Straub (1937) found that influenza A virus, administered under anaesthesia, in mice and ferrets produced a necrosis of the epithelium of the finer bronchioles. There has been a good deal of discussion over the relative roles of virus and bacteria in producing lung lesions in influenza. It is interesting to note that in this series there was a more dramatic response to antibiotics in Group 4 cases, and, although there was a relatively small number of these, there was a suggestion that the beneficial response was due to the presence of a severe secondary antibiotic-sensitive bacterial infection. The lack of response in Group 3 cases might have been because the condition was a more predominantly virus infection which was insensitive to the antibiotic drugs used.

The relative rarity of classical lobar pneumonia in present-day general practice should be noted. In my practice only three cases of this condition have been met with in the past five years. During this same period some 40 cases of unilateral lung infection were seen, having the general picture of the cases described under Group 3.

Summary

A report is presented on 223 cases of clinical influenza seen during the epidemic of last winter.

Difficulties in accurate diagnosis are discussed and the clinical features of influenza described.

The incidence and type of lung involvement are discussed. Signs of lung involvement were found in 17% of the cases. The particular frequency of a "bronchiolitis" or "pneumonitis" is noted. There were no deaths. There was an absence of any real response to antibiotic drugs in this group, but a good effect was obtained in the four cases with pneumonic consolidation.

A correlation is attempted between pathological and clinical features and the relative roles of virus and bacteria.

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EFFECT OF CORTISONE ON REACTION OF SKIN TO ULTRA-VIOLET LIGHT

BY

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Recent investigations have revealed an increasing number of diseases the symptoms of which disappear or are ameliorated during the administration of cortisone in doses that are massive compared with the physiological hormone requirement. An explanation of the mechanism of this action has been sought in the rather basic changes produced in the organism. One of the central problems in this respect—the effects of cortisone on the reactivity of the organism when subjected to various stresses—still remains to a large degree unsolved.

With the use of an adjusted dose of radiant energy as a stress I have studied the change in reactivity caused by massive dosage of cortisone; the radiation was applied to a tissue (skin) in which its effects were easily observable. The results of such an experiment may be thought to be of general interest.

Material and Method

Experiments were made on 14 patients treated with massive doses of cortisone. (The preparation used was cortone acetate, or 11-dehydro-17-hydroxycorticosterone-21-acetate, produced by Merck and Co., Inc., U.S.A.) Nine of the patients suffered from rheumatoid arthritis, one from rheumatic fever, one from neurocirculatory asthenia, one from bronchial asthma, one from ulcerative colitis, and one was a suspected case of brain tumour. Eight of the patients were females and six were males. The average age was 41.5 years.

A mercury quartz lamp (2.5 amp., 220 volts) was the source of the radiant energy. The lamp was 19 cm. from the focus, and an opaque plate with five holes for the exposure was placed at this distance. (The diameter of the holes was 6 mm., and their centres were 15 mm. from each other.) In order to ensure that the amount of radiant energy would be constant, at every session the lamp was on for five minutes before the actual exposure. Thus the terminal radiation due to an increase in the temperature of the lamp may also be regarded as identical at the different sessions.

The volar surface of the forearm was selected for the exposure, using a different site each time, since it is known that the sensitivity of the skin to ultra-violet light is greatly reduced by previous exposure to it (Ellinger, 1932; Schulze, 1946). As the experiments were made during the period from December to February it can be assumed that, at the latitude of Helsinki, the sensitivity of the skin of hospital patients would not have been reduced by exposure to sunlight during the intervals between treatment. At the exposure the opaque plate with the holes was pressed against the site of the skin to be treated. The middle part of the forearm was chosen for the exposure during the administration of cortisone. Before and after its administration the exposure was directed on each side of this area (areas possibly less sensitive to radiation).

The duration of the exposure through the different holes was $\frac{1}{2}$, 1, 3, 6, and 6 to 20 minutes. After preliminary tests an attempt was made to adjust the length of the longest exposure in such a way that it would produce blister formation.

The reactions of the skin were read 6 and 24 hours after the exposure. Ellinger (1932) recommended a reading after 7 and 24 hours. Attention was paid: (a) to the shortest exposure which produced a visible reaction in the skin; (b) to colour changes at the site of the exposure—these were classified according to Schulze (1946), in three groups: (1) red erythema, (2) red erythema and brown pigment, and (3) brown pigment only; and (c) to blister formation at the site of the exposure and to the diameter of the blister.

Results

The results obtained are given in the Table. These show that the reactivity of the skin to radiant energy was on an average reduced during a massive dosage of cortisone. A protective reaction appeared in the skin only after a dose of radiant energy about twice

that effecting a similar reaction before the cortisone. The type of cutaneous reaction also changed on the administration of cortisone. Instead of the previously erythematous reaction, there tended to be an increase of brown pigmentation. A suppression of the reactivity of the skin to higher doses of radiation was also observed. In spite of the use of greater amounts of radiant energy during the cortisone treatment than those required to produce a burn blister of second degree before its administration, blister formation now occurred in only a few cases.

Every change in reactivity of the skin seen during the cortisone treatment returned to normal after treatment (see Table). Any deviation in the results obtained

TABLE Showing the Effect of Massive Doses of Cortisone on the Reactions of Skin to Ultra-violet Light

	Before Cortisone	During Admini- stration*	After Cortisone†
Minimum exposure required to produce a skin reaction observable after 6 hours. Mean	41 sec.	88 sec.	72 sec.
Type of reaction at site exposed for 6 minutes. Reading 6 hours after exposure			
No. of cases with:			
Red erythema	7	2	6
Red erythema and brown pigment	7	9	7
Brown pigment only	0	3	1
Maximum exposure at one site.			
Average	11.1 min.	15.1 min.	14.1 min.
No. of cases with vesicles after this exposure	9	3	10
Sum of diameters of the vesicles	45 mm.	11 mm.	43 mm.

* Cortisone had been administered for at least five days. The average dose before exposure was 1,038.6 mg. The minimum dose was 500 mg.

† The administration of cortisone had been stopped on an average 5.2 days previously. Administration had been carried on for an average period of 18.8 days, and the amount of cortisone given during this time was on an average 1,969.3 mg.

after treatment from those made before it depends possibly on the short interval between the end of the administration and the exposure (average 5.2 days): the reactions may still have been under the suppressing influence of cortisone. This is also supported by the finding that among the rheumatoid arthritis patients only five had developed a severe relapse at the time of the control exposure, after disappearance of the symptoms during cortisone treatment. In the remaining four, relapse occurred as late as one to five days after the exposure.

Discussion

The above experiments show that a massive dosage of cortisone reduces the sensitivity of the skin to radiant energy. It may be questioned whether such an action is favourable. Is it an inhibition of the protective mechanisms of the body, or does it mean a true increase in resistance?

The view that the observed phenomenon should be regarded as a suppression of the normal protective mechanisms is supported in particular by observations made in connexion with various infectious diseases. It has been found that massive doses of cortisone inhibit or prevent the typical symptoms of acute infectious diseases, such as fever, the development of inflammatory tissue changes, a rise in erythrocyte sedimentation rate, the production of antibodies, etc., whereas, for instance, the growth and propagation of organisms in bacterial infections proceeds even more rapidly than normally (Germuth and Ottinger, 1950; Glaser *et al.*, 1950; D'Arcy Hart and Rees, 1950; Bjørneboe, 1951). Similarly, the obvious reduction of the mineralo-corticoid

secretion of the adrenal cortex—which secretion plays an important part in the normal protective reactions of the organism—also supports the view that the observed effect is due to a suppression of the normal protective mechanism of the body. Massive doses of cortisone have been observed to produce atrophy of the adrenal cortex in experimental animals (Nichols and Miller, 1949; Stebbins, 1950; Antopol *et al.*, 1951). This finding corresponds with the clinical observations on man of symptoms suggesting Addisonism (Sprague *et al.*, 1950), and of a decreased excretion of 17-keto-steroids during massive administration of cortisone (Wilkins *et al.*, 1951).

Accordingly there are findings which suggest that cortisone in massive doses is not a means for fighting against the primary cause of a disease, but, on the contrary, a factor preventing the, generally expedient, protective reaction of the organism itself. Since most of the symptoms of diseases are expressions of the protective reaction of the body, it is obvious that a factor suppressing this reaction eliminates the majority of the symptoms of various diseases. It is quite a different question whether such a "cure" of the symptoms is desirable, for diseases in which one may with certainty ascribe the symptoms to a wrong overactivity of the protective mechanism are somewhat rare.

Summary

A change, mainly a suppression, in the reactivity of skin exposed to a mercury quartz lamp was observed during the use of massive doses of cortisone. The minimum exposure required to produce an observable reaction in the skin was approximately doubled. Instead of the earlier red erythematous reaction the skin tended to react with an increase of brown pigment. Blister formation occurred much more rarely than normally.

The observations possibly suggest, in support of earlier studies, that massive doses of cortisone are not a universal means of protection against the causative agents of disease, but, on the contrary, a factor suppressing the protective mechanism of the organism.

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A former instructor in philosophy and novitiate in a monastery who had only brief medical experience as an orderly in an eye and ear infirmary in Boston was said to have established a brilliant reputation as a ship surgeon in the Royal Canadian Navy (*The Times*, November 22). He served in the Canadian destroyer *Cayuga* in Korean waters and successfully performed various operations, such as amputations and removing a bullet close to the heart. According to the Navy's statement nothing has occurred to indicate that he did not possess the competence of a fully qualified medical man; he is nevertheless to be discharged from the Navy for misconduct.