D., for having carried out the bacteriological investigations; also to the officer commanding the Royal Air Force Hospital, Aden, for his encouragement, and for permission to prepare this paper. The provision overseas of references and photostatic copies of publications by the librarian of the Royal Society of Medicine has been greatly appreciated.

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E. T. Ceder and L. Zon (*Publ. Hlth. Rep.*, Wash., November 5, 1937, p. 1580) issue a preliminary report on the treatment of psoriasis with massive doses of crystalline vitamin D and irradiated ergosterol. They point out the frequency of psoriasis, its tendency to occur in the winter, and its diminished prevalence in summer and in the Tropics. The benefit derived from ultra-violet irradiation combined with the application of coal tar is possibly due to the production of a substance similar to irradiated ergosterol. This substance may have toxic effects or produce deleterious effects in children, in rats, and in those who have a recently calcified tuberculous focus. Massive doses of vitamin D, 300,000 units daily, given for chronic arthritis, produced involution of the associated psoriasis. Fifteen established cases of psoriasis were treated with similar doses of vitamin D in sesame oil, given after meals by the mouth. Two brands were used; one produced involution in ten out of twelve and the other one out of three cases in six to twelve weeks. No other treatment was given. All the patients but one developed a progressive hypercalcaemia. Six out of ten in one group gradually relapsed in one and a half to five months. The benefit given may be due to any of the components of irradiated ergosterol, and if it is to be continued necessitates a small maintenance dose.