often numerous small implants, so-called, scattered about the peritoneal surface of the adjacent bladder, rectum, or sigmoid. In the vast majority of cases following such resection there is sufficient interruption of the pituitary-ovarian hormonal axis to allow for regression and atrophy of these small areas of tissue.

4. Chronic Infection

In considering chronic infection as the underlying cause in patients complaining of dyspareunia I would like to mention two types. The first, where there is residual tubal or tubovarian infection which has resisted all treatment by conservative means, such as rest, heat in all forms, and chemotherapy, and where gross palpable masses remain, producing persistent contact pain. The only resort in such patients is obviously the surgical removal of the affected tubes and that portion of the ovary involved, once again being a good conservative and salvaging the normal functioning ovarian tissue, as these patients so often are in the younger age group. It has been our experience in a few such cases in the last few years to obtain very satisfying resolution and symptomatic relief through the administration, by means of an indwelling polythene catheter in the vein, of a continuous penicillin drip, a 24-hour dosage of 25 to 30 million units.

Lastly, I mention the case where on pelvic examination one finds no grossly palpable disease or displacements, where the only finding exhibited by the patient is some tenderness to palpation in the parametrial areas and a general hypersensitivity of the uterus and adnexal areas, especially on movement of the cervix and uterus. There may or may not be some mucopurulent discharge from the cervical os.

In recent years one does not often hear the term "foci of infection," though it is still applicable, and certainly in regard to the cervix. Even where there have been no previous pregnancies the cervix may be the site of chronic low-grade infection, deep-seated in the endocervical glands. The result is a chronic congestion of the cervix and the immediately surrounding tissues, the parametrium, and the utero-sacral ligaments, which become painful on contact.

The infected cervical glands are deeply placed in the endocervix beyond the reach of medicinal douches or vaginal suppositories or local applications. The infection is removed only by actual cauterization or surgical excision. Cauterization carefully but thoroughly done will be successful in a great many cases. Where the infection is more severe or where there are extensive old lacerations, or some type of repair is necessary, a wide conization or partial or even complete amputation of the cervix should be done, to remove the site of infection and thus relieve the symptom of pain.

Summary

Conditions requiring surgical treatment may be the sole problem in relieving dyspareunia, but it is pointed out that such conditions should not be overlooked in the patient who appears to present only a marked emotionally disturbed problem.

Conditions causing dyspareunia and requiring surgical treatment have been presented generally as those of congenital and those of acquired origin.

It has been pointed out that the gynaecological surgeon should always be conscious of the fact that his technique of operation, either vaginal or abdomino-pelvic, may produce this undesirable symptom.

ANTIMALARIALS IN TREATMENT OF SJÖGREN'S SYNDROME

BY

J. M. HEATON, M.A., M.B., D.O.

*Research Assistant, Institute of Ophthalmology, London ;
Lately Tutor in Ophthalmology, University of Bristol*

There is considerable evidence that Sjögren's syndrome is a form of systemic lupus erythematosus (Heaton, 1959). The therapeutic effect of antimalarials on systemic lupus and cutaneous lupus erythematosus is well known (Page, 1951 ; Prakken and Molhuysen-van der Walle, 1954), and it has been noted that these drugs relieve photophobia in patients with systemic L.E. (Hill, 1957). It was therefore thought worth while to try the effect of the drugs on patients with Sjögren's syndrome.

Methods and Results

25 patients with Sjögren's syndrome were treated with antimalarials. Two drugs were used: chloroquine sulphate and hydroxychloroquine sulphate ("plaquenil"). As more hydroxychloroquine became available most of the patients on chloroquine were changed over to it as it is reputed to be less toxic. Every patient had been treated before by orthodox methods, often for many years, and usually with only slight benefit.

The results are summarized in the Table. It is not easy to assess the improvement in patients with Sjögren's syndrome but an attempt has been made by classifying the results as "no change," "improved," and "greatly improved."

Dosage.—The dosage of chloroquine used was 300 mg. daily for three weeks, then 150 mg. daily; this is the dose usually recommended for cutaneous L.E. The dosage of hydroxychloroquine was 800 mg. daily, and this was reduced to a maintenance dose of 400 mg. daily after 8 to 12 weeks if the patient's symptoms had improved. Much larger doses of hydroxychloroquine (up to 2,000 mg. daily) have been used with safety in cutaneous L.E. to get full therapeutic benefit from the drug (Goode, 1958). Possibly more patients with Sjögren's syndrome would have improved if larger doses had been used. It is not known for how long it is necessary to continue treatment; in four cases the drug was stopped and the eyes became worse within a month, while in one case the eyes have remained in a satisfactory state for three months after stopping treatment.

Effects of Treatment

Eight patients failed to improve on antimalarials. Three of these had toxic effects which necessitated stopping the drug before it could be effective and three had had radiotherapy to their eyes in an attempt to relieve their symptoms. This may have been a factor in their failure to improve, as no other patient had previously had radiotherapy.

It took four to eight weeks of treatment before any improvement was noticed; this is similar to the findings in the treatment of cutaneous L.E. and rheumatoid arthritis with antimalarials. The ocular irritation improved first and then the photophobia. In those patients who were not "greatly improved" it was usually a little photophobia that remained. Many patients said that their eyes felt moister, but no change in Schirmer's test was noted; this, however, is a rather crude test.

Table Showing the Results of Treating 25 Cases of Sjögren's Syndrome with Chloroquine and Hydroxychloroquine

Case No.	Age and Sex	Duration Ocular Symptoms (Years)	Duration Treatment Chloroquine (Weeks)	Response to Chloroquine	Duration Treatment Hydroxychloroquine (Weeks)	Response to Hydroxychloroquine	Side-effects	Remarks
1	43 F	5	6	None	8	None	None	
2	59 F	6	—	—	20	I.	"	
3	57 F	2	8	I.	14	G.I.	"	Stopped treatment 1 month, became worse; improved when restarted
4	53 F	10	4	None	12	None	"	Had 2 courses of radiotherapy to eyes
5	51 F	4	—	—	20	I.	"	
6	68 F	6	4	None	4	None	Yes	Nausea, diarrhoea, malaise with both drugs
7	72 F	8	—	—	12	I.	"	Diarrhoea on 800 mg. daily. Tolerates 400 mg. daily
8	68 F	18	12	G.I.	—	—	None	Stopped treatment 3 weeks, became worse. Improved when restarted
9	63 F	2	—	—	20	G.I.	"	
10	53 F	3	—	—	16	I.	"	On systemic cortisone and corticotrophin for rheumatoid arthritis
11	54 F	3	12	I.	16	I.	"	
12	69 F	6	16	I.	—	—	"	Stopped treatment 1 month, became worse. Improved when restarted
13	74 F	11	—	—	16	None	"	Had 2 courses of radiotherapy to eyes
14	64 F	5	—	—	8	I.	"	Stopped treatment 3 months, eyes have remained I.S.O.
15	48 F	5	8	I.	16	I.	Yes	Nausea with both drugs; tolerates 400 mg. hydroxychloroquine daily. Stopped treatment 1 month, became worse; improved when restarted
16	48 F	8	—	—	20	G.I.	None	
17	60 F	3	22	I.	—	—	"	
18	60 F	13	2	None	2	None	Yes	Nausea and diarrhoea with both drugs. Has chronic colitis
19	35 F	7	—	—	12	G.I.	None	
20	52 F	10	—	—	8	None	"	
21	70 F	3	—	—	20	"	"	Had 1 course radiotherapy to eyes
22	67 F	3	—	—	2	"	Yes	Itchy erythematous rash
23	82 F	6	—	—	12	I.	"	
24	66 F	20	—	—	12	I.	None	
25	56 F	14	—	—	12	I.	Yes	Nausea on 800 mg. daily; tolerates 400 mg. hydroxychloroquine daily

I.=Improved. G.I.=Greatly improved.

Objectively, the palpebral conjunctiva became less red, the corneal changes lessened, and there was much less staining with rose Bengal. In every case some staining of the conjunctiva with rose Bengal remained.

Other features of Sjögren's syndrome also improved and the patients felt generally better, including those who had had radiotherapy to their eyes. One of the most remarkable features was the melioration of their arthritis.

Complications of Treatment

The side-effects of chloroquine treatment include nausea, dyspepsia, and diarrhoea; visual disturbances, with difficulty in accommodation and flickering before the eyes; corneal changes; pruritus; dermatitis; urticaria; bleaching of the scalp hair, eyebrows, and eyelashes; vertigo and tinnitus; nervous disturbances; malaise; leucopenia; and agranulocytosis. Most of these complications are rare.

Ten patients in the trial had chloroquine, and side-effects occurred in three of them. These were fairly minor in nature and resolved rapidly when the drug was stopped. None of the corneal changes reported by Hobbs and Calnan (1958) as being ocular complications of chloroquine treatment were seen; but some of these changes would be difficult to differentiate from those of Sjögren's syndrome, as epithelial wrinkling and dots appear in both conditions.

Hydroxychloroquine is probably less toxic than chloroquine (Goode, 1958), and its side-effects are not so well known; these include nausea, dyspepsia, diarrhoea, dermatitis, malaise, and nervous disturbances.

Twenty-two patients in this trial had hydroxychloroquine, and six of them experienced side-effects. These were all fairly minor in nature and resolved rapidly on stopping the drug or, in three cases, on reducing the dose. Sugar-coated tablets of hydroxy-

chloroquine are now available, and are said to reduce the incidence of nausea and dyspepsia.

Conclusion

From the plethora of treatments recommended for Sjögren's syndrome, which range from cervical sympathectomy to sealing the four puncta on the surgical side, and vitamins, oestrogens, testosterone, and steroids on the medical side, it is evident that there is no entirely satisfactory treatment at present for this condition. The results of this clinical trial suggest that further trials of antimalarials in Sjögren's syndrome would be worth while. If the encouraging reports on the effect of antimalarials on rheumatoid arthritis are substantiated, this would be an additional reason for using them in Sjögren's syndrome, as two-thirds of these patients have rheumatoid arthritis.

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The American National Library of Medicine has just issued *Fungus Infections*, a bibliography on systemic and superficial fungus infections. This is another in its series of selective bibliographies on subjects of current interest. Copies can be obtained free from the Acquisition Division of the Library, 7th Street and Independence Avenue, S.W., Washington, 25, D.C., U.S.A.