organs. The liver (weight 2,090 g.) was somewhat enlarged and oedematous. Microscopical examination showed mild fatty degeneration and a scanty infiltrate of lymphocytes in the portal tracts. The trachea and main bronchi contained mucopus, and both lobes of the left lung were consolidated. The microscopical picture was that of pneumonia, though only very few polymorphs were found in the inflammatory exudate. There were numerous ulcers in both tonsils and at the base of the tongue. Histological sections showed massive necrosis in the floor of these ulcers, but again there were only very few neutrophils. The bone marrow of the sternum, the vertebral column, and several long bones appeared normal to the naked eye, but smears and sections revealed a complete absence of all myeloid cells, with the exception of a few scattered promyelocytes and eosinophilic myelocytes. The bulk of the cells were erythroblasts and lymphocytes, with a normal distribution of megakaryocytes.

COMMENT

The cause of death was undoubtedly agranulocytosis and pneumonia. Jaundice develops in many cases of agranulocytosis from all causes, usually as a terminal event. It is therefore difficult to say in this case whether it was due to liver damage from chlorpromazine or to the agranulocytosis.

It is generally agreed nowadays ("Any Questions," 1957) that regular blood counts can do little to prevent agranulocytosis due to drug therapy. The present case therefore underlines once again the need for caution in the administration of drugs of the phenothiazine group.

Our thanks are due to Drs. C. H. Catlin and J. H. Molloy, under whose care the patient was admitted.

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Intra-articular Prednisolone

Although prednisolone (Δ^1 -dehydro-hydrocortisone) has been available for systemic administration for several years, it is only recently that it has been prepared in a form suitable for intra-articular injection.

So far only three reports have been published on its use by this means. Hagedorn (1957), in surveying the results of its administration to 89 patients suffering from various joint and periarticular soft-tissue lesions, concludes that it produces the same effect as hydrocortisone in less than half the dosage. Moreover, he states that it is completely free of the local exacerbation of symptoms that is known to follow the local use of hydrocortisone in 25 to 30% of cases. On account of this complete absence of subjective and objective side-effects, the small doses needed, and the fact that the effect of prednisolone is equal to that of hydrocortisone, he concludes that it is the drug of choice. Thompson (1957) and Newton (1957), although not quoting the number of cases subjected to trial, suggest that there is no significant difference between prednisolone in its acetate or higher ester form and hydrocortisone, although Thompson considered that the results were significantly better when it was injected into the small joints of the hand.

PRESENT INVESTIGATION

In view of this apparent contradiction of evidence the results of a short controlled trial of prednisolone acetate ("hydrodeltalone") in 79 patients suffering from rheumatoid arthritis are recorded. The difficulty in assessing results in

this condition was to some extent eliminated by confining the trial to the elbow- and knee-joints, both of which are readily accessible to measurement of joint swelling, joint temperature, and range of movement. The trial was also confined to joints in the acute stage, as, although the steroids could be expected to produce only a temporary relief of symptoms, this period of relief could be accurately measured in days or hours. Eighty patients were accordingly selected and injected with equal doses (25 mg.) of either hydrocortisone or prednisolone acetate at random. After the effect of one injection had been judged to have worn off, the other steroid was injected. At the time of the injection with the prednisolone the patients were not told that a "new drug" was being tried, and to all external appearances the content of the syringe appeared the same in each case.

Every patient was asked to give an assessment upon the speed of the effect, the incidence of local reaction to the injection, and the duration of the effect.

This inquiry was correlated with a subjective examination of the joint involved to estimate improvement in swelling and range of movement.

Results.—Of the 80 patients treated in the manner described, one failed to return for assessment and six have been excluded from analysis as they failed to show any response to hydrocortisone, although all responded to the

Results

Drug	Average Onset of Relief	Average Duration of Relief	No. of Patients with Increased Joint Pain
Hydrocortisone ..	30 hours	6.5 days	38
Prednisolone ..	20.3 "	8.1 "	15

prednisolone. The results in the remaining 73 patients are shown in the Table. The average onset of relief was 10 hours earlier in the case of prednisolone, the average duration of relief two days longer, and the incidence of side-effects 27% lower. There seemed to be little difference in the intensity of the effect between the two drugs in similar doses. Statistical analysis of the results by 2×2 contingency confirms the clinical impression that prednisolone produces the more rapid and longer duration of relief than hydrocortisone ($\chi^2 > 11$, $P = 0.001$).

CONCLUSIONS

It would appear, therefore, that prednisolone acetate gives a significantly longer period of relief, a much lower incidence of local reaction, and a slightly more rapid onset of effect in the acutely inflamed rheumatoid arthritic joint than hydrocortisone acetate. That six patients responded to prednisolone who were resistant to hydrocortisone would suggest that the former might prove of value where such a resistance is already known to exist.

Although the present trial was confined to those suffering from rheumatoid arthritis, experience with 284 patients suffering from a wider range of articular and soft-tissue lesions suggests that this rapidity of action, reduction in the incidence of local exacerbation, and duration of effect can also be observed following local injection of prednisolone.

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