Summary

1. Female and male hormone can be implanted in tablet form in as large amounts as desired without injury.
2. Female hormone was implanted to allow a small infantile uterus to develop and to make it ready for conception, and this was done successfully.
3. Male hormone was implanted to control serious menorrhagia caused by fibroids. Good results were obtained in the case of women near the menopause.
4. Male hormone was unable to influence successfully existing recurrences of carcinoma of the breast following an operation or x-ray treatment. To what extent male hormone can have a prophylactic action against such recurrence is not yet determined.
5. The general effect of implants of male hormone on women is discussed.

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SULPHONAMIDE TREATMENT OF BACTERIAL AND TRACHOMATOUS CONJUNCTIVITIS

BY

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The idea of developing specific chemical substances for the treatment of bacterial infections is as old as bacteriology itself. In 1881 Koch failed to cure anthrax with mercurial salts; however, in 1904, with Ehrlich's success in protozoan infections the search for drugs of chemotherapeutic value began again. It has been only within the last few years, by haphazard trial and error, that the value of the sulphonamide group of synthetic compounds has been discovered. In 1908 Gelmo described the preparation of sulphanilamide in a purely scientific paper; by the substitution of various molecules he produced different compounds, including dyes. In 1932 Domagk, using a compound patented for dyeing, cured streptococcal infections in mice; this was then sold as prontosil.

The term "sulphonamide" is a generic one and embraces the following compounds: prontosil rubrum, prontosil soluble, rubiazol, uleron, sulphanilamide, proseptasine, soluseptasine, and M & B 693 (sulphapyridine). It appears that there is little difference in the effect of these drugs, the trade names of which have been given. It is said that they do not stimulate leucocytic activity, are not simple germicides, and do not affect the rate of production of specific immunizing bodies, either in quantity or in quality. Probably they act by neutralizing a metabolic function or

an enzymatic activity. The balance of evidence indicates that the sulphonamides affect the invading organism in the sense of producing a bacteriostatic action which in many cases is not sufficient to effect sterilization without the co-operation of the defensive mechanism of the host. The foregoing preface consists of extracts from various recent publications.

In the case of trachoma, however, Julianelle has shown that blood from trachomatous persons contains no demonstrable substance capable of inactivating or neutralizing the infective agent, as measured by the development of experimental trachoma in monkeys. The drug diffuses readily to all tissues and fluids of the body; experimentally it may be found in the eye within fifteen minutes of ingestion. This is the reason why it has been proved to be such a successful chemotherapeutic agent in certain bacterial diseases.

Preliminary Procedures

When its influence on trachoma is being investigated some attempt at scientific observation should be made. After the clinical condition of the conjunctiva has been diagnosed as a veritable trachoma a detailed description of the observations on which the diagnosis has been based should be noted before treatment is begun. This should include:

1. Cultural examination of the conjunctival flora. The conjunctival sac should be filled with sterile broth, which should be allowed to remain for a few minutes before being removed with a pipette for sowing on blood-agar and other media.

2. A slit-lamp examination of the tarsal conjunctiva of the everted upper lid. In the case of trachoma some or all of the following signs may be present: (a) papillary hypertrophy consisting of polygonal areas separated by interstices, forming a mosaic or marquetry; (b) on each of the polygons a congeries of plume-like capillaries; (c) bleb-like excrescences or follicles; (d) cicatricial lines in the epithelium and subepithelial tissue. Signs *a* and *b* are found in most forms of chronic conjunctivitis.

3. A slit-lamp examination of the corneal periphery in its upper fifth to note: (a) subepithelial grey infiltration; (b) corneal rosettes or limbal follicles; (c) Herbert's peripheral pits; (d) neo-vascularization of the normally clear corneal tissue, especially by reflected light.

4. A momentary application of Graddy's or Knapp's forceps may be made in some cases to the conjunctiva to see if gelatinous material is expressed from the bleb-like excrescences.

5. Epithelial scrapings from the upper tarsal conjunctiva should be made and stained with Giemsa for the detection of the epithelial inclusions which are characteristic of any virus disease.

These procedures should be carried out after there has been a cessation of all forms of treatment for about ten days; this, of course, should be maintained while the drug is being given.

Technique of Treatment

The derivative of sulphonamide which I have used has been M & B 693 (sulphapyridine), and the adult dosage has been 3 grammes the first day, divided into six doses and given with an equal quantity of sodium bicarbonate at intervals during the patient's waking hours; after this the daily dosage was 2 grammes, given similarly for nine days. It is not necessary to employ larger doses or to wake the patient up at night so that treatment may extend throughout the twenty-four hours, as is advised in acute bacterial diseases. During the treatment all articles of diet likely to contain sulphur are forbidden, including

purgatives. The patient should be kept under strict medical supervision with attention to possible blood changes.

After the drug course has been completed all the above-mentioned procedures should be repeated; then any difference between the condition before and after treatment may be noted. Mere naked-eye observation before and after treatment is not of much value. It may be advisable to repeat the drug course after an interval of ten days, the examinations before and after treatment being again carried out.

In my latest case, that of a young English lady infected with trachoma, the bacteriological cultures before treatment showed a heavy growth of pneumococci and haemolytic streptococci, while after treatment by sulphapyridine there were only a few sparse colonies of non-pathogenic staphylococci and diphtheroids. There had been some blepharitis, which was cured by the treatment, but I had not suspected a bacterial infection of this severity. The phenomena of trachoma remained unaltered. That the gelatinous matter contained in the bleb-like excrescences or follicles of Stage IIa of trachoma—which was the clinical state of the conjunctiva—would be absorbed would have been too much to expect from any drug, whether ingested, injected, or applied to the surface of the membrane.

Discussion

Up to the present the drugs of the sulphonamide group have been found to be without effect on any virus disease, and most of us believe that it is to this class that trachoma belongs. In my opinion the good results which have been reported in the treatment of trachoma by these drugs have been procured by the elimination of superimposed bacterial infections. Remarkable results may be expected from this form of treatment in many cases of bacterial conjunctivitis and blepharitis.

It has been suggested that trachoma is becoming a rare disease in England, but between December 5, 1939, and January 12, 1940, I examined fifteen persons with the disease in an active and contagious stage, seven being of British birth and eight being Jewish refugees from Germany. Perhaps the most important of these was a private soldier from his regimental barracks.

The John Burford Carll Laboratory,
Westminster Hospital Medical School.
January 13, 1940.

Professor Giuseppe Bastianelli, director of the Istituto di Malariologia "Ettore Marchiafava," Policlinico Umberto I, Rome, has sent the prospectus of an international course in malariology, to be held in Rome from July 15 to September 10. There will be lectures and demonstrations in haematology, protozoology, malaria parasites, and microscopical diagnosis, pathology of malaria, clinical study and treatment in the wards, entomology in relation to mosquitos, and the epidemiology and prophylaxis of malaria. The programme also includes practical work and laboratory demonstrations, instruction in the survey of a malarious area, and residence in experimental stations and in a centre of induced malaria. Several excursions have been arranged, some obligatory and others optional. The course is open to post-graduate physicians only. It will be held in French if required and if ten students at least are attending; but in any case interpreters will be available. The fee amounts to 400 lire, of which 300 will cover all practical demonstrations and free travel in connexion with obligatory excursions. Extra fees are charged for the optional excursions to Sardinia and to Northern Italy. Applications must reach the director before June 20.

EPILEPSY TREATED WITH EPANUTIN

BY

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During the past year forty-three sane male epileptics at St. David's Hospital have been treated with epanutin (sodium diphenyl hydantoinate). In the majority of cases the drug was given in place of phenobarbitone or prominal or rutonal. Several patients had also been having, in addition, mixtures containing bromides, belladonna, borax, chloral hydrate, or pilocarpine nitrate, etc. In such cases the mixture was continued, so that the present investigation indicates the results only of the substitution of epanutin for the barbiturates.

The date was noted when each patient appeared to be receiving his optimum dose of epanutin, and the subsequent period of months was compared with a corresponding length of time before starting treatment. None of the patients concerned had shown a marked seasonal incidence in fits during past years, and therefore the comparison of the two periods was considered to be fair. In regard to incidence of fits the following results were obtained:

Great improvement	..	..	..	20 cases (46.51%)
Improvement	..	..	..	7 „ (16.28%)
No change	..	..	..	6 „ (13.96%)
Worse	..	..	..	1 case (2.32%)
Treatment discontinued	..	..	..	9 cases (20.93%)

Total 43 cases

Effects of the Treatment

It will be seen that twenty-seven patients, or approximately 63 per cent. of the cases, have derived benefit from treatment. Among those cases regarded as showing great improvement one man who had had twenty-six major fits in the four months before treatment has had *none* in the four months following optimum-dose treatment. He has had, however, rather more observed attacks of petit mal. On the other hand, practically all cases showing great improvement have had fewer observed attacks of petit mal as well as grand mal, but several of the men have stated that they experience more "sensations." In addition, they all, with one exception, have appeared to improve psychologically, being brighter, more intelligent, and less introspective and hypochondriacal. Some of the men say that they feel better than they have done for years, one in particular mentioning that he felt as if he had "begun a new life." Even in those cases in which no improvement in the incidence of fits has been recorded the patients say that they are happier and more alert.

In the nine cases in which treatment was discontinued various toxic symptoms and signs had been manifested. In two cases there were pyrexia and skin rashes resembling respectively rubella and urticaria. In one case there was hypertrophic gingivitis, with nausea and vomiting. The other six cases showed some or all of the following symptoms and signs: tremulousness, intention tremor, ataxic gait, nystagmus, ptosis, slurring speech, insomnia, and mental confusion. Most of these toxic effects disappeared within a few days after cessation of treatment.

The patients' ages range from 17 to 58. Successful treatment has not been more marked at one age than at