SOME REMARKS ON THE BACTERICIDAL PROPERTIES OF ZINC OXIDE.

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Zinc oxide is probably that substance most generally in use in the local treatment of skin-diseases, both unmixed and, to an even greater extent, in conjunction with other substances in a number of powders, liniments, salves and ointments. But although zinc oxide occupies such a prominent position in dermatology, we really know very little indeed about its action upon the skin.

The descriptions (as a rule somewhat brief) in the dermatological and pharmacological text-books emphasize zinc oxide's drying qualities, and its power to form, purely mechanically, a protective covering for the surface of the skin. In common with other insoluble, finely-ground powders, zinc oxide has also the power to bind many substances through adsorption, whereby it can counteract the effects on the skin partly of external, active, chemical irritants, and partly also of irritating substances which may possibly develop in the skin itself under pathological conditions.

Finally a few text-books mention that zinc oxide has a slightly antiseptic action, but very little weight seems to have been laid upon the last-named circumstance, since it has probably been assumed that zinc oxide, as a practically insoluble substance, could not be expected, except to a very slight extent, to give off free zinc ions and thereby evince bactericidal properties.

It is, however, zinc oxide's bactericidal qualities which I propose to discuss here, since there is reason to believe that these qualities are of greater significance than is commonly supposed.

I became aware of the significance of this phenomenon through a series of experiments, the object of which was to determine whether or not the drying and adsorbent action of various insoluble powders would have an inhibitory effect on bacteria in ordinary plate-cultures.

These experiments were carried out simply by strewing the sterile powders—those involved were talcum, kaolin and zinc oxide—over the surface of a Petri-dish containing agar inoculated with staphyloccoci.
Whilst talcum and kaolin seemed to have no influence whatever on the development of the colonies, a distinct sterile zone appeared around each little deposit of zinc oxide. It seemed, therefore, that zinc oxide possessed special bactericidal properties which were not present in the other powdered substances, and it occurred to me that it would be interesting to investigate this special property more closely.

I made, therefore, with the aid of a tablet machine, a number of small flat tablets of zinc oxide of 1 cm. diameter. These tablets were sterilized and placed on the surface of agar which had been melted in Petri dishes and inoculated with a culture of various bacteria. The medium's acidity was pH 7.5. When these dishes were placed in a thermostat for twenty-four hours, a circular sterile zone, varying in extent with the various bacteria, appeared around each zinc oxide tablet. In the case of _B. pyocyaneus_, of which two different strains were examined, there was no sterile zone whatever, and in that of two strains of _B. coli_ only the suggestion of such a zone. On the other hand, in the case of _B. subtilis_, which in some other respects possesses far greater powers of resistance, and of which two strains were tested, a distinct sterile zone appeared. Results were most favourable, however, where staphylococci and streptococci were involved. In the case of the strains of staphylococci tested, which were grown from various skin-diseases, the extent of the sterile zone varied from 2 to 6 mm., and in the case of streptococci similarly cultivated from the skin, the extent of the sterile zone varied from 6 to 8 mm.

These experiments showed that, at any rate as far as concerns the two classes of bacteria of most importance in the pathology of the skin, _i.e._ staphylococci and streptococci, zinc oxide undoubtedly has an inhibitory effect under certain conditions. Its action, as will be seen, is not limited to the area directly covered; it would appear that the active substance is an actually bactericidal one, capable of diffusion into the surrounding substratum.

This interesting and, at first glance, mysterious phenomenon can probably be explained in the following manner:

Zinc oxide, although practically insoluble in pure water, reacts readily to acids, and forms, even where many of the weak organic acids are concerned, soluble compounds. This being the case, the possibility arises that zinc ions can be given off in considerable quantities, and this establishes the possibility of a bactericidal action. Staphylococci and streptococci of the skin are essentially acid-forming microbes, and where a colony
of these cocci is in course of development, acid will be diffused into the medium. The possibility is thereby created for the activation (so to speak) of the zinc oxide, since the latter now partially dissolves with the formation of a compound which can give off free zinc ions and thus have an inhibitory effect upon further development.

That the formation of acid really is a deciding factor is confirmed by, among other things, the observation that the inhibitory action of zinc oxide is increased very considerably when agar, the reaction of which has an acid tendency, is used instead of neutral agar. When agar of pH 5·5 is employed, the sterile zone in the case of staphylococci is almost twice that which appears when agar of 7·5 is used.

I have made some comparative tests between pure zinc oxide and commercial zinc oxide (oxydum zincicum venale), which latter has from olden times been the preparation most commonly employed in dermatology. The pure zinc oxide exhibited, on the whole, the weaker action, and the explanation of this circumstance probably lies in the difference in the actual nature of the two preparations. Commercial zinc oxide represents zinc oxide in an amorphous form, whilst oxydum zincicum purum is crystalline, and it has been determined by chemical measurement that amorphous zinc oxide is somewhat more soluble than crystalline in pure water, and is also more rapidly and readily soluble in acid than the crystalline form. Similar diversities may be observed between, for example, the crystalline and amorphous forms of chloride of silver.

There is every reason to assume that a similar bactericidal process to that which has been demonstrated in vitro also takes place when zinc oxide is applied to the skin. In this connection it is worthy of note that the very preparation which has been longest and most faithfully employed, namely commercial zinc oxide, seems to possess the strongest bactericidal properties, and that these are especially pronounced where the two classes of bacteria of greatest importance in dermal pathology, i.e. staphylococci and streptococci, are involved.

This assumption can in reality explain many of the beneficial effects which zinc oxide undoubtedly has on various skin-diseases where infection by the bacteria mentioned plays a part. In contrast to bactericidal substances such as, for example, mercuric chloride, which attacks the bacteria and the cells of the skin indiscriminately, and which rapidly becomes changed into inactive compounds, zinc oxide is apparently a substance which is in itself almost neutral, but which, where acid-producing
bacteria are in course of development, is split up by the acid formed into active compounds. In applying zinc oxide to the skin, therefore, we apply a substance which, while not acting as an irritant upon the dermal cells, exhibits a definite bactericidal action exactly in the places where it is needed. It will readily be appreciated that a substance possessing these qualities is, from a therapeutic standpoint, in many respects more valuable than a disinfectant which, though more potent, is neither so elective nor so enduring in effect as zinc oxide.

In cases of folliculitis, furunculosis and other undoubtedly primary infections of the skin zinc ointment frequently gives far more favourable results than can be obtained by the use of definitely bactericidal agents, such as ethyl alcohol, mercuric chloride, etc., and the explanation of this lies probably not alone in zinc oxide's protective and drying action, but also in its, in certain respects, especially favourable bactericidal effect.

However, the bactericidal action of zinc oxide and its curious elective property are, perhaps, most significant where the diseases under treatment cannot be said to be actually of bacterial origin, but where, in any case, infection plays a considerable part. Pityriasis simplex ("eczema seborrhoicum" of the German authors) is an example of this class of disease. The causative agent of this affection has not yet definitely been agreed upon, but we know that streptococcal infections, the nature of which can be confirmed not only culturally, but also clinically, are very frequently included in the syndrome, and it is probable that staphylococcal infections also play a prominent part here. In its more pronounced forms this affection is characterized by a combination of eczematous and infectious changes, and it is well known that attempts to influence the latter by means of strong disinfectants almost invariably lead to an exacerbation of the eczematous symptoms. By the use of pure zinc ointment, however, amazingly favourable results upon the whole symptom-complex can often be obtained, and these must probably, to some extent, be attributed to zinc oxide's bactericidal qualities, which, where such an exceedingly irritable affection is involved, fully comply with that important condition, ability to injure bacteria without irritating the skin to any noticeable degree—a property which is lacking in most other disinfectants.

It is probable that secondary bacterial infections have a share also in many other skin-diseases. Their significance has probably been underestimated in cases of eczema and the various forms of dermatitis, although
their complication with folliculitis, impetigo, lymphangitis and other similar symptoms is a frequent indication that the bacteria appearing in these affections at any rate can possess pathogenic qualities. It is assumed also that in such cases zinc oxide will exhibit a considerable bactericidal effect, without, like most other disinfectants, irritating the skin.

In zinc oxide’s effect upon the skin, therefore, a definite and by no means inconsiderable bactericidal action can, presumably, be counted upon, in addition to its protective and adsorbent powers. Both as a therapeutic agent in the case of fully developed infections of the skin, and as a prophylactic against secondary infections of various skin-diseases, a certain importance must be accredited zinc oxide. The unusual phenomenon which distinguishes its bactericidal action, i.e. its dependence upon the presence of acid, gives zinc oxide a peculiar position among the bactericidal substances. Whilst, as has been stated, zinc oxide must be regarded as almost neutral as far as the actual cells of the skin are concerned, it will be split up by the acid-producing microbes into disinfectant compounds, so that the microbes, so to speak, weave the rope for their own necks. Its action will thus in some degree be limited to those places where it is needed, and it will be possible to a greater extent than with other disinfectants to injure the bacteria without irritating the skin. It is my opinion that this quality partially explains the established position which it has been possible for zinc oxide in its various forms to maintain in dermatology, where the question is so frequently one of combating an infection of the skin without, at the same time, irritating the latter.
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