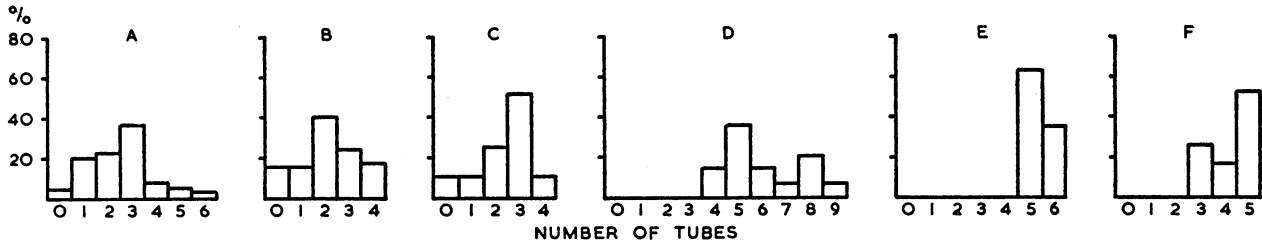


and C). Statistical analysis showed no difference between normal controls and multiple sclerotic patients or between "chronic" and "acute" cases.

Statistical Significance of Results

Sera Compared	Statistical Significance of Difference
Acute M.S. against Normal	N.S. $P > 0.7$
Chronic M.S. " " "	" $P > 0.9$
Acute M.S. " " Chronic M.S.	" $P > 0.7$
Hashimoto's disease " " Normal	$P < 0.001$
Rheumatoid arthritis " " "	$P < 0.001^*$
"Non-rheumatoid arthritis " " "	$P < 0.001$
Rheumatoid arthritis " " Non-rheumatoid arthritis	$P < 0.01^*$

* Cochran's modified "t" test for unequal variance was applied.



Distribution of immuno-conglutinin titres. FIG. A, Normal. FIG. B, Acute multiple sclerosis. FIG. C, Chronic multiple sclerosis. FIG. D, Hashimoto's disease. FIG. E, Classical rheumatoid arthritis. FIG. F, Other "rheumatic" disease.

Sera from 14 patients with Hashimoto's disease serologically and/or pathologically confirmed showed markedly raised immuno-conglutinin titre, distributed as in Fig. D. These were mostly cases with very high antibody titres (tanned red-cell test), and in view of the small size of this group no attempt was made to correlate the immuno-conglutinin and antithyroglobulin titres.

The 22 patients with rheumatic disease (Figs. E and F) were divisible into those with true rheumatoid arthritis (11) and those with conditions such as osteogenic arthropathy, ankylosing spondylitis, etc. (11). The former of these two subgroups had a significantly higher conglutinin titre than the latter ($P < 0.01$), but both differ significantly from normal ($P < 0.001$).

Tests on cerebrospinal fluids gave uniformly negative results.

Discussion

Our normal distribution of immuno-conglutinin differs from that given by Marks and Coombs (1957) but corresponds more closely to some of their analyses for individual months. However, as both the normal controls' and the patients' sera were obtained at the same time it is perhaps justifiable to assume that the incidence of minor infection influencing the immuno-conglutinin titre is the same in the two groups.

To the primary question posed—namely, whether cases of multiple sclerosis show an elevated immuno-conglutinin titre in the blood—we are able to elicit a definitely negative answer in both acute and chronic cases. This contrasted sharply with our findings in Hashimoto's disease, and the test thus gave similar results to the globulin-consumption test applied by Field and Ridley (1960) to these two diseases.

The results obtained with sera from cases of Hashimoto's disease gave the results one would expect from a confirmed auto-antibody disorder; high immuno-conglutinin levels were found in all cases we examined. It would be of interest to reinvestigate all these cases after varying periods of treatment to observe variations of immuno-conglutinin with depression of antibody titre and clinical improvement.

All cases of clinical rheumatic disease had a raised immuno-conglutinin level independent of the result of the Rose-Waaler test, and this may indicate some stimulus not detected by the common serological tests applied in rheumatoid disease.

Summary

Serum immuno-conglutinin levels have been studied to assess the presence or absence of antigenic stimulus.

The serum from patients with multiple sclerosis showed normal immuno-conglutinin levels and distribution.

Immuno-conglutinin was markedly raised in Hashimoto's disease and in rheumatoid arthritis.

We are indebted to Dr. E. J. Field for suggesting the investigation and defining its scope and purpose; to Drs. Henry Miller, Malcolm Thompson, and G. S. Owen for sera; and to Mrs. D. Weightman for statistical analyses.

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Preliminary Communications

Treatment of Herpes Simplex with 5-Iodo-2'-deoxyuridine

The numerous and continuing studies on the prophylaxis and treatment of herpes simplex suggest that there is no satisfactory therapeutic regime for this recurrent virus infection. Immunological techniques, either by repeated autoinoculation of successive lesions as advocated by Hruszek (1933) or by multiple smallpox vaccinations as demonstrated by Schiff and Kern (1954) and earlier workers, are no longer regarded by most dermatologists as acceptable or effective forms of treatment.

Lazar (1956) showed that a new disease site could be initiated after the use of unmodified material containing the live virus, and Kern and Schiff (1959) have negated their earlier work by a controlled trial where they managed to "cure" nearly as many patients with a heat-killed inactive vaccine as with the active vaccine. These workers suggest that any benefit obtained may have been due to inoculation of foreign protein or other substances within the vaccine or to "suggestion." Of more recent interest are the observations of Alexander (1962), who showed that temperature increases were

associated with attacks of recurrent menstrual herpes and that taking aspirin had some preventive action.

Though controlled trials are lacking, x-ray therapy, dabbing with rectified spirit, and, in more recent years, the application of an antibiotic-hydrocortisone cream are thought to expedite resolution, though clearance is unusual under seven days. In severe cases crusting and inflammation may last for two to three weeks.

Prusoff (1959) showed 5-iodo-2'-deoxyuridine (I.D.U.) to be a metabolic antagonist of the use of thymidylic acid in the synthesis of deoxyribonucleic acid, and Herrman (1961) showed that it was an inhibitor of herpes simplex and vaccinia viruses in tissue culture.

Since I.D.U. apparently blocks the metabolic pathways of virus synthesis, the continued presence of the drug might suppress D.N.A. synthesis and would be of therapeutic value.

Recent studies by Kaufman, Nesburn, and Maloney (1962) and Corrigan, Gilkes, and St. Clair Roberts (1962) have confirmed that topical application in the eyes produces a significant antiviral effect and is an efficient treatment in cases of herpetic corneal ulceration. Those studies naturally suggested the use of this compound in herpes simplex infections of the skin.

Case Material, Methods, and Results.—The 0.1% topical solution was used in the first 11 cases which presented when it was decided to treat cases of recurrent herpes simplex with skin involvement; the 0.5% ointment was used in two later cases. The first three cases were treated with hourly applications of the solution, though subsequent cases had the solution applied hourly during waking hours only. The ointment was applied four times daily. The Table summarizes our results.

Skin Lesions Treated with I.D.U.

Case No.	Sex and Age	Site	Duration Prior to Treatment	Previous Attacks	Normal Duration (Weeks)	Treatment Time for Resolution
1	F 9	Upper lid	3 days	Corneal dendritic ulcer 6 weeks before and coincidental	—	3 days
2	M 38	lip	4 hours	Coincidental. Primary corneal dendritic ulcer	—	2 "
3	F 36	" "	4 "	Coincidental dendritic corneal ulcer. 2-3 attacks a year for 20 years	2-3	2 "
4	M 38	Upper lip + nostril with adenitis	24 "	4-6/yr for 6 yrs	2-3	3 "
5	F 14	Upper lip, right hand		2-3/yr for 10 yrs	2-3	2 "
6	F 20	Upper lip		2-3/yr for 6 yrs	2-3	3 "
7	M 23	Right cheek		2-3/yr for 5 yrs	2-3	4 "
8	M 42	Upper lip		2-3/yr for 15 yrs	2-3	3½ "
9	F 26	Cheek	7 days	1-2/yr for 6 yrs	2-3	3 "
10	M 27	Upper lip	5 × 5 cm. 18/12 since malaria; almost continuous herpes	—	—	5 "
11	F 8	lip	3 days	Nil	—	3 "
12	M 30	lip	3 "	2-3/yr for 5 yrs	2-3	3 "
13*	M 57	Nose	4 "	1-2/yr for 10 yrs	2-3	

* This case showed definite clinical improvement, but not complete resolution: probably treatment was not conscientiously carried out.

DISCUSSION

The relief of symptoms and the marked resolution of the eruption within 24-72 hours of starting treatment was noted by all patients. From experience of past episodes it was expected that the lesions would persist for 7 to 21 days, in some cases even longer. One patient failed to respond to treatment, and it is probable that in this case the treatment was not conscientiously carried out. None of those successfully treated have so far failed to respond or suffered a recurrence. It is appreciated, however, that a long follow-up will be necessary before it can be claimed that the drug has completely eliminated the virus at the site of infection.

Although herpes simplex when it affects the skin is usually regarded as a trivial infection it can give rise to serious complications. Jones (1959) stressed the dangers of the virus-laden kiss and made a plea for a national campaign to prevent the blight of ocular herpes by making everyone aware of the infectious nature of cold sores. Three of our cases of dendritic corneal ulceration had a previous history of periocular involvement; an even more serious and sometimes lethal complication is Kaposi's varicelliform eruption, which occurs as a complication of atopic eczema in infants and young children.

SUMMARY

The results of treatment of 13 consecutive cases of herpes simplex of the skin with a 0.1% topical solution or a 0.5% ointment are summarized. There was rapid subjective amelioration of symptoms in all cases and healing of the lesions within two to five days. This was less than the usual period in all cases.

The importance of treatment of skin lesions of herpes simplex is discussed in relation to the other complications of this disease.

The best method of application of I.D.U., the effective concentration, and the frequency of application have still to be determined; it is too early to say whether the cure is permanent or whether there will be recurrences.

ADDENDUM.—Since this paper was submitted five further cases have been treated with equally good results.

We wish to thank Messrs. Smith Kline & French for supplying the I.D.U., and especially Dr. H. D. Darcus and Dr. Johnston for the helpful information they supplied during this investigation.

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