breaks of the disease in their herds during the last ten or fifteen years. I also found that several men, in all probability, contracted the disease on their fingers or wrists, and in one case it was communicated by a cowman to his wife as before mentioned.

I am also impressed by the fact that though the results produced by accidental inoculation direct from a case of cowpox to the human being broadly go through the same stages as those produced by vaccine lymph, yet they differ in the appearances at the various stages, and probably run a more severe and protracted course. This may possibly be due to accidental introduction of organisms producing more intense inflammatory reactions, or the preparation of the lymph for vaccination may modify the activity, and thereby subdue the intensity of results obtained.

As this disease chiefly prevails in milk cows, and usually affects a whole herd, it should, I think, be made notifiable. For in process of milking the scabs are knocked off, and the contents of

Fig. 2.—Showing appearance of cow's teats about twentieth day of disease.

the vesicles are sure to contaminate the milk; the scabs and products of secondary inflammation and sloughing must also to some extent find their way into the milk, and the result of drinking such milk, should any small abrasion be present in the mucous membrane of the upper alimentary tract, raises some speculation. Dairy farmers' knowledge of this may perhaps partly account for the apparent rareness of the disease. If notification were made compulsory, and if the disease was confirmed by competent veterinary inspectors as likely injuriously to affect the use of the milk for human food, surely its sale ought to be stopped until danger had passed. As the disease is rare, probably insurance against its occurrence could be made at a trifling cost.

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ON MALARIAL FEVERS AND QUININE.*

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As all observers of malarial fevers know, quotidian fever and double and triple fever, and irregular and remittent, may be caused by any of the three well-known parasites, it is supposed by several different broods developing independently. There may of course be mixed infection also. As a matter of fact parasites in different stages will be found in any malarial blood at the same time, but there is generally a preponderance of organisms of the same size. Haemolysis, or breaking down of the blood discs, is more

or less rapidly going on during an attack, most rapidly when the sporulation is most complete. But the fever only manifests itself when enough of the poison manufactured by the parasites in the red cells is set free in the blood plasma to cause its physiological action on the nervous system. This poison is probably a protein derivative, and the dose required to cause fever manifestations is large but varies with the individual. We know as a case grows worse the fever anticipates, more cells break down, and more poison is set free. As an attack grows less the fever is postponed, fewer cells break down, and less poison is set free. The development of antibodies is but a small factor in the cure of malarial patients. Immunity to the disease, as we all know, is a thing of very slow growth and very many attacks.

In two or three days, according to the nature of the organisms, the asexual parasites sporulate, but doubtless very many infected cells break down before their uninvited guests reach this stage. The parasites doubtless, too, die prematurely from many causes. Why should they alone in Nature be free from accident and disease?

We know that in malaria there are profound changes in the quality and composition of the blood. (1) There is a great diminution of the red cells, much greater than can be accounted for by the ratio of cells infected. (2) The haemoglobin content of the discs is much reduced. It has been known to fall as much as 50 per cent. (3) The resistance of the discs is lowered. In normal blood nothing happens to the discs when added to a 0.41 per cent. salt solution, whereas malarial blood discs haemolyse at once. (4) There is a leucopenia, but as pointed out by Christophers and Stephens, there is both a relative and an actual increase of the large mononuclear cells. The meaning of this is unknown.

I think we may take the lowering of the resistance of the blood discs to be Nature's method of cure. If the infected discs break down before the asexual parasites can sporulate, a permanent cure ensues, unless, indeed, Schaudinn's theory be correct, namely, that the gametes may revert under favourable conditions to the asexual type. In other words, he supposed that the gametes are not only sexually perfect parasites but may also act the part of resting spores. It is a plausible theory, but there is no evidence to support it. It is much more likely that some spores may become encysted in certain internal organs and await the favourable turn of the tide when the human body becomes again a suitable habitat.

We come now to the action of quinine. Intimately connected with malignant malaria in the tropics is blackwater fever—acute haemoglobinuria. As pointed out by Koch, it nearly always occurs in patients taking quinine. Quinine lowers the resistance of the blood discs, and so does malaria, but we do not give it to our patients on the principle of *similia similibus curantur*. This action of quinine can easily be demonstrated *in vitro*. The amount of neutral quinine hydrochloride required to haemolyse 1 c.cm. of red cells at 37° C. is from 0.001 to 0.0008 gram. In blackwater fever during an attack it was only 0.0008 (Stephens and Christophers). Doubtless the proportion required to cause lysis of inhabited blood discs is very much less than in the case of uninhabited. When quinine is given in large doses for a considerable time to a person the resistance of whose blood has been greatly lowered by frequent attacks of malignant malaria, a time comes when, in spite of the natural safeguards of the system, an explosive breakdown of the blood discs will take place. But when quinine is judiciously given in malarial fever it causes the gradual premature breakdown of infected cells before their guests can sporulate. Thus the cycle of Golgi is cut short, and a cure is effected as far as the patient is concerned, for the time being at any rate. It is doubtful if the drug has any effect in cutting short the cycle of Ross, so that it is possible a patient may be cured as far as he himself is concerned, but still for a time be able to infect mosquitos. In other words, quinine cures malarial fevers by destroying the homes and food of the *Plasmodia malariae* before they can sporulate asexually; but yet the "cured" patient may remain a source of infection to his neighbours for some time. All observers admit that the gametes are practically unaffected by quinine. I have seen crescents very quickly disappear under moderate injections of soamin.

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