ALASTRIM IN JAMAICA.*

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PLATES XII TO XX. (FIGURES 1 TO 15.)

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In September, 1920, one of us was invited by Dr. Deeks, of the United Fruit Company, to go to Jamaica to observe the epidemic of Alastrim which had prevailed there since May, and the following description of the disease is based upon the impressions gained during a stay of twelve days in Kingston, together with the observations of Dr. Moody, who had been studying the clinical phenomena since the beginning of the epidemic. The United Fruit Company gave me their most generous assistance, and to their officers, and especially to Dr. J. L. McLean, my thanks are due.

The name Alastrim is of Brazilian origin and is derived from a Portuguese word meaning to spread or strew about, hence something spread, a mantle or cloak. Other names such as Amaas, Sanaga pox, Kaffir pox, or milk pox, and, indeed, many others, have been applied in various countries to what seems to be the same disease.

In all these epidemics, which have been numerous, the great question has concerned the identity of the affection with smallpox, and in spite of the continued attention which has been devoted to it, this question is still unsettled. It is not even known whether it has always been the same disease in the various epidemics, but at least they have had in common the main feature which seems to distinguish them from typical smallpox, namely, the mildness of the affection and the very low mortality. Cleland and Ferguson, Armstrong, Green and others describe an epidemic of this kind which occurred in Australia in 1914, in which the mortality was very low and in which

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Green found experimentally that vaccination with standard vaccine was less effective than in true smallpox. Dickson and Lasselle and Scheult described an epidemic in Trinidad, and Korte, Plehn' and Grant have discussed the similar or identical Sanaga pox and Amaas in Africa. It is probably in Brazil that this condition has been most widespread, and there are papers describing it by Carini, Ribas and Aragao. The last named in his paper of 1911 states that in the epidemic then progressing there were at least 250,000 cases, with a mortality of only 0.5-2 per cent.

The descriptions given by these authors correspond minutely with what we have observed in Jamaica, and we have little hesitation in concluding that we were dealing with the same disease. It is less easy to be sure as to the relations between Alastrim and the mild forms of smallpox which have been observed in the southern United States in epidemic form from 1900-1905. The long-continued epidemic occurrence of a very mild form of smallpox in various parts of Canada suggests the possibility that there, too, the disease may be more closely allied to Alastrim than to the severe smallpox of other epidemics. Indeed, a survey of the older literature on smallpox shows that there have been many epidemics of exceedingly mild character and the whole difficult question of the general uniformity of smallpox is brought up.

In Jamaica the epidemic of 1920 appears to have started in Kingston in May, and it is thought that the infection must have been brought from Cuba, where there were many cases of this disease. Cuba is only a few hours distant, and there are frequent boats between Santiago and Kingston. But it may have come from South America, where it is reported that there were many cases. Traffic between the ports of the United States of Colombia and Kingston is direct, and less direct communication with other ports on the northern coast not very difficult.

The exact mode of introduction was not determined. From Kingston it spread throughout the island and a few cases were reported from each of many rural districts and villages. In September the number of cases in Kingston, at any one time, was variously estimated at 400-700, of which about 325 were isolated in a building outside the city.

The disease was recognized as Alastrim by Dr. Hunt, the S. M. O. in Kingston. The panic among the people which would have ensued upon the outbreak of an epidemic of severe smallpox was thus averted,

and the Central Board of Health was able to do much to control the spread of the disease by systematic vaccination and revaccination. More than 100,000 successful vaccinations have been performed up to the present date. The government also gave all the help it could to the government bacteriologist in the work reported in this paper.

COURSE OF THE DISEASE.

Through the kindness of Dr. Murray, the District Health Officer, we were able to follow the search for incipient cases, and thus see in their houses those in whom only the first symptoms of illness were appearing. All other stages could be observed at Bumper Hall, the isolation hospital.

In all, up to the present time, 2,333 cases have been reported. The illness begins after an incubation period which is generally thought to be fourteen days, but which in the course of an epidemic it is difficult to determine accurately. The following evidence bears on this point:

Case 1. Nurse at Bumper Hall, not vaccinated. Headache and pain in the back began fourteen days after she took up duty and was exposed to infection.

Case 2. Was up in Kingston for three days, the epidemic being prevalent in Kingston only, and returned to his country district, where no cases had hitherto occurred. Symptoms developed ten days after returning.

Cases 3, 4 and 5. Infants born at Bumper Hall, free of any signs of the disease. Nursed by their mothers. Rash appeared on the tenth, eleventh and twelfth days after birth.

Case 6. Exposed to infection, so far as he knows, only twice, once thirteen days before, and a second time three days before the onset of symptoms.

Case 7. Developed symptoms eleven days after leaving Kingston where he had been at a school in which some of the scholars were infected.

The onset is sudden with headache and fever, often with some general aching, malaise and vomiting. Apparently none of these symptoms are very severe in most cases, and a complaint of backache was generally elicited only by direct questioning, and then usually in the case of women. In children convulsions sometimes occur at the onset. In 202 cases the incidence of these various symptoms of onset was as follows:

Headache in 172 cases.....	85 per cent.
Pain in back in 111 cases.....	54 per cent.
Pain in limbs in 41 cases.....	20 per cent.
Vomiting in 32 cases.....	10 per cent.

Backache was severe in only forty-five cases; the other patients

described their pain as moderate. The combination of headache, vomiting and pain in the back occurred in only twenty-one of the patients, and of these only six vomited more than once.

The temperature at the onset may rise to 104° or 105° F., but is generally in the region of 103° F. It persists with slight variations for three or four days and then rapidly falls to normal as the rash appears, or even before its appearance. The temperature then remains low for four or five days, but rises again as the rash matures. In mild cases there is no secondary rise of temperature, and in severe cases the rise appears to be dependent on the extent of the rash and the degree of bacterial infection of the skin, since there is only a slight rise when the pus is practically free from bacteria. The patient is often not conscious of the secondary fever, although his temperature may be 102° F. After a few days the temperature again returns to normal and stays there unless complications, such as boils, occur.

In a few of the very severe cases the fever may resemble the typhoid type, persisting for fourteen or fifteen days before falling to normal. The temperature at the onset is no sure index of the severity of the case.

Most of those seen in the pre-eruptive stage were not particularly sick, although they generally stopped work. The eruption appears after three or four days (21 times after 2 days, 75 times after 3 days, 70 times after 4 days, and 36 times after 5 days), and is usually first seen on the forehead, wrists and forearms. Of 202 cases, the location of the first rash as noticed by the patient was as follows: Face, 120; wrists and forearms, 52; both arms and face, 27; scrotum, 1; inner side of knee, 1; elbow, 1. The first sign of the eruption is usually in the form of a few small widely separated papules or nodules which are very superficially placed in the skin, slightly elevated, but not hard or shotty on palpation. During the next day or two many more nodules appear, and then suddenly a great number, so that the whole face and trunk, as well as the arms and legs, are studded with them. (Figs. 1 and 2.)

Other patients begin with the appearance upon the forehead and cheeks of a translucent reddish nodular or irregular thickening of the skin. The skin of the forehead becomes rigid and finely mammillated, like shagreen leather, and later when these nodules become pustular there is a great tendency to confluence. Elsewhere on the body the pustules are usually quite discrete and reach a much larger size. (See Figs. 3, 4, 5 and 6.)

Two forms could thus be distinguished, but in neither form could one observe any definite umbilication in the early stages.

The development of the rash is often accompanied by oedema of the subcutaneous tissues, especially about the nose and eyes. In the majority of cases this oedema is slight, but in others it is so bulky as sometimes completely to close the eyes. It appears on the third or fourth day of the rash, and reaching its height on the seventh or eighth day, rapidly disappears.

During the third and fourth days of the eruption the nodules assume a more vesicular appearance, and a clear or opalescent fluid can be withdrawn with a fine pipette—in each case only a very minute droplet. During the following days, the fifth to the ninth or tenth, the eruption becomes definitely pustular. The skin of negroes offers a poor opportunity for the observation of the details of the appearance of such eruptions, but in the white patients there could be seen a red halo about each pustule. The thin epidermis over the pustule itself is stretched, so that the surface glistens and all the pustules bulge forward as smooth hemispherical projections. About the eighth day of the rash the pus begins to be inspissated, and the middle of the roof of the pustule sinks and dries a little, so as to become somewhat opaque. This produces a distinct secondary umbilication, such as is also seen in smallpox, but this is not the characteristic umbilication produced by the epithelial strands in the early stages during vesicle formation (Fig. 7).

Further desiccation produces crusts which loosen readily and are rubbed off, each leaving in the negro a small patch of depigmented pink skin fringed with partly desquamated epithelium and surrounded by a zone of deep brown pigmentation (Fig. 8). There is, as a rule, no deep pitting or scarring, and although the pigmented spots remain for months, they gradually fade and the skin is left practically smooth (Fig. 9). Slight pitting occurs in some cases, but it is by no means so deep and disfiguring as that following smallpox.

With the appearance of the eruption the patients feel a sense of relief, the temperature falls, and there is little complaint of headache or other symptoms; but with the development of the vesicles and pustules there is burning pain in the affected skin which often keeps them awake at night. They are much relieved if any one will puncture their pustules and squeeze out the contents. This we did in many cases, primarily to secure the contents, and next day always found the eruption dried up and the patient much more comfortable. There is

no noticeable odor about these patients, in which respect they are in sharp contrast with those affected with smallpox.

The soles of the feet and palms of the hands become studded with deeply sunken pustules which are painful and greatly disable the patient, since they can not stand nor grasp anything without extreme suffering. During the height of this disability they lie in bed, and some of them complain of being very ill and are drowsy or show great mental depression. Their appetite generally continues good, however, even in spite of the intense sore throat from which a few suffer. Suddenly, next day they are again bright and cheerful, and after that convalescence proceeds without interruption. But in most cases there is very little of the feeling of severe illness and the greater number of the patients move about and try to amuse themselves.

The eruption is usually distributed pretty evenly over the whole body, being more closely set as a rule on the face and forearms, where it first appears. There were few, if any, cases of typical confluent eruption over extensive body surfaces, although a number of patients presented a completely confluent pustular exanthem over the face which later, in healing, left a rough crusted and suppurating surface. In many instances there were, when the eruption was mature, little groups of pustules, all of which could be evacuated by pricking one. Frequently some irritation or the presence of some lesion of the skin independent of the disease led to the outburst of a closely set crop of pustules in one or more places. One man, a policeman, who wore a uniform very tight under his arms, developed an almost confluent patch of pustules in the margins of the axilla. Others who had scratched or abraded the skin showed corresponding groups of pustules. The scalp is very generally affected even in mild cases, but the lesions are usually few in number. Pocks are frequently present on the hard and soft palate, less often on the uvula, pillars of the fauces, and mucous membrane of the mouth. In a few cases the frenum of the tongue was affected. Hoarseness and aphonia have been noted in a number of the severer cases and lesions found in the larynx. In several of the fatal cases the larynx and trachea have been studded with pocks in the mucous membranes. The external genitalia are also affected, especially the prepuce, which becomes much swollen and gives rise to pain and difficulty in micturition. Pocks are generally present on the edges of the eyelids, although the infraorbital space is often left free. None have been seen on the conjunctiva. The eruption seems to be slightly more profuse on the back than on the front of the

trunk. It is not more sparsely distributed between the knee and ankle than elsewhere.

Apart from the inconvenience and pain caused by the eruption, there are few constitutional disturbances, and complications are uncommon. Delirium was never noted. Menstruation did not occur in women unless a period were due, and even then none complained of excessive loss of blood.

Blood counts were made in forty-eight cases with the following results: Before the onset and for the first 3-4 days of the rash the leucocyte count is normal or much diminished. In only 3 cases was it as high as 10,000, and in the great majority it ranged between 2,000 and 7,000. As the eruption matures the count rises to about 15,000, and in a few cases in which the pus of the pustules was much infected with bacteria the leucocyte count was 25,000. Differential counts so far as completed show about the normal ratio, with a few myelocytes. There is no secondary anaemia.

The urine was examined in fifty cases, but albuminuria was never found except where it was readily explained by some other cause, such as an urethral discharge. In three cases there was bronchitis with blood-stained sputum, lasting a few days.

Boils formed the most frequent complication, coming on about the fifteenth day after the onset of the rash and proving sometimes very troublesome. Impetigo also occurred in several cases as the rash was disappearing.

A mild conjunctivitis sometimes arose in those cases in which there were pocks on the eyelids, but never led to serious results.

Laryngitis was fairly common. The patients complained of extreme sore throat, and there was sometimes swelling of the cervical lymph glands. Usually this passed off after a few days, but in some of the cases which were studied at autopsy there was a profound destructive change in the tissues of the fauces, the pharynx and the glottis, involving also the tonsils.

The prognosis is very good. Of 2,333 cases reported to date ten have died. Of these seven were adults, five women and two men. Of the women four were six or seven months pregnant, all of whom displayed a marked tendency to haemorrhage. The other case had a confluent rash and died on the eleventh day. Of the men, one was fifty-six years old and died during convalescence. The other had extensive lesions in the mouth and throat and was dying when admitted to the hospital. The children died within the first month of

life, contracting the disease shortly after birth. Two macerated fetuses were born a month after the mother had an attack of alastrim, with what appear to be pocks on their skin.

HISTOLOGICAL CHANGES.

In order to make a study of the histological changes in alastrim, pieces of skin were excised from several cases with pocks in various stages of development. Of these the most instructive are the very early stages, and after studying these it seems that it would have been desirable to excise similar pieces during the pre-eruptive stage. Naturally some of the sections from such pieces of skin might not represent the future site of a pock, but it seems that in some places, at least, recognizable microscopical alterations could be found in the corium before the slightest evidence of the exanthem was visible to the naked eye. The late stages are of relatively little interest microscopically. The materials from several autopsies, including those in new-born infants, were also preserved for study.

The earliest stage of the eruption in our possession is from the patient Hall, who began to feel ill on September 9, and in whom the rash first appeared on September 14. Skin was excised on September 16—that is, on the third day of the rash. The appearance of this eruption can be seen in Fig. 3, taken at the time of the excision; Figs. 10 and 11 show the microscopical changes.

It is to be observed that in the corium involved in the projecting papule there is an intense inflammatory reaction, although changes in the overlying epithelium are as yet only in their inception. This must be interpreted as evidence that the infective agent begins its activity in the corium, extending later into the epithelium. It is quite clear, since the eruption bursts out almost simultaneously over the whole body, that the organism concerned must be carried by the blood stream. In view of the infectivity of the fluid contents of the pocks, any other explanation of their origin than this seems untenable. In that case it is not surprising to find the earliest evidences of its influence in the terminal capillaries of the corium and of its papillae, and there seems to be little support for the suggestion that this somewhat hypothetical organism is essentially a parasite of the epithelium.

The blood vessels in the depths of the corium are as usual surrounded by a few wandering cells. These are very well preserved mononuclears with some highly amoeboid cells with basophilic granules. As the upper layer of the corium is approached in the area of

the beginning pock, the small blood vessels with their attendant lymph vessels become surrounded by a dense mass of cells, which spreads off into the crevices of the adjacent tissues. Polymorphonuclear leucocytes are numerous, especially among the cells which are wandering toward the skin surface away from the vessels, but most of those about the blood vessels are distorted and misshapen mononuclear cells among which definite plasma cells with bluish protoplasm and unstained halo about the nucleus may be seen. Certain areas of the superficial layer of the corium are especially oedematous and thickly infiltrated with wandering cells. The papillae of these areas are widened by oedema and contain wandering leucocytes. Over these the epithelium is in some cases quite unchanged, or at most shows a beginning vacuolation of the cells. In those places which can be definitely recognized clinically as beginning pocks the epithelium is much more relaxed and separated into loose cells. At some points in such areas there may be distinct rounded spaces evidently filled with fluid which presses aside the epithelial cells. Such spaces are generally loaded with leucocytes as well. But in these areas the affection of the papillae and superficial layer of the corium appears to be more advanced than that of the epithelium.

Wherever there are areas of infiltration of the corium, the overlying epithelium begins to show the remarkable vacuolation especially well described by Unna as balloon-like. The vacuoles seem to us to be in the nucleus of each cell, for they are always surrounded by a thin film of nuclear substance or a band of nuclear substance extends across the vacuole connecting its opposite walls. Occasionally the nucleus is flattened and pushed to one side, but in most cases it appears to inclose the vacuole. The separation of such cells by accumulations of fluid and leucocytes is often accompanied at this stage by the necrosis of the overlying epithelial cells which stain solid pink.

We were unable to observe umbilication in the early stages in this disease and there is no occasion for the discussion of the theories as to its production. We see no such fan-like necrosis of the central epithelium in a pock as was described by Weigert in his explanation of the umbilication. Spaces merely arise in the epithelial layer and coalesce into the cavity of the developed pock. There are sometimes numerous bridges of epithelium left, stretching between the top and the floor of the pustule in alastrim just as in smallpox.

The later stages constitute a progression of the same process. The vesicle appears to arise within the epithelial layer and to become grad-

ually more and more filled with leucocytes. Around the margins of the pustule the lower layer of epithelium which forms the floor is unbroken, but in the middle in nearly all cases it is destroyed, and the dense infiltration of leucocytes is continuous from the corium into the cavity of the pustule. The infiltrated corium forms the floor of the pustules and the papillae disappear from this surface (Fig. 12).

Another early case, that of Burton, was studied by excision of a piece of skin on the third day of the rash. The vesicle (Fig. 13) is more definitely formed than in the case just described and lies chiefly in the upper layers of the epithelium, so that sections passing through the margin show it bounded below by the flattened keratohyalin layer and superficially by a hyaline pink staining layer of keratinized and necrotic cells. But when the center of the vesicle is approached it is found that at least two papillae of the corium with the oedema and infiltration described above project as it were into the cavity of the vesicle and are no longer covered by any remnant of the Malpighian layer. The extensive infiltration about the vessels of the corium underlying this poek is as conspicuous as in the other cases.

No bacteria have been found in the sections of such pustules, although they occasionally appear in smears of the purulent contents. When examined with dark-field illumination, certain minute granular bodies with slight dancing motion could be seen in great numbers in the fluid taken from the pustules. These were found also in the filtrate from the same material after passage through a Berkefeld filter. They correspond fairly well with the bodies described by Prowazek, Paschen and others, but we hesitate to express any opinion as to their nature in the lack of any evidence.

In sections through the skin lesions in the earliest stages there are to be seen small bodies lying among the leucocytes which surround the blood vessels in the corium, which resemble in some degree those described by Councilman and many other writers on smallpox. They are also found in considerable numbers between the cells of the epithelium, but are rarely seen within leucocytes or epithelial cells. They resemble very small rounded cells 1 to 4 microns in diameter, with a deeply stained, rounded, solid nucleus and a delicate irregular cytoplasm which takes a faint pink stain. Some have no recognizable cytoplasm. The irregularity in size and form makes it impossible to feel sure that they represent anything more than isolated cell fragments, but they are quite numerous in the affected areas, absent elsewhere, and are by no means always in any suggestive juxtaposition

with distorted cells. When they lie in an isolated position between epithelial cells it seems difficult to interpret them as cell fragments. In later stages of the development of the pock many of them can be seen engulfed by leucocytes.

The histological description of such bodies—even including the Guarnieri bodies, which these may perhaps represent—has led to no useful result, owing largely, it seems, to the extreme irregularities in form which constitute so good a disguise for any questionable organism. Until some significance can be given to these structures, therefore, by experimental studies, including their isolation and the demonstration of their living nature, we can only look upon them as interesting details in the morphology of the lesion.

Healing of the pustules occurs in the way so often described for smallpox, but it leaves behind so little pitting or scarring that we must regard the changes described in the corium as slight when compared with those of smallpox, although they seem profound enough in the sections.

There were three autopsies upon the bodies of women, two of whom were pregnant, and autopsies were also performed upon several macerated fetuses born after the mother's attack of alastrim, and in most instances showing marks of pocks upon their skin (Fig. 14).

Case 1. A pregnant woman in whom death occurred on the twelfth day of the rash. She was admitted bleeding from the nose, mouth and uterus. The mouth and throat were lined with a thick layer of necrotic material which involved the larynx. The trachea showed pock-like elevations throughout its entire length, and even the bronchi showed traces of the same eruption. The lungs contained numerous scattered haemorrhages. Similar petechial haemorrhages were found in the skin, heart muscle, kidneys, bladder and intestine. No lesions were seen in the fetus. Post mortem decomposition had proceeded so far that the microscopical sections are of little value. Sections through the pocks in the trachea show a thickening of the epithelium with a dense covering of bacteria, but this elevation does not closely resemble one of the cutaneous pocks.

Case 2. Also a pregnant woman at the seventh month. The skin was covered with well-formed pustules. The pharynx and larynx were lined with necrotic material of a dark greenish-black color with much loss of substance. The trachea showed pocks throughout its entire length, and the bronchi were similarly affected. There were some small areas of broncho-pneumonia in the right lung. Haemor-

rhages were few, the largest being a subserous haemorrhage over the uterus. The first two feet of the jejunum presented a remarkable condition, being dark and haemorrhagic with a great deal of oedema. In places the lumen seemed occluded by a gelatinous mass produced by the thickening of the wall.

The tissues from this case were well preserved, but sections of the organs showed no especial abnormality except in the case of the intestine, in which the section shows an extreme oedema with haemorrhage. The lumen is filled with a coagulated material, but the section is insufficient to explain the nature of this process. Section of the trachea shows patches of swollen and necrotic epithelium which apparently represent what appeared on gross examination as pocks.

Case 3. A woman who died on the eleventh day of the rash. The pocks were scabbing on the face, but on the body were confluent in places, frequently haemorrhagic, and abraded. The throat was clear and the trachea showed no eruption. A few areas of lobular consolidation were found in the lungs. The other organs showed no evident alterations.

Microscopically all the organs were studied, but no changes referable to the alastrim were observed except those in the skin. The bone marrow of the femur is entirely composed of fat, with scarcely any myeloid cells.

Sections from the tissues of the macerated infants showed only tissues so badly decomposed as to be worthless. Sections taken through the areas thought to be pocks in the skin show an elevation of the whole epidermis with haemorrhage, but not the characteristic lesion as seen in the adult skin.

It is evident that the virus passes readily through the placenta into the foetal circulation, for of twenty cases admitted after attacks of alastrim, there were eight abortions at about the sixth month, and in each case the macerated foetus was marked with scars of the disease. In two cases the abortion occurred eight weeks after the onset of the disease in the mother. Two children were also born alive with marks of alastrim. One of these was born at full term with nine scars of pocks on the face, twenty-two on the trunk, and a few on arms and legs, including some on the soles and palms. The other child born at the seventh month had pigmented scars on the arms and legs. The mother had the onset of her attack eight and a half weeks before. The remaining ten women went through normal labor and gave birth to normal full-term children.

There were also two women who gave birth to full-term infants showing unmistakable eruption of alastrim, although neither mother ever contracted the disease herself, and both had been vaccinated a month or six weeks before delivery.

In the second case the history was as follows: Mother vaccinated on January 10 developed vaccination fever on January 15 and 16. Declares she has not been ill otherwise and shows no pock marks. Child born on February 10 with universal pustular rash in which the pustules are beginning to relax and are umbilicated. Wassermann of mother and child negative. Child died 5 days after birth.

RELATION OF VACCINATION TO ALASTRIM.

In describing Sanaga pox, Plehn states that vaccination with ordinary calf lymph was successfully performed in thirty-six of forty children six months after recovery from the disease. Ribas, too, found that vaccination of persons who had recovered from alastrim less than a year before was successful in 46 per cent. of the cases; Rudolph in 27 per cent. Aragao vaccinated nineteen persons who had recovered from an attack of alastrim less than a year before and was successful in eleven cases. Rabbits and calves inoculated with alastrim material were in no way immunized against vaccine. Others, too, have been impressed by the fact that alastrim confers little immunity from vaccination with cowpox. Green, experimenting with material from the Australian epidemic, found that inoculation of monkeys and calves produced pustules, but that after recovery these monkeys and calves were susceptible to vaccination with cowpox. His experiments further showed that vaccinia protected against the Australian disease in 25 per cent. of the cases. Variola infection had this effect in 40 per cent. On the other hand, vaccinia protected against variola in 100 per cent., while variola protects against vaccinia in only 50 per cent.

Dr. Moody's study of the relation of alastrim to vaccination in this epidemic gave the following results: 206 cases were observed with regard to the severity of the affection in non-vaccinated and vaccinated cases and these may be recorded in the following table:

	Non-vaccinated.	With scars of successful vaccination.	With history of successful vaccination, but no scars.
Severe Cases	40	16	10
Medium Cases	24	22	22
Mild Cases	14	34	24
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Total	78	72	56

He suggests that the proportion of severe cases is higher among the non-vaccinated, but that since none of these people were vaccinated more recently than twenty years ago, not much stress can be laid upon the figures.

In children the disease seems to run a milder course, both as regards constitutional symptoms and rash. Eighty cases were studied, varying in age from sixteen days to thirteen years, and a similar table constructed for them shows the following:

	Non-vaccinated.	With scars of successful vaccination.	With history of successful vaccination, but no scars.
Severe Cases	14	0	2
Medium Cases	10	4	0
Mild Cases	20	22	4
Total	44	26	6

Thus there is evident a general tendency to a milder type, and the effect of successful vaccination is shown in the greater proportion of mild cases as contrasted with the non-vaccinated group. Nevertheless, it is clear that in spite of vaccination, which in these children could not be of very remote date, there were many cases of alastrim. One mother whose child had the disease was vaccinated successfully about the middle of July and returned to the hospital on August 19 with a well-marked vaccination scar and alastrim in the sixth day of the rash. Of fifty-five of the patients actually ill with the disease in Bumper Hall, I found that twenty-four had never been vaccinated, twenty-eight claimed to have been vaccinated in childhood or at school; one, a child with moderate rash, presented an active vaccination pustule hardly healed, while two others had definite vaccination scars. Such evidence, however, is of little value except, perhaps, in the last three, because the statement of the twenty-eight who said they had been vaccinated in childhood was not supported by the presence of a visible scar.

Physicians and medical health officers in Kingston were somewhat divided in their opinion as to the efficacy of vaccination with the standard cowpox vaccine as a protection against alastrim, but those who saw many cases, such as Dr. Murray, felt that the protection was entirely to be relied upon. He had vaccinated more than five hundred contacts among whom not a single case of alastrim arose. Dr. Moody vaccinated twenty persons who had been in contact with the disease without an instance of subsequent infection. Dr. Murray also dem-

onstrated cases of alastrim in the unvaccinated members of some families while the others living in the same house escaped because they had been vaccinated.

It is difficult to form a very precise idea of the efficacy of vaccination in protecting against alastrim, but since among the actual cases of the disease there were so very few that presented indubitable evidence of having been recently vaccinated, and since the escape of those successfully vaccinated is so well attested in large numbers of cases, it seems necessary to believe that vaccination is an extremely effective protection.

Vaccination is employed naturally because it is difficult to draw a sharp line between alastrim and smallpox. An effective protection must be held to be evidence of their extremely close relationship, while any failure to protect might be regarded as an indication that alastrim is a different disease, since the great effectiveness of vaccination as a protection against smallpox is attested by the experience of more than a century, and is absolutely established in spite of the recurrent outcry of ignorant people who attempt to interfere with the use of this great triumph of preventive medicine.

With regard to the effect of vaccination after recovery from alastrim, Dr. Moody makes the following report: Sixty cases were vaccinated during convalescence at periods varying from fifteen days after the onset of the rash up to the twelfth week. Of these, fifteen showed no sign of a "take" in two weeks, and of these fifteen, twelve were re-vaccinated with three "takes." The method used was that of simple incision through the surface layers of the skin, after which the liquid virus was rubbed in. Of the forty-five who "took" there were none who gave a typical reaction as compared with normal controls vaccinated at the same time with the same batches of lymph. Instead, the incision healed over and no sign of take was visible before the seventh or eighth day, when a few papules were seen in the line of the incision. The papules increased but slowly in size and by the fourteenth day were raised about 2 mm. above the surface of the skin. The lesion ran a very indolent course. No induration or swelling of the arm was noted and in only a few cases were there fever, general malaise, adenitis, or even an areola for more than 0.5 cm. around the lesion. Even in these the symptoms were hardly noticed. On pricking the vesicles a small quantity of clear fluid was obtained. The lesion was multilocular, and when the top of the vesicles was removed it was seen that the base was composed of exuberant granulations

rising above the level of the skin. The lesion disappeared, as a rule, in four weeks, and the resulting scar was not the depressed pitted scar of typical vaccine, but a scar slightly raised and subsequently contracting to the general level.

The process differs from that of typical vaccinia, therefore, in the tardy development and slow course of the lesion, the small size of the vesicles, their exuberant base and imperfect umbilication with the atypical scar thus produced, and the insignificance of local and constitutional reaction. The suggestion is made that something capable of causing this reaction exists in the lymph apart from the protective factor, but this can hardly be maintained, since in that case many normal persons unsuccessfully vaccinated ought to develop this peculiar lesion. Something of its appearance can be seen in Fig. 15.

ANIMAL EXPERIMENTS.

With regard to the transmission of these mild diseases to animals, the following may be said: Carini produced Guarneri bodies in the cornea of rabbits with pus from alastrim, but Rudolph failed in the same experiment. Aragao was able to produce a typical corneal reaction in rabbits with Guarneri bodies, but could not transfer this effect to a second rabbit. Nor could he produce any lesions in the skin of rabbits or calves by inoculation of the alastrim material. Vorwerk failed to produce any effect by inoculating the contents of a pustule from Sanaga pox in the skin of a calf, and similarly Nägele failed in rabbits and calves with the material from cases of Amaas. Green inoculated the Australian material in monkeys and calves and secured positive results. He inoculated other monkeys and calves with true variola and compared the effects, and states that the Australian disease is different from vaccinia and variola in calves, but very like them in monkeys. Vaccinia in calves fails to protect against inoculation of the Australian disease, and in turn inoculation with the Australian virus fails to protect against either vaccinia or variola.

We inoculated rabbits with blood from cases of alastrim in the eruptive febrile stage, thinking that at that period the infective agent might be present in the circulation. Blood was injected intravenously, into the testicle and allowed to flow over the scarified cornea. There were no results. Other rabbits were inoculated in scarifications in the skin and in the cornea with the contents of pustules from typical cases, but although they were most carefully watched for

many days, the scarifications healed without the formation of any recognizable lesion. The corneas never showed the slightest opacity, nor any translucent nodules such as are described by Paul, although carefully examined with a lens. The scarifications healed quickly and the cornea returned to normal.

Three calves were inoculated in the skin of the flank with material freshly obtained from the skin lesions of typical cases of alastrim, but these, too, failed to develop any vesicle or pustule, and the scarifications healed smoothly at once.

We were thus entirely unsuccessful in transmitting the disease, in however localized a form, to rabbits or calves.

It is pretty generally agreed now that the so-called Guarneri bodies which occur in the epithelial cells about a smallpox pustule, and which appear in much greater numbers in the epithelial cells of the rabbit's cornea when either vaccinia or variola is inoculated, are fairly specific in their relation to these diseases, and that they do not represent the aetiological agent, but rather the reaction of the cell to its presence.

v. Prowazek, Paschen, Hallenberger and others have written much recently concerning minute bodies which are present in the lesions of vaccinia and variola and are also found, according to Aragao, in alastrim. v. Prowazek, their discoverer, regards them as the actual cause of these diseases. They can pass through a Berkefeld filter which removes bacteria, and the filtrate will produce the typical corneal lesion in rabbits. They can be concentrated by passing the filtrate through a colloid filter made of agar after which the second filtrate is inert. Hallenberger describes the morphology of these minute bodies in detail and shows them as extremely small round, dumbbell-shaped or dividing bodies, sometimes unequally parted so as to look like an exclamation mark. They do not move except to assume a slight dancing motion; they are not stained by ordinary bacterial stains, but can be colored by Giemsa's stain, although Aragao states that their characteristic staining is only to be attained by the use of Löffler's mordant.

We were able to demonstrate these minute bodies by dark-field illumination in the fresh material from the alastrim pocks, where they appear as very numerous, extremely minute, rather refractive particles in fairly active Brownian motion. When this material was passed through a porcelain filter the same particles were still to be seen. They were inoculated into the skin and cornea of a rabbit, but with no result.

Very few of the proofs ordinarily demanded to show the aetiological relation of an organism to a disease have been satisfied in this case. These nondescript minute granules stain rather more specifically than other granules; they are present in great numbers in smallpox and vaccinia pustules and in the epithelial cells. They go through a porcelain filter and the filtrate, whether on account of their presence or that of some other living organism, produces a characteristic corneal lesion. When they are filtered out by the colloid filter, whether alone or in company with something else, the filtrate no longer produces the corneal lesion.

In the case of the alastrim material our uniform failure to produce any lesions made us incapable of adding any evidence for or against these claims.

DISCUSSION AND CONCLUSIONS.

We are still in the ignominious position of being unable to state with absolute certainty the relation between smallpox and cowpox or vaccinia. This uncertainty must continue until the organisms concerned are isolated in pure culture so that their biological characters may be compared, just as types of pneumonia or dysentery could never have been distinguished without the study of pure cultures of the bacteria. The literature which extends over more than one hundred years is full of arguments based upon inoculation experiments, but it remains clear that it is difficult to transmit smallpox to calves, that it has usually been done in vaccine institutes where there was a chance of the development of cowpox, and that in this apparently simple question uncertainty persists. The reasoning in all this literature seems extremely loose and the dogmatic conclusion found in most textbooks, to the effect that vaccinia is merely smallpox attenuated and permanently altered by passage through calves, unjustified. All this literature is reviewed by Tomarkin and Carriere and by many others. It is mentioned here without any intention of discussing it, merely to show that it is equally difficult to discuss the relations between smallpox and alastrim. No definite and final statement of their relation seems possible until the causative organism is isolated in pure culture from typical cases of each disease and compared.

The immunity conferred by an attack of one of these infections or by the inoculation of the virus to produce a local lesion, while of enormous practical value in the prevention of disease, is not a sharp enough test for the separate identity of these closely related diseases.

Vaccination almost absolutely prevents infection with smallpox, but a mild smallpox or varioloid may sometimes occur in successfully vaccinated persons. Vaccination may sometimes be successfully performed after recovery from smallpox.

Vaccination apparently afforded a powerful protection against alastrim, but there were many cases in persons who had been successfully vaccinated, and successful, if atypical, vaccination was possible after recovery from alastrim. These occasional departures from strict reciprocal protection were probably more numerous between vaccinia and alastrim than between vaccinia and smallpox, but this questionable difference is not a sufficient basis for a sharp distinction between smallpox and alastrim. Dr. Deeks tells me of two cases in which alastrim occurred in persons who had recovered from true smallpox.

Cross complement fixation carried out by Kolmer and others showed that antibodies arise in the serum of vaccinated animals and of persons who have recovered from smallpox, but that these antibodies are in both cases capable of combining with the antigen (contents of pustules) derived from both smallpox and vaccinia. This shows a close relation between these conditions, and probably would show a similar close relation to alastrim. The method seems useless, however, in an attempt to show a distinction between alastrim and true smallpox, although there might be quantitative differences.

One of us (L. M. M.) has made four tests by vaccination of the production of an allergic reaction in persons who had recently recovered from alastrim, using as control normal persons who had not had the disease, but who had been recently vaccinated. There was absolutely no allergic reaction in any of these cases, of whom two were white people, although it was well defined in the recently vaccinated controls. In three of the alastrim patients there afterwards developed, however, the indolent vaccine lesion described above.

The evidence is scarcely sufficient to warrant the statement that alastrim is a disease quite distinct from true smallpox. The effort to distinguish them is the more difficult on account of the extraordinary variation in severity in what has in various epidemics been regarded as true smallpox. Mild cases of smallpox often show, however, only a few scattered poeks and a slight fever, while in alastrim the initial fever is high and the body is covered with poeks often broadly confluent, and yet the patients are not very sick, the liability to secondary infection is slight and the mortality trifling.

Clinically and histologically the eruption is somewhat different

from that in smallpox in that early umbilication is lacking. Inoculation experiments in animals failed in our hands, but the results of others suggest differences between alastrim and smallpox. Although there are very few recorded instances of the transportation of this disease to other climates, we feel that it would probably maintain its identity in any climate.

The disease is as easily communicable as the most severe smallpox, but its spread has been restricted by prompt vaccination and revaccination. No consideration could excuse neglect of this preventive measure or of the proper quarantining, even though the death rate is low.

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EXPLANATION OF PLATES.

PLATE XII.

- FIG. 1. *D. H.* 8th day of rash.
- FIG. 2. *J. M.* 8th day of rash, 11th day of disease.

PLATE XIII.

- FIG. 3. *Hall.* 3d day of rash, 5th day of disease. Eruption confluent on forehead.
- FIG. 4. *Hall.* 5th day of rash.

PLATE XIV.

- FIG. 5. *Hall.* 7th day of rash. Patient ill and photographed in bed.

PLATE XV.

- FIG. 6. *Hall.* 9th day of rash.

PLATE XVI.

- FIG. 7. *Mrs. W.* 9th day of rash, 11th day of disease. Many of the pustules show central desiccation.
- FIG. 8. *D. E.* 4th week of disease. Crusts still adhere to face, but the body shows smooth depigmented areas with zones of pigmentation.

PLATE XVII.

- FIG. 9. *G. W.* 4 months after severe attack of alastrim. Pitting is practically absent and only faded areas of pigmentation remain.

PLATE XVIII.

- FIG. 10. *Hall.* Papule at 3d day of rash showing infiltration about the vessels of the corium and balloon-like degeneration of the epithelium.
- FIG. 11. *Hall.* Vesicle in 3d day of rash, near a hair follicle, with hyalinization of overlying epithelium.

PLATE XIX.

- FIG. 12. *Williams.* Margin of a pock at 9th day of the rash. Compare Fig. 7 from the same patient at the time of excision of this pustule.

FIG. 1.

FIG. 2.

PLATE XII.

FIG. 3.

FIG. 4.

PLATE XIII.

FIG. 5.
PLATE XIV.

FIG. 6.
PLATE XV.

FIG. 7.

FIG. 8.

PLATE XVI.

FIG. 9.
PLATE XVII.

FIG. 10.

FIG. 11.

PLATE XVIII.

FIG. 12.

FIG. 13.

PLATE XIX.

FIG. 15.

FIG. 13. *Burton*. Vesicle in 3d day of rash showing infiltration of the corium and projection of a papilla into the edge of the cavity in the epithelium.

PLATE XX.

FIG. 14. Macerated foetus with distinct marks of alastrim pocks upon the skin.

FIG. 15. Vaccination of patient at the 13th day after the onset of symptoms of alastrim. Photograph taken 10 days after vaccination shows the superficial marks left by the alastrim at about the 20th day and the atypical vaccine pustules.