CHAPTER III

FILTERABLE VIRUS DISEASES OF MAN AND ANIMALS (CONTINUED)

VARICELLA: CHICKEN POX

VARIOLETTE (FRENCH); WASSERPOCKEN (GERMAN); MORBILLIONE (ITALIAN)

Definition.—Varicella is a markedly contagious disease, characterized by a cutaneous eruption that is confined to the superficial layers of the skin. Chicken pox is usually a harmless disease and is rarely malignant. Death never results from this disease, and as a rule there are only mild constitutional symptoms associated with it. The exact cause of chicken pox is unknown, but it is thought to be caused by a filterable virus.

History.—Undoubtedly chicken pox has existed since ancient times, though it was confused with smallpox (see Chapter II) until the nineteenth century. By most of the early physicians this disease was regarded as a benign form of smallpox. Chicken pox has always been a mild disease, but it was early recognized to be highly contagious and is one of the most important diseases of children from the standpoint of loss of time from schools, and is an important consideration in institutions such as hospitals for children. We are informed by Vaughan that even during the latter half of the nineteenth century Hebra, of the Department of Dermatology in the University of Vienna, taught that chicken pox is a mild form of smallpox. There is no question as to the relation of chicken pox to smallpox since it is now well known that neither condition will give any immunity against the other, although an attack of either disease confers an immunity against a subsequent attack of the same disease. Chicken pox is found everywhere. No age is exempt, although the majority of cases occur in the fifth or sixth year. It has been estimated that 5–2 per cent of adults have had the disease during childhood. The disease is more prevalent in girls than in boys, and among white children than among colored children.

The virus of chicken pox.—Little is known concerning the virus causing this disease. Numerous attempts have been made

to infect human beings artificially with varicella material and to transmit the disease to laboratory animals. Bryce,(1) in 1816, inoculated vesicular material taken from cases of chicken pox, representing all stages of the disease, into the skin of children who had never had smallpox or chicken pox. None of the children developed lesions. Hesse inoculated one hundred thirteen children with varicellous material and in seventeen of them obtained a slight local reaction, while nine developed a general reaction. Other investigators have had more or less success, but in general, the reports dealing with experimental chicken pox are at most unsatisfactory. In animals practically no success has been met with. Rivers and Tillett(2) have succeeded in inducing lesions in rabbits and monkeys with material taken from chicken-pox vesicles, a description of which will be given under Virus III infection. The possible relation of varicella to herpes zoster has been the subject of numerous papers during the last few years. Le Feuvre(3) is of the opinion that these two diseases are related etiologically. Suggestive data in this connection are contained in the work of Landa, and Silberstern,(4) Meldrum,(5) Matthews,(6) Pereira,(7) and others. Ziel(8) also speaks of a "zosteriform" chicken pox; Cozzolino,(9) Höffmann,(10) and Netter and Urbain(11) have reported work which suggests the identity of the virus of herpes zoster and varicella. Recently, however, Scheer(12) reports herpes zoster and coincident varicella in a brother and sister developing simultaneously, one zoster and the other varicella. Fourteen days later, the child having zoster developed varicella and Scheer concludes that zoster offers no protection to chicken pox.

In the differential diagnosis of this disease the physician has been concerned chiefly with smallpox. Histologically, smallpox vesicles are found to contain so-called vaccine bodies, while chicken pox vesicles do not contain these. The lesions produced upon the rabbit's cornea with vaccine virus contain vaccine bodies, while the lesions produced with chicken pox are very minor and do not contain inclusion bodies.

Though the virus of chicken pox has not been discovered we may state definitely that it is not related to the virus of small pox and probably is unrelated to the virus of herpes zoster.

Incubation period.—The incubation period of chicken pox usually ranges from fourteen to twenty-one days. The period of incubation varies from four to twenty-one days but for public health purposes, twenty-one days is considered the maximum.

Symptoms.—Mild prodromal symptoms consisting of general malaise may precede the eruption. Usually the first symptom of the disease is the eruption. In rare cases a scarlatiniform erythema is noted preceding the rash.(13) The eruptions begin first upon the head and trunk, then extend to the extremities. They appear in successive crops over several days. The trunk is usually more extensively involved. Lesions usually appear upon the face and in some cases may be numerous in this locality. With the eruption there is usually a slight rise in temperature to 99° or 100° F. The beginning lesion is a small erythematous spot which gradually develops into a vesicle containing a clear fluid. The vesicles are small, pinhead in size to pea size, round or oval, very superficial and thin walled. In some cases the contents of the vesicle may become purulent. After one to three days the lesion dries up and a thin yellowish crust is formed. The lesions are always discrete and irregular in distribution. Several stages of development of the lesions may be noted at a given time. The mucous membranes are usually attacked, a few lesions occurring on the hard and soft palate. Itching may or may not be a prominent symptom. The disease may be complicated by secondary infection, and measures should be instituted to avoid this.

Immunity.—One attack of chicken pox confers a definite immunity. A number of investigators have attempted to induce artificial immunity in susceptible children by vaccination with the contents from varicella vesicles. In 1913, Kling(14) obtained success with this procedure. This method of inducing artificial immunity has also met with more or less favorable results in the hands of Handrick,(15) Rabinoff,(16) Michael,(17) and Greenthal.(18) The latter in 1926 obtained nineteen "takes" among thirty-six persons vaccinated with the vesicular fluid of chicken-pox lesions. Greenthal concludes that this method of producing immunity serves to check the spread of the disease. In his hands the immunity lasted less than eighteen months in one instance and more than six weeks in another. Greenthal attempted to inoculate guinea pigs with varicellous material by the coal-tar method employed by Teague and Goodpasture(19) in herpes zoster, but his experiments were unsuccessful.

Pathology.—The vesicle of chicken pox is multilocular. According to Unna its cavities are formed by the reticulating liquefaction of groups of prickle cells in the middle and upper portion of the rete. Ormsby states that the septa are formed of cells

between the cavities that have not undergone liquefaction. The contents of the vesicle is said to consist of granular coagulated fibrin and ballooned cells. The corium shows œdema and vascular dilatation, but practically no infiltration of leucocytes.

Prevention.—Cases of chicken pox should be isolated. Kling favors vaccination with chicken-pox virus during epidemic conditions. Greenthal's work also suggests the advisability of this. Hess and Unger(20) were able to obtain immunity to varicella in thirty-seven of thirty-eight cases following the intravenous injection of vesicular fluid. This method of immunization should receive further attention, and the duration of such induced immunity should be accurately determined.

HERPES ZOSTER; SHINGLES

ZOSTER, ZONA; GÜRTELFLECHTE (GERMAN)

Definition.—Herpes zoster is an acute disease characterized by the appearance of groups of vesicles, usually following the course of a nerve trunk, and accompanied by neuralgic pains or itching. The distribution of the lesions is usually unilateral, and generally is not recurrent.

Symptoms.—Hyperæsthesia, itching, or pain may precede the appearance of the herpetic lesions of zoster. The pain may be localized or extend beyond the site of the future eruption and in some cases the glands near the site of the eruption become enlarged and painful. The vesicles appear along the course of the affected nerve and tend to occur in groups of two, three, or more, in patches separated by normal skin. The vesicles, which may be the size of a large pea and contain a clear fluid, later develop into pustules. In some instances groups of vesicles coalesce and are deeply situated in the skin. The lesions develop in successive groups and finally dry up and form a yellowish crust that leaves a pigmented area on the skin. In few cases ulceration may take place. Usually the disease runs its course within two to three weeks but may be prolonged in some cases. The pain in herpes zoster may be very mild or severe depending upon the case, and may be transitory, disappearing with the lesions, or persist for long periods of time after all symptoms of the disease have subsided. While the disease is not prone to recur, many cases of two or more attacks are on record. The eruption may occur in different localities, and upon the basis of its place of attack the types of the disease have been designated. Dermatologists now recognize the following types of

zoster: Zoster frontalis, ophthalmicus, capillitii, facialis, nuchæ, brachialis, pectoralis, abdominalis, and femoralis.

The virus of zoster.—The true etiologic agent of herpes zoster is unknown. It is thought that infection, and mechanical and chemical trauma are its chief causes. Rosenow and Oftedal(21) have reported the experimental production of zoster lesions in animals following the injection of certain streptococci which they isolated from the tonsils and pyorrheal pockets of patients suffering with zoster. Sachs(22) has described an epidemic of some sixty-nine cases of the disease that occurred in Breslau in 1901 which indicates the infectious nature of the malady. Hay(23) is of the opinion that the enlargement of the lymph glands in zoster indicates its infectious character. The relation of herpes zoster to varicella has been mentioned above. The affection has also been noted in connection with focal infections by Lain,(24) with malaria by Winfield,(25) with syphilis by Brown and Dujardin;(26) and by other authors it has been noted with eclampsia, pyæmia, septicæmia, meningitis, manipulations of the spine, gunshot wounds, and other injuries, and following the extraction of teeth. Also it appears that this infection may follow the ingestion of arsenic, and poisoning with monoxide, carbon dioxide, and other substances.

In connection with the possible relation of herpes zoster to chicken pox Greenthal(18) states that while working with the virus of chicken pox he developed a mild herpes zoster. He had had chicken pox during childhood. Recently one of my patients developed a mild herpes zoster although he had suffered an attack of chicken pox only a year before. Examples such as these can be multiplied. We believe that herpes zoster and chicken pox are independent diseases and are caused by different agents. These agents may be closely related, but they appear to be specific.

Lipschütz(27) reports that he has been able to demonstrate the presence of inclusion bodies in the lesions of zoster that are similar to the bodies found in other forms of herpes and in many other diseases that are caused by filterable viruses. From the vesicles of herpes simplex and herpes genitalis a virus can be recovered that is infective for rabbits, producing in them an encephalitis to which they succumb within a few days. The virus can be recovered from the brain of the infected animal. Cole and Kuttner(28) in 1925 examined nine cases of herpes zoster and attempted to infect rabbits with fluid from the vesicular

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lesions. These authors were unable to isolate a single strain of herpes from these cases. During the following year McKinley and Holden(29) in their studies on experimental encephalitis in rabbits attempted to isolate a strain of herpes from three cases of herpes zoster but were unsuccessful. It seems apparent that the virus of herpes zoster is not infective for rabbits at least when it is inoculated subdurally. As mentioned above, Teague and Goodpasture(19) were able to inoculate guinea pigs with herpes virus quite easily after the skin had been rendered susceptible with previous coal-tar applications; in this way they produced experimental herpes zoster.

The evidence points to a filterable virus as the etiologic agent in herpes zoster. Mechanical and chemical traumatism may be factors assisting in the development of the infection. As pointed out by us in another publication(30) the herpes virus may remain latent in the tissues (ganglia, nerve trunks, etc.) and pass down the nerve trunks under certain favorable conditions and manifest itself in a cutaneous lesion.

Incubation period.—The exact period of incubation in herpes zoster is unknown.

Animals susceptible.—Man is the natural host for the virus of herpes zoster. According to the experiments of Goodpasture and Teague guinea pigs under certain conditions are also susceptible.

Immunity.—Herpes zoster is not prone to recur. However, instances in which several attacks of the disease have occurred in the same patient are on record. These observations may be taken as both positive and negative evidence for immunity. At present the question remains unsettled. Herpes zoster does not protect against chicken pox nor does an attack of chicken pox protect against herpes zoster. Chicken pox, however, confers a definite immunity against a subsequent attack of varicella. On these facts alone should be based the opinion that these two conditions are separate and distinct entities although they may be similar and the causative agents may be closely related.

Pathology.—The chief changes in herpes zoster are found in the posterior roots of the spinal nerves, in the root fibers of the posterior columns of the cord, and in the peripheral nerves. These changes consist of interstitial inflammation and degenerative changes of the ganglionic centers. Sunde(31) found active inflammation, multiple small hæmorrhages, and round-cell infiltration in and around the Gasserian ganglion on the affected side of a patient having herpes zoster frontalis. There was also

a round-cell infiltration between the nerve fibers and a fibrinopurulent exudate associated with the presence of a Gram positive (both diplococci and chains) coccus. Regeneration usually takes place, but in some cases the destruction is complete and permanent. The cutaneous changes involve both the epidermis and the corium. Unna describes the changes in the epithelial cell as a "ballooning degeneration." The cells within and around the vesicles have a cloudy protoplasm and frequently contain a number of nuclei which resemble protozoans. These were once thought to be parasites, but it is now known that they are nuclei. In the corium there is also dilatation of the capillaries, œdema, and moderate leucocytic infiltration.

Herpes zoster is a self-limited disease and usually terminates within a few weeks at most. Herpes simplex tends to recur, and its appearance is not related to the nerve distribution. Herpes zoster should be differentiated from eczema and from chicken pox, which in some cases closely resemble it clinically.

VIRUS-III INFECTION

Virus III was discovered by Rivers and Tillett(2) while attempting to produce chicken pox in rabbits. The agent produces gross as well as microscopic lesions in the cornea, skin, and testicles of rabbits, and infection with this virus results in an immunity against subsequent infection with the same material. In the beginning Rivers and Tillett believed that this virus was the cause of chicken pox, but further work disclosed the fact that virus III is indigenous to rabbits and that it can be differentiated from vaccine virus as well as herpes virus. These authors demonstrated that the localization of the virus of varicella in the human skin is influenced by irritation. The effect was observed in five of fifty-one patients. In one case the lesions beneath an adhesive-plaster irritant were found to be more numerous than on other parts of the body. In another case napkins were irritants, and the lesions of chicken pox were located at the site of the irritation. In another case the tie and collar served as an irritant. This suggests that the virus is in the circulating blood. Rabbits were found to be susceptible to the virus recovered from the blood of varicella patients, which when inoculated into the testicles of rabbits produced redness, swelling, and œdema, although no ordinary bacteria could be demonstrated. The virus was capable of serial transmission through rabbits by means of testicular inoculation and resisted the action of 50 per cent glycerol for twenty-nine days.

Andrews and Miller,(32) and Miller, Andrews, and Swift(33) have also described a filterable virus infection of rabbits occurring in apparently normal rabbits and in animals inoculated with rheumatic-fever material. It is quite probable that these viruses, if not identical with virus III of Rivers and Tillett, are closely related to it.

In later experiments Rivers and Tillett demonstrated that virus III is filterable through Berkefeld N and V candles, and that the virus is destroyed by heating to 55° C. for ten minutes. These authors found that the intradermal inoculation of virus III into rabbits results in more-uniform lesions than those obtained by smearing the virus on the scarified skin. Immunity to virus III was produced by intradermal, intratesticular, intravenous, intracerebral, and intranasal inoculations. This immunity persists for at least six months. Passive immunity could not be produced in normal rabbits by immune serum taken from immunized animals. Serum from immunized animals, however, possesses virucidal properties for virus III either in vitro or when injected simultaneously with the virus into the same part of the skin. Rivers and Tillett state that virus III is immunologically distinct from both vaccine virus and the virus of symptomatic herpes. Serum from several patients convalescing from chicken pox possessed no virucidal activity against virus III. The authors conclude that the experimental evidence shows no relation of the virus to that of varicella.

In 1926 Rivers,(33) convinced that virus III was indigenous to rabbits and that it was not related to chicken pox, reported his experiments with varicella material inoculated into monkeys (vervets). In this work he was able to demonstrate that following intratesticular inoculation of varicella material into monkeys there appeared nuclear inclusions characteristic of those found in several other filterable virus diseases. These inclusions were observed in the glandular cells of the testicle removed on the sixth day and stained with eosin. In a second monkey showing a similar gross reaction to the inoculation the testicles were removed on the eighth day but no inclusions were found. These results offer encouragement for the future study of chicken pox and should receive further attention.

Virus III has apparently been excellent material with which to study some of the more fundamental problems in relation to the general problem of the filterable viruses. Many interesting experiments suggest themselves with material at hand such as this. Pearce and Rivers have carried on some interesting work

with this virus in connection with tumor growth and malignancy. These authors found that transplantable rabbit neoplasm does not develop in animals immunized to virus III as it does in non-immunized animals. They believe that this resistance to the neoplasm is nonspecific and is due to a more effective resistance of the host. In other experiments these authors were able to show that animals inoculated with virus-III-infected tumor material developed a more serious disease than animals receiving non-virus-bearing tumor material.

Virus III should receive further study in an effort to confirm the interesting results that have been obtained by Rivers and his associates and to extend as far as possible our fundamental knowledge concerning the filterable virus infections.

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RUBEOLA; MORBILLI; MEASLES

Definition.—Measles is a specific, highly contagious, febrile disease which is characterized by catarrhal manifestations of the upper respiratory tract, suffusion of the eyes, and a definite cutaneous rash. While the etiology of measles is not definitely determined it is thought by some to be caused by a filterable virus and by other investigators to be of definite microbial origin.

History.—Measles is one of the most readily communicable of all diseases. Man is universally susceptible. It is probable that this disease is as old as the human race though in olden times it was confused with smallpox. Sydenham(1) in 1847 first gave an accurate description of this disease which eliminated much of the confusion between measles and smallpox that had gone before. Later, for a time, measles was confused with scarlet fever, and even to-day there are cases of German measles that offer difficulty in arriving at an early diagnosis between these two diseases. Koplik in 1896 described small, irregular, red spots, the centers of which are the seat of minute bluish-white specks, on the mucous membranes of measles cases. These spots, now designated "Koplik spots," appear before the cutaneous eruption and aid materially in the diagnosis of this disease.

While measles is considered one of the commonest diseases of childhood, it is by no means limited to this age group. According to Vaughan(2) there were 67,763 cases of measles with 4,261 deaths among the soldiers of the Union Army during the Civil War, while during the World War in the year 1918 the Surgeon General's report gives 48,900 cases of measles for the United States Army. Pneumonia is a frequent complication of this disease, and the relatively high mortality is due to this complication. Wherever people are brought together in crowds, and particularly in time of war, there are susceptible individuals, and epidemics of measles are to be expected.

Distribution of measles.—Man is universally susceptible to measles, and the distribution of this disease is limited only by the distribution of its natural host.

The virus of measles.—The specific etiological agent in measles is undetermined. It is known from the work of Goldberger and Anderson that the virus of measles is present in the secretions from the nose and throat of measles cases, and that the specific agent is capable of passing through the pores of a Berkefeld filter. Blake and Trask(3) were able to induce the disease in monkeys with material obtained from the nasopharynx of active cases, and further demonstrated that the virus is filterable. This virus resists drying and freezing for twenty-four hours but is destroyed at 55° C. Hektoen(4) produced measles experimentally in two students, while Anderson(5) has also succeeded in inducing the disease in monkeys. Nevin and Bittman(6) claim to have induced symptoms of the disease in guinea pigs following the injection of blood from active cases of the disease. Duval and d'Aunoy(7) have obtained similar results. None of these experiments has resulted in the isolation of any known bacterial forms, though Mallory has described certain minute bodies in the endothelial cells of the capillaries of measles cases.

Caronia(8) recently reported the presence of an organism consisting of very minute granules and occurring in pairs in the blood, bone marrow, cerebrospinal fluid, and filtrates from nasal secretions of cases early in the course of the disease. This organism may be cultivated anaërobically from material that has been passed through a Berkefeld filter. Further, according to this investigator, the disease may be produced in susceptible individuals following the inoculation of this culture intravenously and the killed culture when injected produces immunity to the disease.

More recently Tunnicliff,(9) Donges,(10) Ferry and Fisher,(11) and Hibbard and Duval(12) have cultivated a nonhæmolytic streptococcus from the blood of measles cases. Tunnicliff has also been able to cultivate another streptococcus from cases of German measles. In forty-two of fifty-two cases this author recovered a streptococcus, although in twenty cases other bacterial forms were found in addition to the streptococcus. Ferry and Fisher and also Tunnicliff have demonstrated that their streptococcus produces a toxin and in this respect is quite similar to the streptococcus of scarlet fever. In this connection Paraf(13) has shown that measles complicated by streptococcus infections can cause a positive Dick reaction to become negative. In later experiments Tunnicliff has shown that the green-producing diplococci isolated before the appearance of the rash and

during the acute stages of the disease are immunologically distinct from similar cocci isolated later during the convalescence of the patient. Guardabassi(14) found from his experiments on rabbits and guinea pigs that the measles virus is filterable, and demonstrated Gram-negative granular formations that measure from 0.4 to 0.6 micron in length and stain pink with Giemsa's. He states that these forms are analogous to those described by Coronia.

Long and Cornwell(15) attempted to isolate a toxin-producing green streptococcus from forty-seven cases of measles but were unsuccessful. In all the cultures made from the blood of these patients during the preëruptive stage of the disease, cultures were obtained in only four instances and these were regarded as contamination.

Degkwitz(16) has been a steady proponent of the filterable virus theory of the etiology of this disease. In his most recent work he states that measles can be produced in human beings with material sterile from a bacteriologic standpoint, with sterile blood from a patient with measles, or with dilutions of blood that have been passed through a Berkefeld filter. This author finds that the nasal secretions are also infective. According to this author the virus of measles may remain alive for several weeks in blood taken from a patient having the disease, provided it is placed in buffered salt solution and kept at 0° C.

Other organisms have been described as the cause of this disease by Salimbeni and Kermorgant(17) who described the cultivation of a spirochæte associated with a Gram-negative bacillus from measles cases and by Sellards and Bigelow(18) who reported the discovery of a small Gram-positive bacillus. Kusama(19) has described the passage through monkeys of a Gram-positive diptheroid bacillus that he believes to be the cause of measles.

It may be said without reservation that the virus of measles is at present unknown. Since so many different organisms have been described as the cause of this disease it appears that secondary bacterial invasion in measles cases is apparently accomplished with great ease. Perhaps future investigations will determine which of the various organisms described is the true cause of this disease or whether we must continue to regard the etiological agent of measles as a filterable and invisible agent.

Incubation period in measles.—The incubation period of measles is usually from eleven to fourteen days.

Symptoms.—The symptoms of measles may be divided into three stages; namely, the period of invasion, the stage of eruption, and the stage of desquamation.

The invasion of measles is gradual. The fever and the catarrhal symptoms increase gradually until the rash appears. The invasion of the disease is characterized by coryza, increased lachrymation and suffusion of the eyes, photophobia, sneezing, and nasal discharge. A hoarse, hard cough usually develops, and the patient may develop a sore throat. On the mucous membrane of the cheeks appear minute white spots, Koplik spots, that are diagnostic of the disease before the rash appears. The constitutional symptoms consist of dullness, headache, pains in the back and legs, and in some cases vomiting and diarrhœa.

The eruption or rash begins about the third to the fifth day of the disease as small dark red spots on the back or behind the ears, at the hair line over the forehead, and on the neck. The first lesions are macules which rapidly change, within about twenty-four hours, to papules. The rash is usually fully developed in from thirty-six hours to three days. As the disease progresses the rash spreads over other parts of the body and appears last upon the lower extremities. As a rule it covers the entire body and may remain discrete or become confluent. Usually the rash lasts about four days, but in mild cases it may terminate within a day or two and in other cases remain for six days or a week. The constitutional symptoms reach their height at the time of the full development of the rash. The tongue becomes coated and somewhat resembles the strawberry tongue of scarlet fever. As the rash subsides the general symptoms become less marked, the fever rapidly declines and within twenty-four to forty-eight hours after the temperature has reached normal the rash disappears.

When the rash disappears a fine branlike desquamation begins. It may last from five days to two weeks and is more marked in the cases where the eruption has been severe.

Measles cases are subject to a variety of complications. As a rule the mortality is low, but in epidemics where the disease is complicated by a terminal pneumonia the mortality may be exceedingly high. In addition to pneumonia other complications, such as meningitis, encephalitis (see chapter on Encephalitis), otitis, chronic conjunctivitis, enlargement of the lymph glands followed by tuberculosis infection, nephritis, endocarditis and pericarditis, gastric disorders, erysipelas, furunculosis,

impetigo, pemphibus, and hæmorrhages, have been observed. Measles may also be complicated by other infectious diseases.

The blood picture in measles is characterized in the early stages of the disease by a lymphocytic leucocytosis and later there is a leucopenia.

Animals susceptible to the measles virus.—Man is the natural host for this virus. Experimentally monkeys, rabbits, and guinea pigs are said to be susceptible.

Immunity.—One attack of measles usually confers immunity. Second attacks are more often reported in this disease than in any of the other eruptive fevers. Age is no barrier to the infection provided the individual has never suffered an attack of the disease. It is quite generally agreed that measles lowers the resistance to other infections more than any other disease. Immune bodies are greatly diminished or disappear within a short time after an attack of measles.

Within recent years the use of convalescent serum has been employed, particularly by Park, for the prevention of measles. The serum is most active after the tenth day following the disease and before three months have elapsed. Five cubic centimeters of this serum are sufficient to immunize a child against measles for a few weeks. Adult serum has also been employed for this purpose, but much larger quantities are required to produce any immunity. Debre, Joanmon, and Papp(20) have employed minute quantities, 0.00125 cubic centimeter, of filtered blood from measles cases for the purpose of immunizing children and state that hundreds of children have been successfully vaccinated in this way without any reactions. The duration of the immunity produced by this method is unknown. According to Baron(21) the use of Degkwitz's protective sheep serum for measles is not encouraging. In this author's experience all persons so immunized developed measles and in some cases with grave results. On the other hand the use of convalescent serum for immunization has met with continued success wherever it has been tried. For the time being this method of prevention in measles appears to be very encouraging, and the dangers of transmitting other infectious diseases may be minimized by careful selection of material to be used for immunization of susceptible individuals.

In 1926 Tunnicliff and Hoyne(23) reported the immunization of goats with their green-producing measles diplococci and found that the serum from these goats protected rabbits against sub-

sequent injections of infective material from measles. Rabbits not so protected developed characteristics of measles when injected with infective material, the symptoms consisting of a rise in temperature, Koplik spots, and a rash. In another paper these authors have described the results of the use of their immune serum in children in which 45 per cent of children who received 4 to 6 cubic centimeters of serum on the fourth day after contact with measles patients remained immune. All infants under one year of age who received serum after the fourth day following exposure developed the disease. Tunnicliff concludes that—

> Although the duration of passive immunity with immune goat serum, as with human convalescent measles serum, is only a few weeks, the serum appears to be useful in preventing measles in very young and sick children, and in stopping epidemics in institutions where the inconvenience of an epidemic is great and the mortality may be high.

Pathology.—The only anatomical changes in uncomplicated measles are those found in the skin and mucous membranes. The skin lesions are inflammatory in character and are thought to be more superficial than those in scarlet fever. Around the blood vessels there is an infiltration of round cells. Œdema and congestion are in evidence about the sweat and sebaceous glands, and the papillæ.

The mucous membranes are the seat of a catarrhal inflammation, and in some cases the inflammation may be of a membranous character. Other anatomical changes depend upon various complications which may appear in certain percentages of measles cases.

Control measures.—Isolation and quarantine are absolutely essential for the control of this disease. Seroprophylaxis, as soon as it can be carried on on a large enough scale, may offer great aid in the prevention of this disease. At present our methods of preventing measles are totally inadequate, even were they rigidly enforced, due primarily to the very nature of the disease. Rosenau (22) states, "the suppression of measles is one of the most difficult problems we have to face, for the reason that the disease is one of the most highly contagious of all infections, and for the further reason that it is most contagious during the preëruptive stage." Further investigations it is hoped will lead to a better knowledge of this disease upon which a practical and definite method of protective immunization may be devised.

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RUBELLA: RÖTHELN: GERMAN MEASLES

Definition.—German measles is a specific, infectious disease of a mild nature; it is characterized by a cutaneous rash which usually appears without prodromal symptoms. Its mortality, if any, is exceedingly low, and in the absence of any demonstrable causative agent it has been thought to be caused by a filterable virus.

History.—From our knowledge of the history of rubella it is believed that German measles probably existed in ancient times

and was confused with scarlet fever and rubeola. Vaughan(1) states that—

> Capable students of the history of epidemiology claim that there is some evidence of the recognition of this disease from measles in the writings of Arabian physicians of the ninth and tenth centuries. We are also told that in the seventeenth century the learned epidemiologist of Sicily, Ingrassias, recognized that occasionally he had to deal with a disease resembling measles but to which an attack of measles gave no immunity. During the eighteenth and a large part of the nineteenth centuries there was much discussion as to the identity or the specificity of rubella and rubeola. These terms were used indiscriminately, and it is now quite evident that they were often transposed by certain authors.

Vaughan believes that the malignant epidemics attributed to rubella by German authors in the eighteenth century were undoubtedly epidemics of scarlet fever. The exact date when German measles was recognized as a separate and distinct disease is not known, although Vaughan states that—

> In 1815 Maton clearly pointed out the difference between scarlatina, rubella, and rubeola. Rubella was given a variety of names; in fact, nearly every clinician who wrote upon the exanthemata of infancy and childhood, for 100 years gave some new name to it. The term rubella was suggested by an English physician, Veale, in 1866 and soon found its way into the medical dictionaries. The name is especially appropriate, being the diminutive of rubeola and expressing at one and the same time the slight import of the disease and its relationship to measles; in other words, rubella means little or light measles.

Distribution.—German measles has long been known throughout Europe and the Americas. No doubt its distribution is limited solely to the distribution of its natural host, which is man.

The virus of German measles.—The cause of German measles is not known. Tunnicliff (see Measles) has found a streptococcus in measles which is different from the streptococci found in rubeola, but so little study has been made of this organism and its relation to German measles that only passing mention of it may be made at this time. German measles, being of such low mortality and of such a mild clinical nature, has received very little study from the standpoint of etiology. That rubella is a disease distinct from rubeola there can be no doubt. Measles gives no immunity to rubella, and in rubella Koplik spots are absent. In the absence of a definite etiologic agent and based upon the possible filterable nature of the virus of rubeola it is also thought that rubella may be due to a filterable virus.

Incubation period.—The period of incubation in rubella is

usually from fourteen to twenty-one days but is subject to great variation.

Symptoms.—Usually there are no prodromal symptoms, although in some cases there may be mild constitutional symptoms before the rash appears. As a rule the first sign of the presence of this disease is the appearance of a rash. The rash is usually composed of very small maculopapules which are pale red in color, discrete, and the size of a small pea. The rash resembles rubeola in many respects and is subject to variation. In some cases the rash is hæmorrhagic and may have a "shotty" feel to the touch. The temperature usually does not exceed 101° F. and may fall abruptly as the rash disappears. In some cases the temperature may reach 103° F. and catarrhal symptoms with sore throat may be present. One of the most constant features of rubella is the enlargement of the cervical lymph glands. This swelling subsides slowly in most cases without suppuration, but in some cases it may persist for long periods of time. I have recently seen a case in which the cervical adenitis has persisted for nearly two years despite all the treatment to reduce it. Forcheimer (2) has described an enanthem of the mucous membrane of the throat in German measles consisting of minute, red points appearing upon the uvula and soft palate which he believes is characteristic of the disease. According to this author these "points" disappear within the first twenty-four hours of the disease.

Duke has attempted to differentiate between two forms of German measles, one of which closely resembles scarlet fever. This disease is known as "Duke's disease" or the "fourth disease." Opinion is not crystalized upon this matter.

In some cases there is no desquamation following the disappearance of the rash, while in others it may be fairly marked. The mortality in German measles is practically nil; complications are rare and when present are very mild in character.

Animals susceptible to rubella.—So far as is known man is the natural host of the infectious agent of this disease and is the only species affected. German measles has not been definitely produced in animals.

Immunity.—One attack of the disease confers a definite immunity against subsequent attacks. Rubeola and scarlet fever offer no protection against rubella and vice versa.

Pathology.—The anatomical changes in German measles are limited to the skin and the accompanying changes in the cervical

lymph glands. Due to the mild nature of this disease there has been a great paucity of material for study, and in general it is believed that in uncomplicated cases of German measles the pathological changes are so mild that no importance should be attached to them.

Control measures.—According to Vaughan the evidence appears to favor the idea that German measles is transmitted chiefly through fomites. Authors are not agreed as to the degree of contagiousness of this disease, although it is generally admitted that it is contagious. Isolation is indicated; and in general the measures employed for measles should be instituted. Vaughan recommends the burning or disinfection of all articles with which the patient has been in contact.

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EPIDEMIC PAROTITIS: MUMPS

Definition.—Mumps is a specific contagious disease characterized by an inflammation of the salivary glands. The parotid gland is usually involved and the submaxillary and sublingual glands may also be affected. In some cases the disease involves the testes in the male and the ovaries in the female. In some cases the first symptoms of the disease may be related to the testes. The disease is caused by a filterable virus.

History.—According to Vaughan(1) this disease has been known since the time of Hippocrates, though it was first recognized as a specific disease by Hamilton in Scotland in 1761. In discussing the epidemiology of this disease this author states that extensive epidemics of mumps occurred in Italy during the latter half of the eighteenth century. Mumps is an important disease in military organizations. Vaughan states that in 1918 there were 166,370 cases of mumps in the United States Army, and the loss of time caused by this disease has been estimated at 2,894,074 days. During the World War there was a total of 213,943 cases of mumps in the American Army. Considering the entire army at home and abroad for the year 1918

Vaughan states that 7,766 men were disabled by this disease for each day of the year. The total number of deaths for the year 1918 attributed to this disease was 151, the actual cause of death for the most part being a complication by pneumonia. In civilian life mumps usually occurs between the ages of 5 and 15 with most cases falling in the age group between 7 and 9 years. It is in this period of life, when the child starts to school, that he comes in contact with the virus from other cases. In armies the disease appears in the age group of 21 to 31 years chiefly. In the early history of mumps the disease was confused with secondary parotitis and practically nothing was known regarding the epidemiological features of the disease.

Distribution.—Mumps is distributed all over the world, and no place or country, it is thought, is ever continuously free from the disease.

The virus of mumps.—In the eighties of the nineteenth century various investigators reported bacterial forms in the blood and saliva of persons having mumps. Vaughan states that "in 1892 Laveran and Catrin found in 67 out of 95 cases of mumps micrococci resembling those already described. The testicular fluid obtained by puncture with a hypodermic needle gave positive results in 12 out of 16 cases. No inoculation experiments were made with these bacteria." Again, "in 1896 Mecray and Walsh found a diplococcus in the discharges from Steno's duct. . . . Granata (1908) for the first time, used filtered saliva in animal inoculations."

Granata used rabbits in his experiments, and his results are regarded as of doubtful significance. In 1913 Nicolle and Conseil,(2) working with filtered saliva from cases of mumps, found evidence of the experimental disease in the monkeys which they inoculated. These experiments were followed by the work of Wollstein(3) in 1918 which placed the filterable nature of this virus upon a sound basis. Wollstein inoculated the filtered mouth washings of children suffering from mumps directly into the parotid glands of cats. Following these inoculations the cats exhibited a small rise in temperature within forty-eight hours and slight local tenderness which Wollstein thought to be due to mechanical injury. In about seven days after the injection there was swelling and tenderness of the parotid and testicles. Wollstein states that "the swelling and pain in the parotid lasted from two to five days, but the testicular swelling rarely subsided in less than ten to fourteen days." There was a gradual in-

crease in leucocytes from the second day following the inoculation. Wollstein says:

> In the third week all the symptoms began to disappear, the leucocytes reaching the normal first, the tenderness disappearing at the same time, and the fever persisting for another week. While tenderness on palpation of the parotids was less marked than that of the testes, and the swelling never reached the stage of marked facial asymmetry, the cats manifested some degree of discomfort in the inoculated parotid. The appetite was only slightly affected and at no period of the experiment did the cats appear especially ill . . . the salivary filtrates from patients ill from one to three days produced these marked symptoms in the inoculated cats. On the sixth day of the disease the effect of the filtrate injection was much less marked and inoculation of material obtained from a patient nine days or longer after onset of the mumps attack was apparently without results.

Transmission of the experimental disease from cat to cat was successful with emulsions made of infected glands and by means of the saliva from inoculated cats.

Regarding the properties of this virus little is known. In view of the apparent ease with which cats can be infected with mumps virus it seems that much information on the nature of the virus may be obtained by further experiment.

Incubation period.—The incubation period of mumps may vary from three to twenty-five days, and on the average it ranges between fourteen and twenty-one days. Experimentally in cats, according to Wollstein, it is from six to seven days.

Symptoms.—Prodromal symptoms consisting of headache, anorexia, vomiting, back and leg pains, and fever may in some cases precede the local swellings. As a rule both parotids are involved and the jaws are painful before actual swelling is noted. Usually the swelling begins on one side, the other gland becoming involved one or two days later. All degrees of swelling may exist depending upon the severity of the case. The submaxillary and sublingual glands may also be involved. The salivary secretion is usually diminished, but in some cases there may be excessive salivation. The temperature ranges between 100 and 104° F. Venous congestion leading to hyperæmia of the brain with headache and delirium may result. Other complications such as orchitis, nephritis, deafness, pneumonia, meningitis, endocarditis, and suppuration may occur in some cases. However, these are rare. The blood picture in mumps is quite characteristic. It consists of a reduction in the polymorphonuclears and an actual and relative increase in the lymphocytes.

Animals susceptible to the mumps virus.—Man appears to be the natural host for this virus. Cats can be experimentally infected. The work on rabbits and monkeys is indefinite.

Immunity.—One attack of the disease confers a definite and in most cases a lifelong immunity to subsequent infection with this virus. The age incidence of mumps indicates that there is very little, if any, natural immunity to the disease.

Pathology.—The anatomical changes in this disease are found principally in the salivary glands. There has been a paucity of material for the study of pathological lesions in this disease, but it is quite generally known that the salivary glands exhibit hyperæmia and œdema, and the walls of the ducts are swollen and obstructed. Pyogenic germs may gain entrance and lead to abscess and suppuration, but this is rare. Other lesions depend upon various complications of the disease.

Control measures.—Isolation and disinfection are indicated as the most efficacious measures for the control of mumps.

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TRACHOMA: GRANULAR CONJUNCTIVITIS

Definition.—Trachoma is a specific, contagious disease, characterized by inflammation and hypertrophy of the conjunctiva; and by the formation of granules, with subsequent cicatricial changes. It is usually of long duration, occurs at all ages, is frequently complicated, and may lead to partial or total blindness. It occurs in three forms; namely, the papillary form, the granular form, and the mixed form.

History and distribution.—Trachoma has been known since ancient times. It has long been endemic in Egypt and is thought to have been carried to Europe by soldiers during the Napoleonic wars. It occurs in Arabia, Belgium, Holland, and Hungary. It is present in Italy and is found to be an important affection among the American Indians in sections of the United States. It is common among the Russians, Polish Jews, Hungarians, Italians, and Irish. It has not been common among the negroes. In the Philippines there is a form of follicular conjunctivitis which is endemic among school children in Pap-

gasinan Province. This is probably not true trachoma, but extensive investigations into the true nature of this affection have not been made. Trachoma seems to have been introduced into the Netherlands about 1860 and is thought to have been carried to Amsterdam by Polish Jews. In a survey made in 1880 it was found that 45 per cent of 2,733 Jewish children were affected. By 1901 through periodic examination and control methods this percentage had fallen to less than 8 per cent. In China, Japan, Egypt, and Russia the disease remains a great public-health problem.

The virus of trachoma.—In 1907 Prowazek and Halberstaedter(1) described inclusion or trachoma bodies in the conjunctival epithelium of cases of trachoma. The exact nature of these bodies remains undetermined. These inclusions consist of coccoid and minute granular bodies. The coarser coccoid bodies stain bluish by the Giemsa method, while the granular forms stain reddish. Scrapings from the conjunctiva injected into the eye of the orang-utan produced conjunctivitis associated with the appearance of similar inclusion bodies. These bodies were regarded by these authors as the cause of trachoma. Later the same workers found similar inclusions in cases of uncomplicated blennorrhœa neonatorum, and their specificity was questioned by contemporary investigators. Herzog(2) suggested the theory that the gonococcus is transformed into small forms within the ephithelial cells and that the so-called trachoma bodies are in reality changed gonococci. Williams(3) regarded the inclusion bodies as degenerated forms of the Koch-Weeks bacillus. Prowazek regarded the trachoma bodies as protozoan in nature, while Noguchi(4) in 1913 claimed to have cultivated these bodies, although his attempts to induce trachoma in monkeys (*Macacus* and *Papio*) with his cultures failed. The exact relation of the so-called trachoma bodies to the true etiology of this disease, then, has remained undetermined. Because of the uniform presence of these inclusions in typical uncomplicated cases of the disease and the occurrence of similar bodies in various other diseases which are thought to be caused by filterable viruses, and in the absence of any other definite etiological agent, the possibility of a filterable virus etiology has been suggested for trachoma. According to Rosenau,(5) "experimental evidence permits no more than the suspicion that the virus may be filterable under some circumstances." However, fairly convincing evidence has been

presented upon this point in the experiments of Bertarelli and Cechetto(6) and of Nicolle, Cuénod, and Blaizot.(7)

Heymann(8) after finding inclusions in cases of gonorrhœal blennorrhœa neonatorum suggested that the so-called inclusion bodies were in reality reaction products of the gonococcal virus. Simon(9) states:

> A thorough study of this question then led to the interesting discovery of the existence of an inclusion blennorrhea as a malady *sui generis*, which primarily affects the genitalia of both male and female and secondarily the eyes of the new born. This type of blennorrhea it is now known may be associated with a gonococcal infection, as well as with other bacterial infections (pneumococci, diphtheria bacilli), but when this occurs the processes are independent of each other.
>
> The discovery of the occurrence of inclusions in connection with blennorrhea of this type naturally threw doubt upon the correctness of Prowazek's view, that the constituent granules making up the inclusions found in trachoma actually represented the trachomatous virus. Various suggestions have accordingly been made to account for their appearance in trachoma, on the one hand, and in inclusion blennorrhea, on the other.

Linder(10) inoculated two baboons with pure inclusion blennorrhœal material and obtained a clinical and histological picture which he states cannot be distinguished from trachoma. Wolfrum(11) inoculated similar material into a human being, and there followed the typical picture of trachoma. Simon suggests the theory that the inclusion bodies may not be part of the picture of trachoma but are found in cases of this disease only when both blennorrhœa and trachoma are present in the same subject.

In 1927 Noguchi(12) produced an experimental trachoma-like condition in monkeys with material obtained from cases of trachoma from Indians at the government school for Indians at Albuquerque, New Mexico. From this material he cultivated upon special media a Gram-negative bacillus which when injected into monkeys produced a granular conjunctivitis that "had an appearance strikingly like that of the human trachomatous conjunctiva in the early stages of the disease." This organism was associated with four of the five cases studied, and the conjunctival disease produced is said by Noguchi to be transmissible in series while the identical microörganism is obtained regularly even in the second and the third passage in monkeys. None of the other organisms isolated by Noguchi from his material was capable of inducing follicular lesions in monkeys. Material taken direct from patients and injected into monkeys did not produce lesions within four months.

This work of Noguchi's represents an important contribution to the knowledge of trachoma as it exists in the American Indian but must, of course, await confirmation in other localities.

Incubation period of trachoma.—Trachoma is a chronic disease. Its incubation period is not definitely known. The recognition of the disease in its early stages is very difficult, and accurate diagnosis usually depends upon changes that appear later in the course of the disease. In the experimental form of the disease, produced by Noguchi in monkeys, the first changes were noted two to four weeks after inoculation with the cultures obtained from trachomatous material.

Symptoms.—There are three forms of granular conjunctivitis; namely, papillary, granular, and mixed forms. Regardless of the form, there are certain subjective symptoms which may be present; such as, photophobia, lachrymation, itching and burning sensations, feeling of a foreign body, pain, and visual disturbance. In some cases there may be no subjective symptoms. The objective symptoms consist of swelling of the lids, narrowing of the palpebral aperture, and dropping of the upper lid. There may be a mucopurulent discharge and the conjunctiva of the tarsus and fornik is reddened, thickened, and uneven, on account of the hypertrophy and the occurrence of granules. Trachoma progresses slowly up to a certain point, then is followed by the cicatricial stage. The papillæ and granules disappear, but the conjunctiva does not return to normal and various degrees of scarring remain. The entire surface of the conjunctiva may be replaced by a cicatricial membrane.

In some cases the condition is acute and is accompanied by marked inflammatory symptoms. Gonococcal infection may be associated with true trachoma; and the diagnosis may be difficult, especially early in the course of the disease. In other cases the symptoms may be so mild and the disease so insidious that it may exist for months without recognition. In fairly severe cases there may be intermissions and exacerbations, and relapses are quite frequent. The disease is frequently complicated by pannus and corneal ulceration. The commonest sequelæ are trichiasis and entropion, ectropion, symblepharon, corneal opacities, staphyloma of the cornea, and xerosis.

Animals susceptible to the virus of trachoma.—Man is the natural host for the virus of trachoma. From experimental sources it may be said that the evidence points to the possibility of infecting monkeys.

Immunity.—That there is a definite racial predisposition to infection with trachoma is borne out by the studies on the epidemiology of this disease. It may be assumed by the same token that there exists some degree of racial immunity and, for that matter, an individual natural immunity. There is, however, no experimental evidence bearing upon this point. Immunity has not been produced experimentally.

Pathology.—In the papillary form a large number of small elevations appear upon the conjunctiva giving a velvety appearance, and if the papillæ are larger, a granular appearance. This form occurs only upon the upper lid. The papillæ represent the hypertrophied conjunctiva thrown into folds and covered by increased epithelium. Within there is a cellular infiltration. In the granular form there are grayish, rounded, translucent bodies or granules which are seen through the conjunctiva. These bodies may be small and round, large and warty, or flattened and succulent. They are principally in the fornix. They may also be found upon the semilunar folds and the bulbar conjunctiva. These granules represent collections of lymph corpuscles in a connective-tissue reticulum, resembling Peyer's patches in the intestines. According to Noguchi the histologic changes present in trachoma as it exists in the American Indian are as follows:

> The essential features of the lesions in the human disease are (1) diffuse infiltration of lymphocytes mingled with plasma cells, extending along the entire length of the subepithelial or adenoid layer; (2) the presence of fairly well defined follicles, consisting of layers of lymphocytes, enclosing a mass of large round or polyhedral epithelioid cells with paler staining cytoplasm and nuclei; (3) ill defined foci of mingled lymphocytes and large epithelioid cells; (4) the presence of Leber cells within the follicle and elsewhere; (5) the presence of fine connective tissue fibrils surrounding or penetrating the infiltrated or follicular areas, and (6) the proliferation of the conjunctival epithelium, which in some places shows several layers of flattened cells, and in others is thinned out to a single layer or even ruptured by protruding follicles. In older lesions the infiltration and follicles have given place to increased numbers of connective tissue fibers, which bind the epidermized conjunctival epithelium to the often deformed tarsus. A few polymorphonuclear leukocytes may be found in the tumid epithelial layer, but their presence is not usual.

In the experimental disease produced in monkeys Noguchi found similar changes.

Control measures for trachoma.—Trachoma has always been associated with poverty and squalor. Unhygienic conditions predispose to the disease. Early diagnosis of the condition is important in order to prevent serious sequelæ. The secretion from

the eyes of trachoma patients is regarded as contagious, and the disease may be transmitted by infected handkerchiefs, towels, washbasins, etc. Isolation of trachoma cases has been advocated, especially during epidemics. In general, early diagnosis of the disease coupled with intelligent care and the institution of strict sanitary measures are indicated.

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INCLUSION BLENNORRHŒA: INCLUSION CONJUNCTIVITIS

Following the work of Heymann in 1909 (see Trachoma) who found in several cases of gonorrhœal blennorrhœa neonatorum inclusions similar to those that had been described in trachoma by Prowazek, it appeared that there existed a separate and distinct type of blennorrhœa not associated with gonorrhœa or trachoma. This type of blennorrhœa primarily affects the genitalia of both male and female and secondarily the eyes of the new born. While this condition may exist along with a gonorrhœal or other bacterial infection, it is now recognized that the processes are independent of each other. The cause of this form of blennorrhœa is unknown. Inclusion bodies are found within the lesions which suggests a filterable virus origin for the disease.

Inflammations of the conjunctiva are of several varieties and generally are divided into the following types: Catarrhal (acute, chronic, and follicular); purulent (ophthalmia neonatorum, and gonorrhœal); membranous (nondiphtheritic or croupous, and diphtheritic); granular (trachoma); and phlyctenular. It is well recognized by ophthalmologists that there are

cases of ophthalmia neonatorum which are not caused by gonococcal infection, and these are believed to be due to infection with simple catarrhal (nongonorrhœal) secretion. In 1913 Cohen(1) reported on the clinical course of conjunctival affections associated with so-called trachoma bodies which was a further study of the cases described in an earlier paper by Noguchi and Cohen(2) published in 1911. The original cases studied by these authors included nine cases of trachoma represented by four stages of the disease, six cases of blennorrhœa neonatorum nongonorrhoica, and six cases of blennorrhœa gonorrhoica in young girls. As a result of these cases there were a number of other cases infected. There were nineteen new cases of trachoma, two new cases of blennorrhœa neonatorum (nongonorrhoica), and twenty cases of blennorrhœa gonorrhoica in young girls. Inclusion bodies were found in the six cases of blennorrhœa neonatorum nongonorrhoica varying from four days to two weeks after birth. Cohen states that—

> The clinical course of these cases resembles that of mild cases of blennorrhœa gonorrhoica, which in its earliest stage is characterized by a diffuse conjunctival congestion with a mucoid secretion from the conjunctiva. The condition remains for about one week, when the conjunctiva assumes a fine papillary appearance, and a few small follicles are seen on the upper fold as well as on the lower. This appearance lasts about two months, when the process regresses simultaneously with the gradual disappearance of the bodies and is followed by a permanent return of the conjunctiva to normal in from three to four months.

In one of Cohen's cases, so-called trachoma bodies were found in an affected eye from the mother and these were demonstrated at intervals for three months. In his study of thirty cases of blennorrhœa gonorrhoica in young girls at Randall's Island Hospital, Cohen was able to demonstrate gonococci and so-called trachoma bodies in practically every case. These bodies persisted even after the gonococci could no longer be found. Likewise in his true trachoma cases Cohen found inclusion bodies.

The interesting feature of this study is the fact that inclusion bodies are found in cases of blennorrhœa which are of neither trachomatous nor gonorrhœal origin. These cases are not trachoma since they bear no clinical resemblance to trachoma and because there is spontaneous cure without sequelæ. In Cohen's opinion "where bodies were found in conjunction with gonococci, and in some cases of typical trachoma, these conditions are to be interpreted as the result of the disease caused by these bodies becoming engrafted on the original affections." Cohen

believes that the term "trachoma bodies" is a misnomer and should be discarded.

While there is nothing known regarding the etiology of this condition there has been a tendency to classify inclusion blennorrhœa with the filterable virus diseases. At present there is no experimental evidence that it is caused by a filterable virus.

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See also Trachoma.

VERRUCÆ: WARTS

VERRUE (FRENCH); WARZE (GERMAN)

Difinition.—Verrucæ, or warts, represent an epidemic, papillary new growth of which there are three recognized types; namely, verruca vulgaris, verruca plana juvenilis, and verruca senilis.

History.—Warts have been recognized since olden times, and legends and superstitions have been connected with their appearance for perhaps centuries. Even to this day there are certain peoples who are prone to regard these lesions with various superstitions. The infectious nature of these growths was demonstrated in 1891 when Payne(1) developed warts under his thumb nail following the removal of warts from one of his patients. Lanz(2) reported similar results in 1898. In 1889 Kuâneman(3) cultivated a bacillus from warts and claimed to have reproduced typical lesions in laboratory animals. Variot(4) four years later produced warts in one of his assistants following the inoculation of blood from small warts. During the next year Jadassohn(5) made seventy-four inoculations with wart material from which he obtained thirty-one positive results and demonstrated that the lesions he produced were typical verrucæ according to their histologic picture. In these experiments this author demonstrated that the incubation period for warts ranges from seven weeks to three months. In 1919 Wile and Kingery(6) reported their brilliant experiments which proved conclusively that warts are due to a filterable virus.

The virus of verruca.—Wile and Kingery began their experiments on the theory that the infectious agent of warts is a filterable virus. In their first paper they point out that certain microörganisms are known to give rise to disorders of keratinization. Examples of this fact, such as the rôle of the gonococcus in the production of blennorrhagic keratoses, the

tubercle bacillus in verruca necrogenica, and the gonococcus in the production of condyloma acuminatum, are mentioned.

Their experiments consisted of the removal of clinical warts and grinding this tissue in a small amount of saline after which the saline emulsion was filtered through the finest Berkefeld filter. In order to obtain the maximum amount of material for their experiments the filter candle was almost entirely covered with melted paraffin leaving only the top end exposed as a filtering surface. After testing their filtrate for sterility small amounts of filtrate were inoculated intradermally into human subjects. Part of their material was preserved in glycerin to be tested later. In the course of about four weeks small wartlike growths appeared in one subject, while a second showed lesions one week later, and a third about three weeks later. In only one case did a wart reach the size of a large pea. This occurred in about eight weeks. In some cases there was a tendency to spontaneous resolution; however, in most cases the lesions persisted for at least seven months. The histologic studies made upon these new growths were typical of true warts. A control which received a filtrate prepared with normal epithelium remained negative. In later experiments the preserved material in glycerin was tested in a similar manner, but results with this material were negative after nearly six months. These authors concluded that "the sterile filtrate of wart material injected intracutaneously is capable of producing localized hyperkeratoses which are clinically and pathologically identical with verruca vulgaris."

In 1921 this work was further extended by Kingery(7) when he demonstrated that lesions could be produced in the second generation from the initial lesions described above. In these experiments the incubation period was found to be nearly six months. There are no data on the properties of the virus of verruca.

Symptoms.—The lesions of warts are unaccompanied by subjective symptoms. When they first begin to appear they are small, flat, shiny areas which increase slowly in size. Later the growth may present a distinct papillary surface. At first it is the color of the skin, then gradually becomes grayish and even grayish black. As a rule there is no pain or itching except when inflammation is present.

Immunity.—There are no data on immunity in this form of new growth. While no experimental evidence is available on the subject, it is generally assumed that there is a natural im-

munity to the virus which varies greatly in degree. This is indicated by the variable period of incubation and the fact that most individuals rarely become infected with this virus.

Pathology.—Histologically warts are characterized by a typical localized acanthosis. The growths begin as an early hyperkeratosis which gradually becomes more marked. In the late stages there is a proliferation of the papillary tufts which later thicken and dip down. In general all the layers of the epidermis are more or less increased in thickness. The granular layer is increased, the rete cells are enlarged, and the intercellular spaces are widened. In some cases there is moderate inflammation, and round-cell exudate is found in the neighborhood of the vessels. All of these changes vary according to the type of growth.

Control measures.—None are indicated. These growths are benign. Rarely do they become epitheliomatous.

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MOLLUSCUM CONTAGIOSUM: EPITHELIOMA

Molluscum sebaceum; Molluscum epitheliale; Acne variioliformis

Definition.—Molluscum contagiosum is regarded as a contagious epithelial neoplasm, or new growth, which is characterized by small tumors the size of pin-heads or peas, usually the color of normal skin but at times pinkish or bright red, with a small depressed central opening. These new growths are believed to be caused by a filterable virus.

History.—The term "molluscum," or "molluscis," is thought to have been first employed by Ludwig(1) in 1739 as a synonym for "mollis" to indicate certain soft tumors, while others believe that the word was used because of the resemblance of certain cutaneous tumors to knots on the bark of the maple. The first clinical description of this disease was given by Bateman(2) in

1817, while Patterson(3) in 1841 studied the secretion from molluscum tumors and called attention to the so-called molluscum corpuscles or bodies. This author believed that these bodies represented nuclei. In 1844 these growths were regarded by Engel(4) as enlarged sebaceous glands, a view which was concurred in by Rokitansky(5) in 1856. Virchow(6) in 1865 regarded molluscum tumors as a lobulated glandular epithelioma. He believed that the molluscum bodies arose from the hair follicles and likened their appearance to swollen starch bodies and fatlike globules, although he thought they were probably the result of a degenerative process involving the epithelium. In later years Bizzozero and Manfredi(7) contended that these peculiar bodies originated from the protoplasm of the cell; Retzius(8) affirmed that they were sui generis, that their size precluded the idea that they could be spores or parasites; Boeck(9) stated that the bodies arose from peculiar epidermal cells, a metamorphosis of the rete cells, and that according to his chemical tests these cells contained no fat and were not amyloid; Lukumsky(10) suggested that the bodies came from cells which had invaded the epidermis. In 1878 Vidal(11) advanced the idea that the molluscum bodies were the product of colloid degeneration.

Angelucci(12) in 1881 described a bacterium, *Bacterium lepogenum*, as the cause of molluscum contagiosum, while Neisser(13) the following year claimed that the specific cause of the disease was a gregarine. In 1886 this author again stated his belief in the parasitic origin of the disease and stated that the molluscum bodies were in reality coccidia and related to the Sporozoa. Graham(14) in 1892 described a micrococcus as the cause of the disease, while the following year Neisser again confirmed his coccidial theory of the origin of the tumors. In 1902 White and Robey(15) recapitulated the trend of thought on the nature and cause of this disease. They pointed out that there are those who believe in the sebaceous origin of the tumors and also those who contend that the tumors originate in the rete. Further, that some authors believed in the contagiousness of the disease, while others were equally certain that it was noncontagious; that one school of thought considered the molluscum bodies as evidence of epithelial degeneration, while others considered these peculiar bodies as parasites. These authors isolated a staphylococcus from molluscum tumors but did not consider it of any etiological significance. They concluded by stating that until that time they considered that

no one had isolated any parasitic body from the growth and that in their opinion the changes produced did not represent a colloid of hyaline degeneration but rather a metamorphosis of rete cells into keratin.

In 1909 Knowles(16) found what was apparently *Micrococcus salivarius* in a few cases of the disease but did not claim any etiological rôle for this organism. It was not until 1919 (nearly one hundred years after the disease was first described) that the epical work of Wile and Kingery(17) on the etiology of this disease appeared. According to these authors the disease is due to a filterable virus. Juliusberg(18) had suggested this possibility in 1905, but the evidence he presented did not substantiate his claims. In 1923 Clarke(19) described a parasite grown from molluscum lesions which he named *Plasmomyxa contagiosa* and which he believes to be the cause of this disease.

The virus of molluscum contagiosum.—Wile and Kingery not only demonstrated that the virus of molluscum contagiosum is filterable but also succeeded in producing experimentally in human beings typical tumors with the sterile filtrate of typical lesions. These authors further showed that the incubation period of the disease varies with the individual's predisposition or susceptibility; in one case it was found to be fourteen days while in another it was twenty-five days, and the microscopical diagnosis was made at the fifty-fifth day. These authors believe that the molluscum body develops late in the stage of evolution of the tumor and further that it represents a degenerative stage in this evolution.

Symptoms.—The tumors of molluscum contagiosum are quite solid and contain a cheesy material which can be pressed out of the growth through the central opening. In some cases the tumor mass extrudes this material spontaneously. Usually the lesions of molluscum are found on the face, around the eyelids, or in the neighborhood of the genitalia, or elsewhere on the body. They rarely occur on the soles of the feet or the palms of the hands. Usually there are only few lesions, a few or a dozen or more, though in some cases they may be very numerous. They are discrete but in some cases several tumors may coalesce. They may become inflamed, or suppurate. In some cases there may be severe itching but this is not common. The lesions may persist for several months or even years in rare cases. While the lesions are usually limited to the skin there have been cases reported in which lesions have occurred upon the tongue and other mucous membranes. The infection is

more frequent in children than in adults and may be transmitted by infected towels or gymnasium mats, etc. It is known to be transmitted directly from person to person in some instances.

Animals susceptible to the virus of molluscum contagiosum.—The disease is primarily a disease of man but a similar disease has been described in animals, especially in domestic fowls such as the pigeon. In a few cases the disease is known to have been transmitted from animals to human beings. Dogs and pigeons are both said to have transmitted the disease to man.

Immunity.—Little is known regarding immunity in this disease. Cases are known to have developed lesions of molluscum several times. That there is a natural immunity to the disease is indicated in the work of Wile and Kingery, who point out that there is a difference in the predisposition or susceptibility of the individual. From the experimental standpoint no conclusive data are available.

Pathology.—The tumors of molluscum contagiosum are essentially epithelial neoplasms. They are surrounded by a thin fibrous capsule and contain lobules of epithelial cells which are separated by thin septa and open upon the surface of the skin through a depressed central opening. It has become a generally accepted view that the tumors arise from the rete since the cells on the periphery of the lobules are of the type found in the basal layer of the rete. The central oval cells contain the so-called molluscum bodies which are regarded by Wile and Kingery as a degenerative stage in the evolution of the tumor. Lipschütz has called a minute organism found in the epithelial cells *Strongyloplasma hominis* which conforms to a general classification of peculiar bodies described by this author (see Introduction). According to modern textbook description three kinds of degenerated cells may be observed in these lesions. First there are large round bodies which contain an eccentrically placed nucleus; then there are oval cells surrounded by normal epithelium which contain a nucleus lying at one pole of the cell; and finally completely degenerated cells which are oval, structureless bodies. The exact nature of the degenerative process is still unknown.

Prevention.—The disease is comparatively trivial and is of no great importance either to the individual or to the community. While personal hygiene, discouragement of the use of the common towel, etc., are indicated, the chief effort should be directed to the proper treatment of the disease in order to eliminate carriers of the infection.

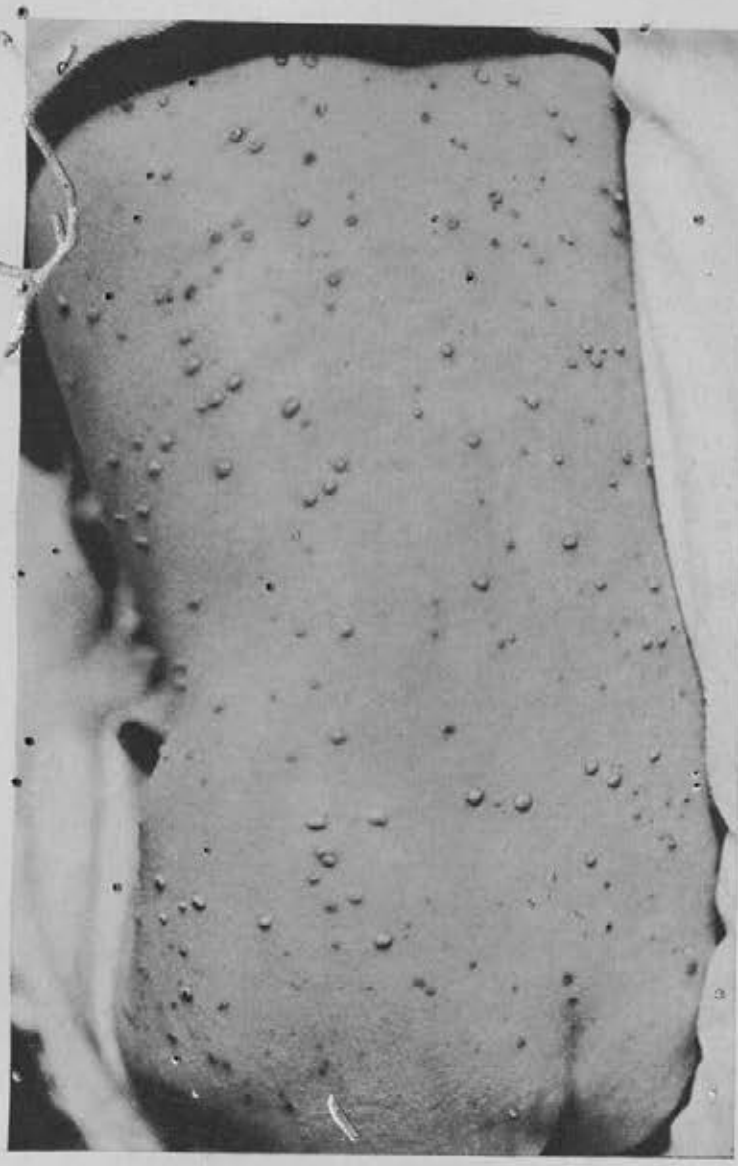

PLATE 6. VARICELLA.

PLATE 6. HERPES ZOSTER ARSENICALIS-LICHEN PLANUS ON FLEXOR SURFACE OF WRIST.

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Fig. 1. Measles. 2. Granulated conjunctivæ in trachoma. 3. Verrucæ digitatæ.

PLATE 7.

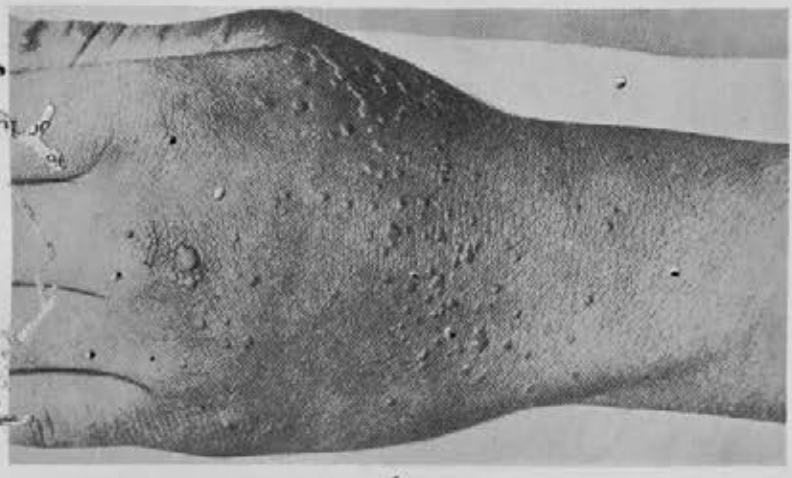

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Fig. 1. Verruca plan juvenilis. 2. Molluscum contagiosum.

PLATE 8.

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ILLUSTRATIONS

Plate 5

Varicella. (After Hartzell.)

Plate 6

Herpes zoster arsenicalis-lichen planus. Patient had a lichen planus shown on the flexor surface of the wrist, for which he had been taking Fowler's solution. (After Hartzell.)

Plate 7

Fig. 1. Measles. (From Hartzell; after Pfaundler and Schlossman.)
2. Granulated conjunctivæ in trachoma. (After May.)
3. Verrucæ digitatæ. (From Hartzell.)

Plate 8

Fig. 1. Verruca plana juvenilis. (After Ormsby.)
2. Molluscum contagiosum. (After Ormsby.)