REFRESHER COURSE FOR GENERAL PRACTITIONERS

CONJUNCTIVITIS AND IRIDOCYCLITIS

BY

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When a patient seeks advice for an inflamed eye it is clearly important for his doctor to make a correct diagnosis as soon as possible, since upon this depends not only the treatment to be adopted but also the prevention of complications.

A careful examination is made in a good light, and the cornea should be studied with a corneal magnifier (loupe) if available. In hospital or private practice certain apparatus is available to the oculist (e.g., a slit-lamp or a special inspection lamp) which may give information not obtainable without its use, but in most cases a correct diagnosis should be reached without such aid if attention is paid to certain clinical features which vary according to the cause of the trouble. Below is a table showing the points of difference

Points of Difference Between Acute Conjunctivitis, Acute Iritis, and Acute Glaucoma

	Conjunctivitis	Iritis	Glaucoma
Age ..	Any	Not children	Elderly
Sex ..	Either	Either	Females more common
Unilateral or bilateral	Either	Either	Unilateral, but the other eye often develops the disease
Symptoms	Grittiness and pain accompanied by discharge. Vision not impaired except by flecks of mucus which can be blinked away, or by the lid margins adhering as a result of dried secretion. (N.B. The presence of a corneal ulcer causes more pain, intolerance of light, and impairment of sight)	Severe pain in and around the eye. Vision is impaired in varying amounts; may be considerable	Intense pain, radiating to the forehead. The pain can be severe enough to cause vomiting. Vision is seriously impaired
Signs ..	A clear cornea, active pupils, and a healthy-looking iris. The conjunctiva is intensely injected, and scarlet in colour; this colour tends to fade towards the cornea. If the conjunctiva is moved by gentle pressure through the lid the injected vessels move with it	The conjunctiva is injected, there is a purple flush round the limbus (circumcorneal injection), which is in contrast to the peripheral scarlet of conjunctivitis. The cornea may be clear, but with a loupe small grey spots may be made out on the posterior surface (K.P.). There may be exudate in the anterior chamber; adhesions between iris and lens (synechiae) may have formed. The iris is swollen and "muddy" and is less bright in colour than its fellow. New blood vessels may be visible in the stroma	The conjunctiva is injected in varying degrees (may be slight in the very old). The cornea is misty, due to oedema, making details of the iris difficult to see. The fundus is not visible for the same reason
Discharge ..	Watery, mucopurulent, or purulent	Watery	Negligible
Tension ..	Normal	Normal	Greatly raised
Pupil ..	Normal in size and reactions	Constricted; sluggish in reaction	Semidilated, oval, inactive

between the three common causes of an acutely inflamed eye—namely, acute conjunctivitis, acute iritis, and acute glaucoma.

By careful consideration of the data included above a general practitioner should be able to decide upon his diagnosis without any more aid than a good light and a corneal loupe.

Acute Infective Conjunctivitis

Signs and Symptoms.—These are indicated above. Discharge may be mucopurulent or purulent. Before any treatment is started a bacteriological examination is advisable if it is easily available, but treatment should not be delayed.

A. Local Treatment

The eye is gently irrigated with lotion. It may be necessary, before the eye can be opened, to bathe off dried crusts of secretion by means of cotton-wool pledgets soaked in lotion. There are a number of eye lotions in use. The important thing to remember is that it is not possible to use an antiseptic in a strength sufficient to have antiseptic value on a delicate tissue like the conjunctiva or the corneal epithelium. Therefore any lotion used merely acts as a diluent and flushes away products of inflammation; thus it does not matter greatly what lotion is recommended (except in conjunctivitis from chemical burns). The following are in common use: normal saline, hydrarg. perchlor. 1/10,000, hydrarg. oxycyanid. 1/8,000, sod. bicarb. 2%, acid. boric. 2% (5 gr. to 1 oz. equals 1% approximately).

Irrigation is carried out with an undine or by means of a dropper, which should be sterile. The patient should be lying down and his head turned to the affected side to prevent infected fluid from reaching the other eye. It is not easy to irrigate one's own eye, so, if possible, someone who has access to the patient should be shown how to do it.

On completion of the irrigation penicillin ointment (oculatum penicillin, 2,000 units per gramme) is placed inside the lower fornix and along the lid margins. This is conveniently done by means of a small glass rod, and again someone with the patient should be instructed in the method, which is to place the glass rod with the ointment in the lower fornix, get the patient to squeeze the lids together, and then gently withdraw the rod sideways while the lids are still together. The eye should on no account be bandaged. Dark glasses with protective sidepieces or, failing this, a lint flap or soft eye-shade may be worn. The patient should be instructed to avoid draughts, strong wind, smoky atmospheres, and any external irritant. If practicable it is advisable to rest the good eye for a day or two in order to prevent the affected eye from being used. The patient must be instructed not to employ handkerchiefs, towels, etc., when treating the eye, but to use cotton-wool and burn it after use. The risk of infecting the good eye and the eyes of others must be explained. Further treatment consists of:

1. Irrigation night and morning, or more often, depending on the amount of discharge and the severity of the attack.

2. The use of oculatum penicillin at intervals of four to six hours by day. The eye must be kept under the

effect of penicillin all the time. As the potency of penicillin ointment lasts about four to six hours in the conjunctival sac it is clear that renewal of it should take place at about this interval. It is of little value to prescribe penicillin in the eye for any inflammation once a day or twice a day; it must be used four- to six-hourly. Furthermore, I believe that if penicillin has not done its work after seven days it is useless to continue with it, and something else should be tried. Penicillin drops may be used, 1,000 or 2,500 units per ml., but their potency lasts for less time than that of the ointment, and liquids so easily escape from an inflamed eye that drops are much less effective. Drops are indicated for prophylactic purposes or in very severe cases where there is much pus. (See below, ophthalmia neonatorum.) If any further treatment is required after seven days penicillin is replaced by sulphacetamide—in the form of ung. sulphacetamidi 20% or guttae sulphacetamidi 20%. In severe cases in which a secondary iritis might develop or in which there is any suspicion of corneal involvement guttae atropinae 1% should be instilled daily.

B. General Treatment

Systemic injections of penicillin 200,000 units twice daily should be used only if the cause is thought to be due to some endogenous infection, or if the case fails to progress quickly. Similarly with the sulpha drugs (by mouth). It should not be necessary to employ the latter unless the inflammation is caused by a penicillin-resistant organism, and I regard it as unnecessary to use both together in most cases. Obviously the patient's general condition must be kept as good as possible, and his adviser will determine from the severity of the case whether he is to be confined. Fresh air is to be encouraged. Some varieties of conjunctivitis require some modification in treatment:

Ophthalmia Neonatorum.—Since the advent of penicillin this disease has become much less dangerous to sight. The treatment adopted (Sorsby) is as follows: oral treatment (sulphadimidine 0.5 g. followed by 0.25 g. every six hours) is combined with local penicillin drops (10,000 units per ml. at intervals of one minute for half an hour and then less often as the discharge lessens). Results are quite dramatic compared with the "pre-penicillin period." These cases should be treated in hospital.

Acute Conjunctivitis from Dacryocystitis.—The lacrimal sac is repeatedly emptied by pressure over the internal palpebral ligament and the eye then irrigated in the ordinary way. As soon as the patient can tolerate it the sac is syringed and penicillin (1,000 units per ml.) is left in it. This is repeated when necessary.

Angular Conjunctivitis.—That part of the conjunctiva exposed by the palpebral fissure is most often involved. The disease is caused by the Morax-Axenfeld diplobacillus, and is cured by the application of zinc drops, $\frac{1}{2}$ gr. or 1 gr. (32 or 65 mg.) to the ounce (28 ml.), which may well be combined with sulphacetamide 20% to counteract secondary infection.

Membranous Conjunctivitis.—The conjunctival sac is immediately examined bacteriologically for diphtheria, and the appropriate treatment undertaken if this is positive. The membrane is stripped off with forceps.

Purulent (Gonococcal) Conjunctivitis.—Treat as ophthalmia neonatorum, see above. These cases should always be treated in hospital.

Acute Non-infective Conjunctivitis

This type is mostly due to injury or corrosive burns. The cause of the trouble is obvious from the history.

Treatment

Foreign bodies must be removed as soon as possible. Examination of the under surface of the upper lid and the upper fornix must never be neglected.

Burns.—If these are caused by acid the eye should be irrigated with an alkaline lotion (lotio sod. bicarb. 2%), and vice versa (lotio acid. boric.). There is always a danger of the raw surfaces adhering, a condition called symblepharon, and this later gives rise to considerable limitation of movement of the globe, with diplopia. To prevent this the fornices are liberally lubricated with guttae paroline or castor oil, and sterile petroleum jelly is placed therein. Daily a glass rod is passed along both fornices to break down any adhesions that may have formed.

Lime Burns.—Any lime remaining *in situ* is carefully removed. The eye is irrigated with 10% ammonium tartrate and the conjunctival sac kept lubricated with "paroline" to prevent adhesions. All except very slight cases of lime or other caustic burns should be treated in hospital because of the danger of corneal damage.

Special Types of Conjunctivitis

1. *Phlyctenular.*—In this disease nodules appear on the conjunctiva or cornea, to which a leash of blood vessels run. It is a common disease of childhood, and there appears to be a very definite connexion between phlyctenular disease and sensitivity to tuberculous toxin. General treatment is therefore important—fresh air, nourishing food, and sunlight should be sought. Local treatment is relatively unimportant unless the cornea is affected, because phlyctenules soon disappear.

2. *Associated with Skin Diseases.*—The importance of such cases is that the conjunctivitis is always secondary, and will not be cured unless the skin disease is cured. Most important are rosacea (in which the cornea is nearly always affected) and conjunctivitis associated with seborrhoea capitis or acne vulgaris. Treatment of the eyes is therefore palliative.

3. *Allergic.*—Characterized by sudden onset and recession, and by being bilateral. Eosinophil cells may be found in a conjunctival smear. In a suspected case it will be necessary to subject the patient to protein-sensitivity tests to find out what he or she is to avoid. Local treatment consists of "antistin-privine" drops (1%) frequently, and "benadryl" by mouth may be justified.

4. *Spring Catarrh.*—This has a seasonal incidence and attacks young people. It is probably allergic. The common form affects the eyelids, in which large follicles "like paving stones" appear. There is a milky secretion. The bulbar form affects the limbus area. Eosinophils are found in a conjunctival smear. The patient complains of a great deal of itching. Treatment is palliative. The antihistamine drugs are used. Trachoma, conjunctival tuberculosis, syphilis, and other diseases are now uncommon, and cannot be considered here.

Chronic Conjunctivitis

The clinical appearances vary considerably. The eye may be severely injected, the conjunctiva swollen and "velvety" in appearance, the lower lids tending to evert and expose the mucous surface, thus adding to the irritation. On the other hand, all that is visible may be a mild degree of conjunctival hyperaemia, or a little epiphora or sticky discharge. In a like way the symptoms can be out of proportion to the signs.

Points Worth Remembering

1. Cases can be made worse and the inflammation may be prolonged by too much treatment—especially by astringents.

2. Many cases are due to some constitutional factor—metabolic (e.g., gout), general debility—poor living conditions, and skin diseases (many of which are in themselves metabolic—e.g., rosacea). It is necessary to treat these underlying factors as well as the eyes.

3. Allergy may be a cause. In such cases there is often an allergic history or family history. Locally the suggestive signs are a very sudden onset (bilateral) and a very sudden cessation of the attack, with frequent recurrences. In women, face powder, mascara, and other cosmetic preparations are sometimes responsible. Most non-allergic cases subside very slowly and reluctantly.

4. In a unilateral case great care must be taken to exclude foreign bodies, misplaced or ingrowing eyelash, dacryocystitis, intranasal infection, conjunctival concretions protruding above the epithelial surface, and conjunctivitis artifacta. In the last-named the type of patient may give a clue, and the inflammation is almost always in the lower fornix. Self-inflicted conjunctivitis is usually produced to escape work or some distasteful duty, and so long as the possibility of it is remembered it is usually not difficult to recognize it.

5. Refractive errors may play a part, and should be investigated.

Treatment of Chronic Conjunctivitis

Mild astringents are used in the form of drops. These must not be prolonged indefinitely. There is usually very little discharge, so that lotions are often unnecessary. At the outset the surgeon may paint the lids with 25% or 50% argyrol. This is done quite firmly (under amethocaine hydrochloride) and the excess silver washed out. For home use the patient is given guttae zinc. sulph. $\frac{1}{4}$ gr. (16 mg.) to the ounce (28 ml.); or Crooke's colossal argentum, twice daily. I have found the following effective: zinc sulphate $\frac{1}{8}$ gr. (8 mg.), sol. adrenalin. 1/1,000 30 m. (1.8 ml.), sol. sulphacetamidi 10%. If allergy is suspected, use guttae antistip-privine 1% three times daily. Some patients need a placebo. Guttae phenolaine is a soothing preparation. The great thing is to prevent the patient becoming a permanent user of drops.

It is as well to tell the patient that chronic conjunctivitis is not easy to cure; a lot depends on general health, surroundings, and finding and eliminating the cause. It is the responsibility of the doctor to be sure that everything is done to eliminate any factors which may be contributing to the condition. It is worth remembering that not all hyperaemic conjunctivae cause symptoms. If the patient is not complaining of gritty eyes or soreness he is best left alone.

Iridocyclitis

For our purpose iritis and iridocyclitis can be considered together. The presence of small grey spots (keratitis punctata, or K.P.) on the posterior corneal surface indicates ciliary activity. Chronic cyclitis—a most insidious and resistant disease—may occur for a long time without any obvious iris inflammation, but sooner or later this takes place; clinically, however, it may only show, in later stages, as iris atrophy.

The end-results of iridocyclitis can have a most serious effect upon vision. Some of these can be prevented by early treatment, particularly adhesions between the iris and lens capsule (posterior synechiae). Such adhesions are caused

by the organization of fibrin into fibrous tissue, and are produced by the formation of fibrin from the vessels of the inflamed iris. When they become fibrous, adhesions are very tough, and often cannot be broken down. Dilatation of the pupil is restricted and irregular; circulation of the aqueous may be interfered with (if the adhesions are extensive), with resultant iris bombé and secondary glaucoma; the transparency of the lens capsule, and later the lens, may be impaired; and finally, synechiae are said to predispose to recurrent attacks of inflammation. (This is probably fallacious.)

The object of immediate treatment is to prevent the formation of synechiae by getting the pupil margin as far away from the lens capsule as possible. For this we use a mydriatic—atropine—and it is clear that a correct diagnosis will greatly facilitate the prevention of adhesions.

Acute Iridocyclitis

The signs and symptoms of acute iridocyclitis have been briefly considered under "differential diagnosis." The treatment is conveniently considered as local and general.

Local Treatment

Some form of mydriatic is instilled as soon as the diagnosis is made. I believe it to be best to use atropine ointment 1% (2% if adhesions have begun) thrice daily. Atropine drops are in common use, but so easily are they spilt over the lids, diluted by the tears, or dabbed off that the drug does not remain *in situ* long enough to be absorbed in quantity. Some form of heat is employed for the relief of pain and to stimulate the blood flow. This can be given as moist heat in the form of hot bathings, or dry heat by means of a Maddox heater. Heat is also used in the form of diathermy (500 mA for five minutes), but this may not be available except in hospital. Dark glasses are worn as a protection against light; a bandage is unnecessary. Relief from vascular engorgement may be obtained by applying leeches to the temple.

Should adhesions form in spite of early application of atropine it may be possible to break them down by means of a more powerful mydriatic injected subconjunctivally. This is called "mydricaine," and it is a combination of atropine 1/60 gr. (1 mg.), cocaine 1/10 gr. (6.5 mg.), adrenaline 1/600 gr. (0.1 mg.), sodium chloride 1/80 gr. (0.7 mg.), and chloretone 1/120 gr. (0.54 mg.), in 5 minims (0.3 ml.) of sterile water. Five minims of this is injected near the limbus, opposite the offending synechiae. Sometimes the patient may develop sensitivity to the local application of atropine. This shows itself as a local reaction: the skin of the eyelid becomes very dry and puffy, the whole of the affected side of the face may become considerably swollen, there is a great deal of itching, and the eye itself becomes more injected. Should this condition arise, atropine must be stopped immediately and other mydriatics employed. We can use hyoscine hydrobromide 1% or duboisine sulphate 1%. A synthetic preparation "lachesine" 2%, has recently become available, and is useful in that it does not give rise to allergic reactions, but it is a good deal less potent than atropine.

Surgical procedures comprise iridectomy, dividing synechiae, iridotomy to produce an artificial pupil, etc., details of which are not given here.

General Treatment

Some oculists advocate protein-shock therapy in early stages of acute attacks. There is not universal agreement about the efficacy of this form of treatment. It is difficult to assess the value of it, because there is no control with

which to compare. Shock therapy is conveniently given by means of an intravenous injection of typhoid vaccine (15,000,000 units), which can be repeated with slightly higher dosage two or three times a week, provided the general reaction is not too severe. For the relief of pain in the acute attack, aspirin, phenobarbitone, "veganin," etc., are in general use. In rare cases of acute pain morphine may be needed.

Specific treatment may be indicated. This depends on the cause of the attack. Therefore as soon as possible after immediate local treatment has begun investigations should be made to try to bring to light any relevant aetiological factor. It must be admitted, however, that, despite the advance made in modern medicine and diagnostic technique, the majority of cases of iritis remain unexplained. Briefly, the following diagnostic methods are used: (a) A careful history. This may give a pointer to the cause, and in many cases the patient's doctor can assist with his knowledge of previous illnesses. (b) Blood examination for Wassermann and Kahn reactions, gonococcal infection, etc. (c) Focal sepsis must be eliminated, and this involves investigation of sinuses, teeth, etc. In women, gynaecological causes must be excluded. (d) Radiographs to exclude sarcoidosis or tubercle, either healed or active. (e) Urine examination, especially for sugar.

Aetiology

The following are the generally accepted causes of inflammation of the uveal tract:

Primary Causes.—(a) Syphilis; (b) gonorrhoea; (c) tuberculosis; (d) focal sepsis; (e) herpes zoster; (f) metabolic (gout, diabetes); (g) allergy; (h) uveoparotitis; (i) sarcoid; (j) undulant fever.

Secondary Causes.—(a) Injury; (b) corneal inflammation (e.g., herpes); (c) post-operative (e.g., endophthalmitis phaco-anaphylactica).

Primary iridocyclitis is an endogenous reaction. The clinical features of individual types sometimes have diagnostic value, and will be briefly mentioned. Any relevant special treatment will also be indicated.

(a) *Syphilis*.—This is probably a less frequent cause than heretofore, owing to earlier diagnosis and treatment of syphilis itself. Some years ago it was said to account for 25% of cases of iritis, but the figure is a good deal lower now. Syphilitic iridocyclitis occurs in two forms—a "plastic" and a "nodular or gummatous" form. The plastic form appears in secondary syphilis, accompanies the skin rashes, and usually occurs between three and twelve months of infection. It is sometimes characterized by excessive formation of fibrinous exudate, but there may be no local distinguishing features. The "gummatous" form occurs in late secondary or early tertiary syphilis, and is distinguished by usually multiple yellowish nodules forming at the pupil margin. Special treatment is of course that for syphilis, the details of which need not be repeated here. It will suffice to mention that iodides may have a beneficial effect on the rapid absorption of nodules in the gummatous type. A mild iritis occurs in congenital syphilis in conjunction with interstitial keratitis.

(b) *Gonococcal*.—Ninety-six per cent. of cases are found in men. There is nearly always an accompanying arthritis or a history of joint pains (usually the knee or ankle), and the primary urethritis has probably subsided. Recurrent attacks are common, and may arise when no evidence of the original attack of gonorrhoea is present. Thus the cause may be difficult to find unless a truthful history is obtained. The local feature is that of a gelatinous exudate which is rather greenish in colour and excessive. Special

treatment in chronic or recurrent cases is prostatic massage. A gonococcal vaccine is sometimes advocated.

(c) *Tuberculosis*.—This usually occurs in children or young adults. The inflammatory reaction is often less acute in tuberculous cases. Nodules may occur rather similar to those of syphilis. K.P. tends to be rather coarse and large, and may easily be visible to the naked eye. Special treatment consists of the usual fresh-air-and-diet regime. The patient should live in the country. Tuberculin injections, beginning with very small doses, can be effective, but, because of the difficulty of assessing the correct dosage, should be given by experts. In ocular tuberculosis large doses of vitamin D (calciferol) are worth a trial—100,000 i.u. daily given in tablet form up to a total of 18 to 33 million i.u.

(d) *Focal Infection*.—There are no local distinguishing features except that often the case takes a more subacute to chronic form. K.P. is produced in crops and vitreous opacities are excessive. Treatment consists in eliminating the focus if possible. Sulphanilamide therapy or systemic penicillin might be useful for the focal infection, but has not any local ocular effect. Autogenous vaccines are used and sometimes seem to modify an attack.

(e) *Herpes*.—Iritis occurs in association with herpes zoster, usually when the cornea is involved, but it may occur independently. It may also arise in conjunction with herpetic keratitis. A virus infection is generally accepted now as the cause. No special treatment is indicated here.

(f) *Metabolic*.—(1) *Diabetes*. There is a tendency for a large number of visible blood vessels to form on the iris, producing a condition known as rubeosis, which is pathognomonic. Hyphaemia is common. General treatment for diabetes is usually already in operation, as iritis is not likely to be an early sign. (2) *Gout*. This disease itself is much less frequent than it was; iritis has been freely attributed to gout in the past, and probably in many cases erroneously. However, a gouty iritis does occur; it is often associated with episcleritis. There is very considerable pain, and the ocular tension is often raised. General investigations—blood uric acid, radiography of joints (if any are affected)—should be carried out. Any positive evidence will entail careful treatment of the underlying metabolic disorder.

(g) *Allergy*.—The subject of allergy is vast, and I believe it to be a very important factor in eye disease, but it can only be briefly mentioned here. There is no doubt that the uveal tissue develops hypersensitivity. For example, recurrent attacks of iridocyclitis occur long after the original cause has been dispersed; this suggests a reaction to a stimulus which would not have been effective prior to the original attack. An allergic cause is difficult to prove and more difficult to isolate, but in a suspected case it is justifiable to try the effect of antihistamine drugs—benadryl (50 mg. thrice daily) or antistin (100 mg. twice daily).

(h) *Uveoparotitis*.—This is an unusual form of iridocyclitis associated with enlargement of the glands and sometimes with cranial nerve palsy. Tuberculosis is usually accepted as the underlying cause. There is no specific treatment.

(i) *Boeck's Sarcoid (Benign Lymphogranulomatosis)*.—This disease is one in which nodules appear in the skin, lungs (particularly the hilar region), lymphatic system and conjunctiva, and other internal organs. Iridocyclitis is not uncommon in the disease and is characterized by the formation of iritis nodules. Uveoparotitis is considered by some authorities to be a variety of benign lymphogranulomatosis.

(j) *Undulant Fever*.—Chronic iridocyclitis is associated with this illness. No specific treatment is indicated.

Chronic Iridocyclitis

There is a form of uveal inflammation which manifests itself in a manner likely to remain unnoticed by the patient for some time. The first symptom is diminution of vision, or maybe rapid increase in presbyopia. On examination only very fine vitreous opacities and fine K.P. are found. With a slit-lamp it is possible to see cells circulating in the aqueous. There is probably no circumcorneal injection (ciliary flush).

In spite of local treatment the disease tends to remain active; very often a secondary glaucoma supervenes, and this is a most serious matter. Very few of such cases resolve, and the eye is usually lost after a period of relapses. Little or nothing is known about this disease. It is attributed to such possibilities as septic absorption, allergic reaction, and tuberculosis—but rarely is anything definite found, elimination of which cures the local disease. Treatment therefore consists of atropine, rest, and complete overhaul; and if secondary glaucoma occurs operative treatment may become urgent.

EXPEDITION TO NIGERIA

M.R.C. SEARCH FOR TROPICAL PLANTS

BY

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In November, 1949, an expedition was sent by the Medical Research Council to Nigeria to investigate certain tropical plants as possible sources of raw materials for the preparation of cortisone. The members of the expedition have recently returned, and, although evaluation of results must wait upon the completion of detailed laboratory investigation, some account of the background of their work and of its progress can be given.

The expedition, under the title of the Medical Research Council Medicinal Plants Survey, consisted of myself and a technical assistant, Mr. W. Read, from the National Institute for Medical Research, with a botanist, Mr. R. D. Meikle, of the Royal Botanic Gardens. During our stay in Nigeria we had our headquarters in University College, Ibadan, and grateful acknowledgment is made of the invitation from the Principal, Dr. Kenneth Mellanby,

and of the laboratory facilities which were made available by Professor R. J. McIlroy and Professor F. W. Sansome, in the Chemistry and Botany Departments respectively.

Origin of the Expedition

To explain the need for the expedition it is necessary to recall the sensational announcements, made just over a year ago, of the therapeutic activity of cortisone ("Compound E," 11-dehydro-17-hydroxycorticosterone; Formula I) in rheumatoid arthritis, and the fantastic discrepancy between the quantity of this compound which could be made available and the potential demand for its use. Although the compound is present in extracts of adrenal cortex, to obtain any considerable amount from this source is plainly impossible. A complicated many-stage synthesis from bile acids is known but is expensive, and the United States journalists have emphasized sufficiently the almost astronomical number of cattle which would be required for the maintenance of a single patient.

Synthetic routes to the adrenocortical hormones have been, and are being, busily explored; but a major difficulty is the introduction of the oxygen atom in position 11 in the steroid ring system (* in Formula I). This structure seems to be essential for the required type of biological activity. Were it possible to begin a partial synthesis

from a natural product with this bit of the molecule "ready made," the problem would be immensely easier. Attention was early directed to sarmentogenin, one of the group of heart poisons, the constitution of which, with an 11-hydroxyl group (Formula II), had recently been proved by Katz, in Switzerland.

Sarmentogenin was believed to occur in the seeds of *Strophanthus sarmentosus* P.D.C., a climbing plant of West Africa, and United States journalists rapidly sketched visions of vast areas of Texas planted with crops which would supply the rheumatoid arthritics of the world. The bubble burst when two of Professor Reichstein's colleagues collected in West Africa authentic seeds of *S. sarmentosus*, and it was shown that they contained little or no sarmentogenin but mainly a new heart poison, sarverogenin, the constitution of which is still undetermined. The origin of sarmentogenin now presented a fascinating scientific mystery.

Sarmentogenin had been isolated by three groups of workers, on each occasion from commercial samples of seed coming on to the market described as seeds of *Strophanthus hispidus*. In each instance pharmacognostic examination indicated that the seeds were not those of *S. hispidus*, but in general corresponded most closely in properties, particularly in colour reaction, with seeds of *S. sarmentosus*. If now, from the Swiss results, the source of sarmentogenin were not *S. sarmentosus*, what seed

FIG. 1.—Bush resthouse at Kagara. The M.R.C. expedition on tour.