FILTERABLE VIRUS AND RICKETTSIA DISEASES IN THE TROPICS.* III.

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In the two previous papers of this series on the filterable virus and Rickettsia diseases we have discussed several of this important group of affections chiefly from the standpoint of what is known concerning the etiology. An historical account of each disease together with data on the distribution, incubation period, symptoms, susceptible hosts, immunity, prevention and control have also been presented. It has been pointed out that while these diseases are, for the most part, not "peculiar" to the tropics, they are prevalent, in most instances, in warmer climates and as such should be considered part of the general field of tropical medicine. The present paper deals with other diseases of this group.

MEASLES
MORBILI; RUBEOLA

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 as yet definitely determined it is thought by some to be caused by a filterable virus and by other investigators to be of definite microbic 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 descriptiontion of this disease which eliminated much of the confusion between measles and smallpox which had existed before. Later measles was confused for a time with scarlet fever and even today there are

* This is the third of a series of articles on the filterable virus and Rickettsia diseases which are appearing in the Review. These articles are adapted from a monograph on this subject which is now in the press (Philippine Journal of Science).

cases of German measles which 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 most common 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 4,264 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 U. S. 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 as yet 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(5) were able to induce the disease in monkeys with material obtained from the naso-pharynx 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 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 have 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 anaerobically from material which 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), Denges(10), Ferry and Fisher(11), and Hibbard and Duval(12) have cultivated a non-hemolytic streptococcus from the blood of measles cases. Tunnicliff has also been able to cultivate another streptococcus from cases of German measles. In forty-two cases of measles out of fifty-two 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) from his experiments on rabbits and guinea pigs holds that the measles virus is filterable, and demonstrates gram-negative granular formations which measure from 0.4 to 0.6 microns in length and stain pink with Giemsa. He states that these forms are analogous to the forms 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 preeruptive stage of the disease, cultures were obtained in only four instances and these were regarded as contaminations.

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 which have been passed through a Berkefeld filter. This author also finds that the nasal secretions are 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 zero centigrade.

Other organisms have been described as the cause of this disease by Salimbeni and Kermorgant[17] (who have described the cultivation of a spirochete associated with a Gram-negative bacillus from measles cases) and by Sellards and Bigelow[18] who have reported the discovery of a small Gram-positive bacillus. Kusama[19] has described the passage through monkeys of a Gram-positive diphtheroid-like bacillus which 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 investigation 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. (1) The period of invasion; (2) the stage of eruption; and (3) the stage of desquamation.

The invasion of measles is gradual. The fever and the catarrhal symptoms increase gradually up 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) which 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 diarrhea.

The eruption or rash begins about the third to the fifth day of the disease. It begins 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 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 fever has reached normal the rash disappears.

When the rash disappears desquamation begins. The desquamation is fine and bran-like. It may last from five days to two weeks and is more marked in those cases where the eruption has been most 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, otitis; chronic conjunctivitis, enlargment of the lymph glands followed by tuberculous infection, nephritis, endocarditis and pericarditis; gastric disorders, erysipelas, furunculosis, impetigo, pemphigus and hemorrhages 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 leucocytósis and later there is a leucopenia.

ANIMALS SUSCEPTIBLE TO THE MEASLES VIRUS

Man is the natural host for this virus. Monkeys, rabbits and guinea pigs are said to be susceptible experimentally.

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. 5 cc. of this serum is 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 of filtered blood from measles cases (0.00125 cc.) 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.

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. Edema and congestion are also in evidence about the sweat and sebaceous glands, and the papillae.

The mucous membranes are the seat of a catarrhal inflammation and in some cases may be of a membranous character. Other anatomical changes depend upon various complications which may appear in a certain percentage 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 out 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 precruptive stage." Further investigations it is hoped will lead to a better knowledge of this disease upon which a practical and definitive method of protective immunization may be devised.

GERMAN MEASLES
(Rubella Rotheln)
(Liberty measles)

DEFINITION

German measles is a specific, infectious disease, of a mild nature which is characterized by a cutaneous rash which usually appears without prodromal symptoms. Its mortality is exceedingly low (if any) 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 rubeola it is believed that German measles probably existed in ancient times and was confused with scarlet fever and rubeola. Vaughan(²) 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 "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 relation-

ship 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 German 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 distinct disease from rubeola there is 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 filterable nature of the virus of rubeola it is thought that rubella may also 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 hemorrhagic and may give 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. We have recently seen a case in which the cervical adenitis has

persisted for nearly two years despite all treatment instituted to reduce it. Forcheimer([23]) has described an enanthem on 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 certain 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 and complications are rare and when present 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 host 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 or 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 same measures employed for measles should be instituted. Vaughan recommends the burning of all soiled

articles or disinfection of such articles with which the patient has come in contact.

VERRUCA

Wart; Verrue (French); Warze (German).

DEFINITION

Verrucae or warts represent an epidermic, papillary new growth of which there are three recognized types: 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 until 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([24]) developed warts under his thumb nail following the removal of warts from one of his patients. Lanz([25]) reported similar results in 1898. In 1889 Kuhneman([26]) cultivated a bacillus from warts and claimed to have reproduced typical lesions in laboratory animals. Variot([27]) four years later produced warts in one of his assistants following the inoculation of blood from small warts. During the next year Jadassohn([28]) made 74 inoculations with wart material from which he obtained 31 positive results and demonstrated that the lesions he produced were typical verrucae 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([29]) reported their experiments which proved conclusively that warts are due to a filterable virus.

THE VIRUS OF VERRUCA

In 1919 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 known microorganisms are known to give rise to disorders of keratinization. Examples of this fact such as the rôle of the gonococcus in the production of blenorrhagic keratoses, the tubercle bacillus in verruca necrogenica and the gonococcus in the production of condyloma acuminate are mentioned.

Their experiments consisted in 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 glycerine to be tested later. In the course of about four weeks small wart-like 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 histological 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 glycerine 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 vurrucae vulgaris."

In 1921 this work was further extended by Kingery([39]) 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.

At the present writing 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 the growth 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 immunity 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 enlarged and the intercellular spaces 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 if ever.

EPITHELIOMA (Molluscum) CONTAGIOSUM

(Molluscum contagiosum; Molluscum sabaceum; Molluscum epitheliale; Acne varioloformis.)

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 which at times become 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[31] 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[32] in 1817 while Patterson 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[34] as enlarged sebaceous glands, a view which was concurred in by Rokitansky[35] in 1856. Virchow[36] 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 fat-like globules although he thought they were probably the result of a degenerative process involving the epithelium. In later years Bizzozero and Manfredi(37) contended that these peculiar bodies originated from the protoplasm of the cell; Retzius(38) affirmed that they were sui generis, that their size precluded the idea that they could be spores or parasites; Boeck(39) contended that the bodies arose from peculiar epidermal cells, a metamorphosis of the rete cell, that according to his chemical tests these cells contained no fat and were not amyloid; Lukomsky(40) thought that the bodies came from cells which had invaded the epidermis. In 1878 Vidal(41) advanced the idea that the molluscum bodies were the product of colloid degeneration.

Angelucci(42) in 1881 described a bacterium (bacterium lepogenum) as the cause of molluscum contagiosum while Neisser (43) the following year claimed that the specific cause of the disease was a gregarin. In 1886 this author again stated his belief in the parasitic origin of the disease and stated that the molluscum bodies were in reality coccida and related to the sporozoa. Graham(44) in 1892 described a micrococcus as the cause of the disease while the following year Neisser again confirmed his coccidal theory as to the origin of the tumors. In 1902 White and Robey(45) 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 up 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 or hyaline degeneration but rather a metamorphosis of rete cells into keratin.

In 1909 Knowles(46) found what was apparently the 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 work

of Wile and Kingery([47]) on the etiology of this disease appeared. According to these authors the disease is due to a filterable virus. Juliusberg([48]) had suggested this possibility in 1905 but the evidence he presented did not substantiate his claims.

THE VIRUS OF MOLUSCUM CONTAGIOSUM

Wile and Kingery not only demonstrated that the virus of molluscum contagiosum is filterable but they 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 and in one case was found to be fourteen days while in another it was twenty-five days and the microscopical diagnosis was made at the 55th 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 a few lesions, two or three 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 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. We have recently seen a case of molluscum contagiosum in Porto Rico diagnosed histologically some time previously by Lambert. This case was a small child, the daughter of an undertaker, and it is possible that the child was infected by the father who became contaminated with the virus during the course of his work. This case is the only case known to have occurred in Porto Rico.

IMMUNITY IN MOLLUSCUM CONTAGIOSUM

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 tumor 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 containing the so-called molluscum bodies 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 *Strongloplasma hominis* which conforms to a general classification of peculiar bodies described by this author. According to modern text book 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 it is of no great importance either to the individual or to the community. While personal hygiene, discouragement in the use of the common towel, etc., are

indicated the chief effort should be directed in the proper treatment of the disease in order to eliminate carriers of the infection.

TRACHOMA

Granular conjunctivitis

DEFINITION

Trachoma is a specific, contagious disease which is characterized by inflammation and hypertrophy of the conjunctiva and the formation of granules, with subsequent cicatricial changes. It is usually of long duration, occurs at all ages, frequently complicated and may lead to partial or total blindness. It occurs in three forms: (1) the papillary form; (2) the granular form; and (3) 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 the province of Pangasinan. This is probably not true trachoma but extensive investigations into the true nature of this affection have not been made. A similar condition is said to be present in Porto Rico. Trachoma seems to have been introduced into the Netherlands about 1860 and is thought to have been brought 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. The disease, however, still persists in this part of the world. In China, Japan, Egypt, and Russia the disease still remains a great public-health problem.

THE VIRUS OF TRACHOMA

In 1907 Prowazek and Halberstaedter[49] described inclusion or trachoma bodies in the conjunctival epithelia of cases of trachoma. The exact nature of these bodies still 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. Scrappings from the conjunctivae injected into the eye of the orangoutang produced conjunctivitis associated with the appearance of similar inclusion bodies. These bodies were regarded by these authors as the cause of trachoma. Later these investigators found similar inclusions in cases of uncomplicated blenorrhea neonatorum and their specificity was questioned by contemporary investigators. Herzog([50]) suggested the theory that the gonococcus is transformed into small forms within the epithelial cells and that the so-called trachoma bodies are in reality changed gonococci. Williams([51]) regarded the inclusion bodies as degenerated forms of the Koch-Week's bacillus. Prowazek regarded the trachoma bodies as protozoan in nature while Noguchi([52]) 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 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 for trachoma, the possibility of a filterable virus etiology has been suggested for trachoma. According to Rosenau([53]) "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 experiment of Bertarelli and Cechetto([54]) and of Nicolle, Cuénod and Blaziot([55]).

Heymann([56]) after finding inclusions in cases of gonorrheal blenorrhea neonatorum suggested that the so-called inclusion bodies were in reality reaction products to the gonococcal virus. Simon([57]) states "A thorough study of this question then led to the interesting discovery of the existence of an inclusion blenorrhea 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 blenorrhea 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 blenorrhea 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 conclusion blenorrhea, on the other."

Linder[58] inoculated two baboons with pure inclusion blenorrheal material and obtained a clinical and histological picture which he states cannot be distinguished from trachoma. Wolfrum[59] inoculated similar material into a human being which was followed by 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 blenorrhea and trachoma are present in the same subject.

In 1927 Noguchi[50] 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, N. M. From this material be cultivated upon special media a Gram-negative bacillus which, when injected into monkeys, produced a granular conjunctivitis which "had an appearance strikingly like that of the human trachomatous conjunctivitis in the early stages of the disease". This organism was associated with four out of the five cases studied and the conjunctival disease produced is said by Noguchi to be transmissible in series while the identical microorganism is obtained regularly even in the second and third passage in monkeys. None of the other organisms isolated by Noguchi from his material were capable of inducing follicular lesions in monkeys. Material taken direct from patients and injected into monkeys did not produce lesions within four months' time.

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

INCUBATION PERIOD OF TRACHOMA

Trachoma is a chronic disease and 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 which 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. These are papillary, granular and mixed forms. Regardless of the form there

are certain subjective symptoms which may be present such as photophobia, lacrymation, itching and burning sensations, feeling of 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 drooping of the upper lid. There may be a mucopurulent discharge and the conjunctiva of the tarsus and fornix is reddened, thickened and uneven, on account of the hypertrophy and the occurrence of granules. (May). Trachoma progresses slowly up to a certain point, and then is followed by the cicatricial stage. The papillae 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 most common sequelae are (1) trichiasis and entropion; (2) ectropion; (3) symblepharon; (4) corneal opacities; (5) staphyloma of the cornea; and (6) 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 born out by the studies on the epidemiology of this disease. It may be assumed by the same taken 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 papillae

are larger, a granular appearance. This form occurs only upon the upper lid. The papillae 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, or large and warty, or flattened and succulent. (May). 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, ressembling Peyer's patches in the intestines. According to Noguchi the histological changes present in trachoma as they exist 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 epitheliod 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 other 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 sequelae. The secretion from the eyes of trachoma patients is regarded as infectious 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.

INCLUSION BLENNORRHEA
(Inclusion conjunctivitis)

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

Inflammations of the conjunctivae are of several varieties and generally are divided into the following types: (1) Catarrhal (acute, chronic, and follicular); (2) Purulent (ophthalmia neonatorum, and gonorrheal); (3) Membranous (non-diphtheritic or croupous, and diphtheritic); (4) Granular (trachoma); and (5) 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 (non-gonorrheal) secretion. In 1913 Cohen([61]) published a report 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([62]) published in 1911. The original cases studied by these authors included nine cases of trachoma representing four stages of the disease, six cases of blenorrhea neonatorum (non-gonorrhoica), and six cases of blennorrhoea 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 blennorrhoea neonatorum (non-gonorrhoica), and twenty cases of blennorrhoea gonorrhoica in young girls. Inclusion bodies were found in the six cases of blennorrhoea neonatorum non-gonorrhoica varying from four days to two weeks after birth. Cohen states "The clinical course of these cases resembles that of mild cases of blennorrhea 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 blennorrhoea 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 blennorrhoea which are neither of trachomatous or gonorrhoeal origin. These cases are not trachoma since they bear no clinical resemblance to trachoma and because there is spontaneous cure without sequelae. 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 blennorrhoea with the filterable virus diseases. At present there is no experimental evidence that it is caused by a filterable virus with the exception of the fact that no known etiological agent has been demonstrated.

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