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BDRL ltr, 13 SEP 1971

(1)

TRANSLATION NO. 197 (P)

DATE: July 1968

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DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland

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On the causes and incidence of glanders in humans, as well as on the measures for the prevention of contagion.

by W. von Brunn

Vierteljahrschrift f. ger. Med. u. off. San.-Wesen, 1919, Vol 58, No. 1, pp 134-161.

I. The causes of human glanders.

The cause of human glanders is the infection with the glanders bacillus. The pathogen may be transmitted to man from an animal ill with glanders, from another glanders-infected person or directly from a culture.

The animal which almost exclusively transmits glanders to humans is the horse. In the literature available to me I have not found a single mention according to which the infection of a human with glanders could be ascribed to any other animal. In addition to the horse, spontaneous illness occurred in: Donkeys, mules (1,2), goats (3,4), dogs (5,6,7) and cats (8) as well as the large predators, even camels (9); all mammals in our climes with the exception of cattle and the domestic rat (1) can be vaccinated.

The donkey is the animal (other than the field mouse) most susceptible to a glanders infection, its involvement is almost invariably acute and for this reason it was used for diagnostic immunization in countries where it is inexpensive; the mule's disease is sometimes acute, at times subacute. The carnivores often fall ill after consuming the meat of glanders-infected animals.

It is possible, however, that an infection of humans by all of the animals susceptible to glanders may occur.

Lorin (10) first proved in 1812 that a horse can transmit glanders to man, in 1821 Schilling (12) described the same most convincingly in Germany by way of one of his own cases. In England Ellioston (13) was the first to recognize the danger to humans from horses with glanders. Rayer (14) observed the illness of a human caused by a horse and was able to reinfect a horse with the pus from this patient.

The danger to man of being infected by equine glanders is not only great because the horse is the animal most susceptible to glanders with which man has the most frequent contact, but mainly because the horse in about 90% of all cases aquires chronic glanders (1) which for a long time may remain without significant externally visible symptoms. These masses of horses ill with occult glanders form a source of constant dissemination of the disease, only through occasional illness of a person is attention directed to a stable with apparently quite healthy horses, which despite complete ability to work are then found to be partly or entirely infected with glanders.

The proof of the fact that it is the horse which is primarily responsib

for human glanders will be established in part II; the patients almost without exception had dealt with glanders-infected horses.

That a person could be infected by another person has been proved by a few incidents, even if it belongs to the greatest of rarities.

Permit me to present 4 pertinent observations.

Bouley (15) infected himself from a sick person, was ill for years, but recovered. Jenckel (16) reports the case of an assistant at the pathological institute at Gottingen, who infected his finger in the summer of 1900 during the autopsy of an agriculturist who had died of glanders; he fell ill 7 days later with lymphangitis and phlegmons on the arm and recovered after incision and several months of sickness. I was privileged to observe this case at the time.

Zawadzki (17), Nencki and Pruszynski (18) report the case of a physician who infected himself during incision of an abscess on a colleague and died.

Finally, the case published by Auer (19) may be mentioned, in which the wife of a glanders-infected groom fell ill with perimetritis and peritonitis due to glanders; this case is almost everywhere cited as a possibility of a genital path of infection, whether justly so seems doubtful to me.

Finally, a "laboratory infection" may be involved, to which physicians and laboratory assistants are particularly exposed. Here, too, I should like to list the cases I found in the literature.

Hartge (20) reports that a Russian regimental veterinary in the bacteriological institute at Dorpat was working with glanders cultures, infected himself without a known portal of entry and died. The patient of Koch (21), a county veterinary, had infected himself with an agar culture during the breakage of a test tube and died; section revealed pulmonary glanders and Koch thinks that an inhaled infection may be involved here. The patients on whom MacCallum (22) (institute assistant) and Hoke (veterinarian) report, as well as Neklindoff (24) himself had infected a finger with the canula during the injection of a guinea pig; the case of Neklindoff was recorded by himself, he was cured after months on the sickbed and operative opening of the very numerous abscesses on the entire body. In addition, 2 cases of fatal glanders are known of employees of a Viennese bacteriological institute due to a court trial; a tube with glanders bacilli broke during centrifugation, both deceased had pulmonary glanders. Ris (25) treated such a patient, the incubation lasted 6 days, the case progressed chronically.

How does the glanders bacillus enter the human body? It is natural that every cleavage in continuity offers a welcome portal of entry, this is clearly evident from the cases described so far and especially from those to be referred to later.

The question whether this bacillus wanders through the intact skin and can thus infect the human body, is not clear and should be negated, if animal experiments are admitted as parallel.

Babes (26) and Cornil (27) report on quite isolated glanders infections among numerous guinea pigs into whose intact skin they had rubbed a glanders bacilli-containing salve, but the cases were still very few in number for an animal which otherwise is quite extraordinarily susceptible, the experiment was successful only if the glanders culture was quite fresh and particularly virulent. The spots at which the penetration of the skin seemed to have taken place always corresponded to the hair follicles. Nocard (28) repeated these tests with guinea pigs and donkeys, only twice with positive success; he stresses in particular that such positive infections are to be ascribed to subsequent lesions which the animals inflict at the site, which after all had become slightly irritated due to the rubbing.

Fritsche's (29) tests confirm only that the smallest separations in continuity already suffice to infect animals with glanders. When he shaved the abdominal wall of guinea pigs, rabbits or mice and rubbed glanders bacillus cultures into these shaved spots, all animals fell ill. Shaving without inflicting numerous tiny injuries must be considered impossible. Loffler (30) also is of the opinion that the glanders bacillus can only enter through wounds.

Generally this path of infection should be rejected for the genesis of human glanders, especially since in Europe thousands of glanders-infected horses are dissected annually and of the personnel engaged in this endeavor only an infinitesimal fraction gets the disease.

Babes (31) however, observed 2 human cases where such a modus of infection could be considered possible — once through the apparently intact skin of the lower leg.

A similar situation exists concerning the repeatedly mentioned possibility of infection by way of the intact conjunctival mucous membrane. Thus in experiments with guinea pigs the infection succeeded if the bacilli-containing fluid is allowed to remain in the conjunctival sac for 2-4 hours (Conte, 32); Dufour (33) was almost invariably able to effect an infection in the guinea pig in this manner, similarly Galtier (34), while Babes and Cherchez (35) only achieved positive success in exceptional cases by careful rubbing into the conjunctiva palpebrarum.

Grafe (36), Neisser (37), Gourfein (38), Boyd (39), Scheby-Busch (40), Nicolle and Dubois (41) and Strzemunsky (42) have published cases of human glanders in which the region of the conjunctival sac alone was involved, or the disease seemed to emanate from there. In these cases, too, we should consider how easily this mucous membrane is injured and that one is accustomed to rubbing it vigorously at the slightest irritation.

The patients were a groom, farmer, countryman, veterinarian, horse trainer and a 12 year old girl who had only one ulcer on the inner canthus, from which for a long time glanders bacilli could be grown (38). Another patient (42) only had a small nodule at the conjunctiva which was extirpated and contained glanders bacilli. In another case (41) only lymphadenitis developed from the primary infection, this was healed after incision; another patient (37) also recovered, although not prior to the healing of various metastatic foci; the other patients succumbed to the disease, no details are known to me concerning Graefe's case (36).

Without a doubt it would be interesting to know the role played by the nasal mucous membrane as infection portal, since the name (Rotz -- snot) points to the conspicuous symptom of the copious malodourous exudate from the nose of the horse and also since it may be assumed that the nasal mucous membrane in horses may easily become the portal of infection in view of the feeding from common cribs and drinking from common buckets. But this does not seem to be the case, the nasal mucous membrane almost never seems to be the portal of entry; Viborg (43) already observed that a horse cannot be infected by light rubbing of pus from glanders-infected horses into the nostrils; if an injury is inflicted, the infection takes place immediately. On the other hand, the nose seems to be a site of localization particularly preferred by glanders; Bollinger's (44) experimental results are especially valuable in this connection; he infected a rabbit at the ear, a goat intraperitoneally; both animals soon showed characteristic nasal glanders.

With respect to human glanders, the study of the cases reported in part II will show that the nose hardly deserves consideration as a portal of entry — although one could imagine that the grooms in infected stables may at times pick their nose with dirty fingers —; usually nasal involvement appears last, if at all.

The oral mucous membrane naturally may offer opportunities for the penetration of bacilli through small injuries, as during the mastication of hard plants, especially if the rough teeth of old horses scratch the membrane; experimental, careful application of bacilli on the oral mucous membrane of animals did not cause infection (Cadeac and Malet, 45). Nor did Decroix (46), who undertook an extremely uninviting test on himself by eating the raw meat of glanders-infected horses, suffer an infection of the oral mucous membrane or the alimentary canal. Staub (47) also reports on such an experiment on humans.

Here we come to the repeatedly mentioned question of infection by way of the intestinal tract. For man it has no significance in locales where no raw meat is consumed, or at least no raw horse meat. Still, this source of infection should be considered. About humans nothing is known in this connection other than the test by Decroix (46). Bonome (48 and 49), in his extremely conscientious and extensive examinations undertaken for the Italian government, came to the conclusion that this path of infection perhaps is the most frequent in horses; the infection as a rule does not adhere to the mucous membrane, an immediate transmigration into the chylous stream takes place, leading to an — only seemingly primary — pulmonary glanders infection. The fact that carnivores easily fall ill through feeding of glanders-infected horse meat has already been mentioned. Hutyra (50), like Bonome, is convinced of the same and bases his assertions on the results of numerous tests with horses, donkeys and guinea pigs. Contrary experience was gained by Cadeac (51) with 12 guinea pigs and Ravenna (53) with 6 out of 7 cats. Lothes (52) has determined by means of extensive tests with horses that the portal of entry was almost without exception the digestive tract, primarily the tonsils, from which the cervical lymphatic glands were attacked.

The examinations of Ravenna (53) as well as Kurloff and Wagner (54) may be of interest, of whom the first determined that the gastric juice of guinea pigs kills glanders bacilli in 6-7 hours, while the latter two authors proved

that they succumb to human gastric juice within ½ hour.

The extraordinarily frequent glanders infection of the horse's lungs has directed researchers to the question whether or not inhalation could lead to infection. We have already seen above (Bonome 48 and 49, Hutyra 50) that another explanation has much more probability. Cadeac and Malet (55) did not succeed in infecting animals in this manner; the same authors (56) have shown further that glanders bacilli cannot withstand the effects of air-drying, especially in daylight; Nocard and Leclainche (57) have confirmed this and have demonstrated on their part that only powder-dry, i.e. ineffectual material is able to penetrate into the respiratory passages during inhalation. Seven cases of human glanders were attributed to an inhaled infection. Lussana and Romaro (58) report on 2 patients, one with acute, one with chronic glanders, Forestier (59) on an acute, fatal case, Koch (21) believes the case described by him to be inhaled glanders, Pilcher (60) also ascribes a case of acute, fatal glanders to inhalation. The two fatal cases mentioned previously, due to breakage of a glanders culture tube during centrifugation, also belong to this category. It suggests itself that inhaled glanders may occur in factories where horse hair etc. is being processed, but such observations have been made only twice. Weichselbaum (61) has seen a rag collector fall ill with glanders, Remy (62) observed the disease in a matress maker; in both cases inhalation was blamed. Thus inhalation seems to play a meager role etiologically. In inhalation experiments an affection of the deeper nasal passages is achieved at the most (Hutyra, 50). The possibility of glanders infection through inhalation is also considered by Leisering (63), Gerlach (64), Pflug (65) and Rabe (66).

Genital contagion has already been mentioned in connection with Auer's (19) case. Tessier (67) and Cooper (68) also found it necessary to point to the possibility of a genital infection based on the observation that one of their female patients (the second recovered) had frank glanders with an ichorous, smelly fluor; nothing further is known hereon in the literature.

Very little can be said about the incidence of an intrauterine infection of the fetus by the mother. It is understood a priori that this may occur only when bacilli are present in the blood stream, i.e. in acute cases. Valentini (69) reports on such a case in a horse, it often appears in cats (Lissitzy, 8); Cadeac and Malet (70) have undertaken 13 tests with donkeys, dogs and guinea pigs, only twice successfully; Loffler (30) also considers this mode possible.

The material to be inoculated may be of various type, of course it must contain the glanders bacillus. It is found in the pus of the glanders ulcers, in the secretion of affected mucous membranes, in the feces in the case of intestinal glanders ulcers, in pulmonary glanders after swallowing of sputum (Cadeac and Malet, 71). The fact that urine is infectious was known to Viborg (43); Weichselbaum (72), Philippowicz (73), Kiemann (74) and Cagnetto (75) found glanders bacilli therin, in horses, donkeys, cats and humans. The bile may also harbor bacilli (Ferraresi and Guarnieri, 76). Whether milk may be infectious is doubtful. The two patients who, according to Loffler (30) fell ill after drinking the milk of a sick mare, may have been infected just as well in a different manner. The bacilli do not seem to be secreted through perspiration (Tromschtschinsky, 77).

The cadavers of humans and animals may of course be very infectious when they are recent, especially after an acute disease. In cases of chronic glanders the pathogen may be limited to a few specifically altered foci and may have lost its virulence even there.

The infective material may adhere to equipment etc., and be transferred from it, but the time involved must not be too long in view of the low resistance of the bacillus to aridity and warmth. Adler (78) reports on the fatal illness of a coach-driver who had slept beneath horse blankets and had drunk from a horse pail in a stable which doubtless contained horses with glanders. In Liegnitz a saddler's apprentice fell ill, seemingly infected during the repair of harness, and in Rotenburg a groom got glanders first on his feet, then on the whole body after wiping his sore feet with rags that evidently had been used previously on glanders-infected horses (Sanitation of the Prussian State, 79).

Dupuy and Thiry (80) saw a patient who had infected his middle finger during the cleaning of his diseased horse's crib.

Finally, Baracz (81) reports on a very peculiar case. A gentleman had had a tooth pulled with an iron instrument by a shoemaker 15 years ago, subsequently fell ill with suppuration at the jaw from the nose and ear with abscesses on the whole body, now here, now there. Glanders was positively diagnosed; 15½ years later the man died.

If I summarize the result of my discussion briefly at this point, the following may be said:

The cause of human glanders almost always is attributable to contagion from the horse. As a rule the glanders pathogen penetrates through a break in the continuity of the skin or the mucous membrane. Evidently a very intimate contact is necessary for infection, usually a direct injury.

II. Incidence of human glanders.

Although the number of publications on human glanders is quite large (the Index Catalogue (82) lists more than 100 up to the year 1901) it almost invariably involves data on one or two isolated cases; considering the interest with which every case is received we can conclude that in most European countries, perhaps with the exception of Russia, Spain, Portugal, Greece and Turkey, only a few such cases remain unpublicized and thus we can rightly designate the occurrence as rare.

Greater numbers of human glanders cases, which generally speaking offer a certain perspective on the incidence of the disease in certain localities, are available e.g. in Germany from the official yearly report (83): From 1886 to 1914, i.e. in 27 years, 40 cases of human glanders were reported in all of Germany. Pedkow (84) has seen 45 cases within 2 years (1892-93), and this exclusively in Berdian County, Iwer Province (Russia). Davalos (85) reports that until 1874 glanders was totally unknown in Cuba, then brought in from America; at once the disease appeared in humans, until 1888 18 cases were counted, until 1893 and additional 89, for a total of 107. In Budapest, von

Koranyi (86) has seen 5 cases; Meyer and Crohn (87) in New York have substantiat , in the years 1906 and 1907, 6 and 3 cases respectively, for a total of 9 human cases, compared to 530 and 470 cases of equine glanders, respectively. Bollinger (88) was able to collect 106 cases from the literature up to the year 1874.

I succeeded in finding a total of more than 242 individual cases in the literature; if we add the 107 Cuban cases (Davalos, 85), Pedkow's (84) 45, and the 9 cases of Meyer and Crohn (87), which surely are not included in the individual observations collected by me, we come to the result that according to the literature available to me a total of 403 cases of human glanders have been published to date. This number is worthless, of course, since one can be sure that in Russia, for instance, probably the most diseased country in Europe, every year a great number of cases must occur, if one single observer is able to count 45 cases within 2 years in a single county, and where according to recent official reports 25,000 horses fall ill with glanders every year (83).

A number of human glanders infections have also occurred during the present war, even a few laboratory infections, as I have gathered from a responsible source by personal communication.

If I briefly examine the 242 individual observations compiled by me in detail, which for the most part were available only in the form of a short reference, I find that in 180 cases it is specifically stressed that the disease was transmitted from the horse; in the remaining 62 cases wither contagion between humans or a laboratory infection is involved, or else no detailed data were contained in the reference; only in 4 cases a remark is found that the patient, to his knowledge, had never had any dealings with horses.

The occupations of the patients were as follows: Groom, horse trainer etc. 53 times, farmer, agriculturist, etc. 23, veterinarian 14, coach-driver 9, flayer 5, cavalryman 6, horse slaughterer and institute assistant 5 each, physician 5, blacksmith 2, trick rider, coach painter, book printer, laundress, rag collector, matress maker each once. Isolated cases of affection of the relatives of a farmer etc. are included in these categories. All in all the female sex was involved only 6 times. Bollinger's (88) statistics reflect a quite similar distribution according to occupations. The differentiation of cases according to acute and chronic character, so far as is evident from the case reports, shows that slightly more than half can be considered acute. The patients with acute glanders almost invariably die, of those with chronic glanders about 1/3 recover.

The breakdown by nationality is as follows: Germans 110, Russians 58, North Americans 23, Britons 36, Hungarians 5, Frenchmen 22, Austrians 14, Cubans 109, Italians 7, Belgians 2, Roumanians 7, Swiss 1 (here the figures from the larger statistics are included).

The publications concerning the 242 individual observations compiled by me are listed in the literature index under numbers 89 to 183.

The imparted figures on the geographic distribution of human glanders are, of course, unable to reflect the actual conditions. I shall therefore list a

short summary of the incidence of glanders in the horse, as reflected in the yearly report on the distribution of animal diseases (83). The following table, which I have prepared on the basis of figures contained in the yearly reports, will be best suited to that purpose.

Year	Germany	Prussia	Mecklenburg Schwerin	Mecklenburg Strelitz	Belgium	France
	Horses actually found to be glanders-infected during dissection				Reported cases	Horses destroyed due to glanders
1888	1044	844	-	7	182	622
1889	1184	983	7	13	158	826
1890	738	612	10	-	124	700
1891	885	763	27	-	212	820
1892	742	645	12	-	169	785
1893	505	440	1	-	107	?
1894	452	361	10	1	85	and Algiers 1103
1895	527	435	4	1	106	1312
1896	448	351	-	1	243	1690
1897	286	223	-	-	194	1349
1898	325	265	-	-	307(166 imported from England)	1175
1899	395	326	-	1	289(124 Engl.)	1354
1900	659	515	13	-	274(135 Engl.)	1484
1901	602	450	27	-	135(74 Engl.)	1092
1902	304	238	4	-	152(60 Engl.)	904 (without Alg.)
1903	269	195	1	-	160	697 (without Alg.)
1904	398	338	-	-	148	653 (without Alg.)
1905	443	398	7	-	138	923 (without Alg.)
	Figures for 1906, 1907 and 1908 were not available.					
1909	298	?	?	?	?	?
1910	332	?	?	?	?	?
1911	265	227	?	?	21	304
1912	331	308	3	?	42	160
1913	362	325	3	?	?	-
1914	256	228	2	?	?	-

In addition, in Mecklenburg-Schwerin: 1916: 35, 1917: 21, 1918: 41.

Year	Great Britain	Italy	Austria-Hungary		Roumania	Switzerland	Russia	
	Reported cases. (Scotland & Ireland very little. London alone over half)	Affected communities (from 1897 reported cases)	Reported cases (from 1893 affected localities)		Reported cases		Europe	Asia & Caucasus
			Austria	Hungary				
1888	1581	187	485		203	40	-	-
1889	2246	268	591		182	28	-	-
1890	1836	131	?		152	26	-	-
			Galicia and Bohemia always hevily diseased					
1891	?	108	?		150	40	-	-
1892	3001	130	?		149	21	-	-
			Localities					
1893	2130	131	15-30	up to 198	?	81	-	-
1894	1436	129	8-17	98-161	213	50	-	-
1895	1602	101	4-20	45-126	99	37	-	-
1896	1310	136	10-21	74-113	118	-	-	-
		Rept'd cases						
1897	1629	458	6-25	44-131	101	-	-	-
1898	1385	317	5-21	84-186	128	95	-	-
1899	1472	203	9-14	69-113	138	93	-	-
1900	1858	478	5-22	42- 89	140	61	-	-
1901	2332	471	5-18	27- 68	794	3[illegible]	-	-
1902	2083	493	4-15	32- 83	531	-	-	-
1903	2499	443	5-21	20-69	730	-	-	-
1904	2612	462	9-29	17-65	315	-	-	-
1905	2068	446	5-23	11-59	283	12	9151	
	Figures for 1906, 1907 and 1908 were not available.							
1909	?	?	?	?	?	?	?	?
1910	?	?	?	?	?	?	?	?
1911	491	332	5-13	27-77	233	25	18,845	3790
1912	315	314	4-16	17-78	353	4	23,477	4151
1913	-	-	-	-	-	-	-	-
1914	-	-	-	-	-	-	-	-

Of the countries bordering on Germany, Holland has reported 114 cases in 1896, even 128 in 1897, but only 18 to 38 cases in the years 1902 to 190[illegible]; the number of horses with glanders has been even lower in Denmark and for years has been limited to a few isolated cases. In 1905 the first Russian data appear, with 9151 reports; just how closely this figure corresponds to reality is hard to judge. Norway and Sweden as well as Luxemburg are almost free of glanders, in Iceland and Bornholm also, glanders is said to be unknown.

The fact that glanders comes to us primarily from Russia is supported by data on the incidence in the various parts of Germany, the eastern provinces are always more affected by a huge majority.

Cases of equine glanders are rare in the German army; other than in the years 1899 and 1895 in which 20 and 10 cases, respectively, were reported, no cases or only sporadic single cases have been observed.

The frequent occurrence in England proper, especially in the London area, is conspicuous.

A British staff veterinarian known to me obtained the following data for me in 1909:

Number of horses in London afflicted with glanders:

1904: 1869, 1905: 1387, 1906: 1382, 1907: 1365, 1908: 1704.

These figures represent 70%, 67%, 68⅔%, 71% of all cases of glanders in Great Britain. The total number of horses in London is estimated at 600,000. The extraordinarily strong concentration of horses in certain metropolitan districts favors contact infection.

In England the legal measures against glanders contagion are considered to be utterly inadequate, especially since insufficient attention is devoted to the stable-mates of glanders-infected horses.

It must be mentioned that no data or almost none were available concerning occurrence of glanders in Africa (other than Algiers), South America (Carini, 184, reports that glanders is rare in Brasil and has a mild course), Australia, as well as the whole of Asia (other than a short remark by Schlie (135) that glanders does occur in China, but not frequently). Of the European countries I lack data on Spain and Portugal, Greece and Turkey.

Concerning the ratio of animal glanders to that of humans, so much is evident from these figures — only those on Germany are usable — that in comparison to horses, the disease in man is infinitesimal, that only under especially unfavorable conditions can a transmission from horse to man take place.

III. Measures for the prevention of glanders transmission to man.

It is obvious that attempts at prevention of glanders transmission to humans must first of all be directed to the annihilation of the disease among horses. Legal regulations and other necessary measures are based initially on the diagnosis.

The diagnosis of equine glanders is not easy clinically, because, as mentioned before, the chronic form of disease is present in about 90%, in which the horses appear externally healthy and able to work.

The clinical symptoms of acute glanders are as follows: It may be either acute from the start or emerge from the chronic, latent form. In the first case, following an incubation period of 3-5 days, a temperature rise to 42°C appears suddenly, chills, strength subsides rapidly, pulse and respiration are strongly accelerated, inapnetence; strong injection of the mucous membranes. After 1-3 days local symptoms, ecchymosis on the nasal mucous membrane, in which yellow, round pustules of lentil to pea size appear, which burst and ulcerate. The secretion is serous, now purulent, mixed with blood. Everywhere in the skin there appear edematous, extensive, painful swellings, which reabsorb within 12-24 hours and leave abscesses; these burst, crater-like ulcers are formed; the lymphatic vessels become inflamed and are felt like thick worms. Here and there ulcers appear in the region of the lymphatic vessels which rapidly spread. Within 8-30 days the horse usually dies of lobar pneumonia. In the horse, acute glanders never turns into the chronic form.

Concerning chronic glanders nothing can be said about the incubation time, it may last many months and years. The skin alone becomes involved, especially where it is tender and the connective tissue is loose, at the inner surface of the thigh, the side of the neck, at the flanks. Coarse, round, painless nodules of hazelnut to egg-size develop, open and secrete an oily, sometimes sanguineous fluid. The ulcer looks like a crater, shows no tendency to heal, the edges are raised. At times the ulcers are situated singly, at times in groups, old and new next to each other, in close proximity are radiating scars. From the ulcers the lymphatic vessels proceed as worm-like (later quite painless) cords far into the surrounding area and may remain unchanged for a very long time. Chronic glanders may attack only the nose, even half the nose, ulcers develop, extravasation, swelling of the lymphatic glands (esophageal glands). These ulcers may heal with a radiating scar. The secretion may be viscous at first, dries into scabs, later becomes purulent with bloody streaks. In chronic laryngotracheal glanders only the larynx and the trachea are involved; chronic pulmonary glanders may exist for years, may even heal, without showing any manifestations. As said before, the horses may remain well and able to work for a long time.

If there are clinical suspicions of glanders and test material can be obtained, the bacteriological test is indicated. Often it may help to extirpate one or several enlarged lymphatic glands and examine them bacteriologically (Bollinger 186, Rieck 187, Rudenko 188 and 189). In addition, the mallein test and serologic methods will be used extensively (cf. later).

The glanders bacillus 1882, first described by Loffler and Schutz (190), has the length of 1/3 to 2/3 of the diameter of a red blood corpuscle, the width is about 1/5 to 1/8 of the length; at times it may grow very long. Often

it looks finely granulated, but these are not spores, only plasma aggregations. It does not form spores, has no inherent motility, but strong molecular movement. It cannot be stained easily, it is recommended to use a concentrated alccholic methyl-blue solution with 0.01-percentual potash lye as mordant in a ratio of 3:1 and to let the cover glass with the material float thereon for 5 minutes. Then it is placed for 1 second in 1% acetic acid with a little tropeolin 00 — the color should be as yellow as Rhine wine — and washed out. The bacilli are stained blue, the cell nuclei less, the plasma not at all.

If a culture is started, the medium should be maintained at body temperature. The growth on potato is characteristic; here a culture with an amber-yellow, transparent appearance develops, which then takes on a reddish hue, similar to cuprous oxide. The bacillus also grows in broth and on agar, and on other media; glycerol is added to advantage and a weakly acid reaction is noted in the medium.

Invariably, if the material is available, the animal test is immediately resorted to, Straus' (191) reaction is carried out, the material is injected into the abdominal cavity of male guinea pigs, where after 2-3 days an inflammation of the testicular cortex develops. The pus forming here should always be examined bacteriologically. If there is cause to suspect other pathogens in the material, subcutaneous injection of cats, guinea pigs or even dogs and donkeys is indicated.

If no material is available for bacteriological tests, other diagnostic methods may be utilized, I am thinking here primarily of the mallein test. Mallein was first produced in 1891 simultaneously and independently by the Russian veterinarians Helmann (192) and Kalning (193). There are several methods of manufacture, of which the one used by the Roux Institute is probably the most common (194). Cultures of the glanders bacillus in glycerol broth are used, filtered after sterilization.

Mallein is used diagnostically in different ways, by way of subcutaneous injection, instillation in the conjunctival sac or cutaneous inoculation. Instillation in the conjunctival sac is the customary method today. This convenient method allows the examination of large stocks of horses in a short time; adequate training and experience of the examiner is important, but then unequivocal results may be obtained with a probability of 90%. The degree of subsequently appearing redness and tumescence of the conjunctiva, the time of its appearance and the duration of its persistence allow a completely unequivocal evaluation. While this method has been in use for a long time abroad — Nocard (195) has tirelessly championed mallein — German workers had declined its use until a few years ago. Now, during the war, the method has proved itself splendidly in mass examinations; of publications I shall mention only the paper by Miessner (196) and refer to the extensive literature thereon in the collective works. The injection method, so customary earlier, is not recommended, since it influences the evaluation of serologic test results. These, however, yield results of unsurpassed certainty, I am speaking of agglutination, complement deflection, conglutination and hemagglutination; they are best conducted simultaneously side by side, and conclusions are drawn from comparison (Miessner 197, Pfeiler and Weber 198, Pfeifer 199, Kliem 200 and numerous other authors). The precipitation method cannot be considered reliable as yet,

in spite of numerous examinations (Pfeiler 201). Anaphylaxis is not suited to the diagnosis of glanders (Kiessner, 202).

If glanders is to be controlled effectively in Germany, its entrance from abroad, especially from the East, must be prevented; newly imported horses must remain in strict isolation until serologic tests are concluded, each horse must have its own drinking and eating vessel. The existing holdings must be examined more or less frequently, depending on the circumstances; when horses of fighting or marching units are involved, one is limited to the mallein eye test, in all other cases the absolutely certain serologic method must be utilized (Kiessner, 203).

As yet we are unable to kill the active glanders bacillus in the body of the sick individual, unless we simultaneously sacrifice the afflicted creature itself. We know of no certain drug against glanders, even if a favorable effect of mallein has not been completely denied (Popescu 204 and Romano 205), it has never been proved; Nocard (57), on the other hand, the most zealous supporter of the diagnostic importance of mallein, speaks against its therapeutic effect. Nikolski (206) recommends vaccination, Salvarsan has not proved itself.

Therefore each glanders-infected horse must be killed and rendered harmless, just as the horses which have died of glanders; it is best to burn the cadaver; if this is not feasible, it must be buried with adequate disinfective agents and care must be taken not to till the spot for a long time — at least one year. All animals in contact with the afflicted horse must be tested and suspected individuals must be isolated until the diagnosis is ascertained, or, under certain conditions, killed like glanders-infected animals. Everything in contact with the animal, the stable with all equipment, straw, harness and wagon must be disinfected. Things of low value are burnt. Whatever can withstand flowing steam is exposed to it for sufficient periods of time. The fact that the glanders bacillus is very vulnerable to heat has been reported by Saunier (207) who used boiling water; glanders cultures die within 2 minutes in boiling water (Cadeac and Malet, 208); that the bacilli die in 10 minutes at 55°C was already known to Abildgaard (cited by Viborg 43); Loffler (30) has confirmed this. It also has little resistance to sunlight (Altuchoff 209, Nowikoff 210, Sirena and Aless 211); drying as such does not work as fast. The cold, on the other hand, affects the flanders bacillus little or not at all; Altuchoff (209) proved that exposure to winter's cold of -17° to -19°C for up to 12 days does not harm the bacillus. Wladimiroff (1) has kept emulsions of glanders bacilli for 5-80 minutes in liquid air at -185° to -190°C, without being able to kill them.

The resistance of the bacilli increases quite considerably if, surrounded by mucus or other material, they are exposed to disinfectants. Unfortunately our convenient and effective gaseous disinfectants fail completely, especially formaldehyde, since the buildings involved here, particularly stables, can never be closed air-tightly and since the gaseous antiseptics have no depth penetration; also, these buildings commonly do not offer favorable conditions for the entry of air and light. We must resort mainly to liquid disinfectants. Of those, the otherwise excellent sublimate is also unsuited, it is too expensive, corrodes metals and does not penetrate deeply enough. Milk of lime and chloride of lime, the first in a ratio of 1:400, the latter 1:800, kill

the glanders bacillus positively within 1 minute, that is a lower concentration by far than is commonly used — 1:2-4 or 5:100 — (Schroder 212). Suitable are also preparations first recommended by Kencki, made of pine tar (e.g. 100 parts water, 10 parts pine tar, and 2 parts caustic potash), tested by Lowikoff (210) and extraordinarily cheap in some areas. The susceptibility of the glanders bacillus therefore is quite considerable; we can only preserve its virulence by intravenous infection of rabbits (Wladimiroff 2). The proper training of persons engaged in the care of horses will always be an important link in the chain of our measures; persons with wounds or cracked hands in particular should not groom glanders-suspected horses; after injuries, thorough cleansing, tincture of iodine and washing with oil of turpentine have proved helpful in the glanders hospitals of the Army, as reported to me by a pertinent source.

The tests of Levy, Blumenthal and Marxer (213) have taken on great significance; they succeeded in immunizing numerous horses by means of killed glanders bacilli; the protection has been absolute for over 4 years, although these horses lived constantly among large stocks of infected horses in Russia. All later researchers, I mention only Machatin and Bautz (214) as well as Koneff (215), have had the same assured success. Pfeiler (216) has even strongly suggested that now, during the war, our entire stock of horses be immunized systematically. Magnin (217) who deals with the history of glanders in the French Army, in 1909 valued the diagnostic methods so highly that he dared to pronounce glanders as the most easily cured equine disease, based on this circumstance.

The legal foundation for the control of animal glanders is laid by the Federal Law pertaining to animal diseases, of 26 June 1909.

Paragraph 1 stresses expressly that all useful domestic animals, including dogs, cats, and fowl, are subject to this law. Designated as suspect are not only those animals which show symptoms that point to the possibility of an outbreak of a contagious disease (animals suspected of disease), but also those animals which, while they do not show symptoms, are presumed to have absorbed the infectious agent (animals suspected of contagion); this exact precision of the concept of suspicion doubtless is quite important. Par 2 assigns the responsibility for the regulation and enforcement of control measures to the Land governments; in every case recourse to complaint against the orders of the police is permitted. According to par. 3 the military authorities are allowed to formulate their own measures for the determination and suppression of epizootics among their own cattle and horse stocks, this also applies to the Imperial Health Office and similar institutes, national stud farms, veterinary schools, and other specifically designated establishments, but all of these authorities and establishments are duty-bound to inform the police of suspicions and outbreaks of an epizootic, its course and termination. According to par. 4 the Federal Chancellor supervises the execution of this law, if an epizootic in threatening dimensions appears at the borders of the nation he causes the threatened States to take joint defensive measures, especially if the disease touches on several States within the Federation. Par. 6-8 deal with the defense against entry from foreign countries. They forbid not only the import of sick and suspected animals and their products, the cadavers and parts of such animals, but also all items which might be carriers of the infective agent,

generally or for certain border regions, or allow this only under certain control measures. All such regulations are to be publicized immediately and submitted to the Federal Chancellor. Par 9-73 deal with the control of epizootics in the interior. Par. 9 regulates the compulsory report of diseased and suspected animals, it covers all persons who might have some knowledge of a suspected illness among them, and simultaneously orders a provisional isolation of those animals. According to par. 10 glanders belongs to these diseases. Par. 11 to 16 deal with the diagnosis of epizootics by the official veterinary and the measures he is to take in urgent cases; the owner of the livestock is allowed to consult another approved veterinary; in doubtful cases the authorities are responsible for a ruling. All livestock markets, yards and slaughter houses must be supervised by official veterinarians, this supervision may be ordered for all livestock that changes its location.

Par. 17-30 contain protective measures against dangerous diseases, first more severe controls of the animals, cleaning and disinfecting rules and more severe ordinances for all markets and industries through which the infective material might spread. In addition, the following may be ordered: Quarantine, guarding or observation by the police of sick, suspected or susceptible animals, certain limitations on the transport of diseased or suspected animals, their cadavers and all items capable of spreading the contagion, limitations on the transport and utilization of animals susceptible to the disease, limitations on the trading of such animals; prohibition of common pastures and the use of certain grasslands, wells, watering places and horse ponds, and transportation with diseased or suspected animals on the public or common streets and passages; closure of stables, farms, communities, of pastures or village fields or parts thereof, single streets or parts of a community; inoculation and veterinary treatment; slaughter of diseased or suspected animals, as far as required by law; the slaughter of animals found at forbidden locations; removal of all material suspected of contagion; cleaning and disinfection; prohibition or limitation of all opportunities for the contact of large numbers of livestock; testing of the pertinent stocks of a certain region; public announcement of the outbreak and termination of an epizootic. In particular, it is ordered, concerning glanders, that all diseased animals are to be killed immediately (par. 42); suspected animals are isolated and observed by the police, with necessary limitations on transportation and utilization or closure; the slaughtering of sick or suspected animals is forbidden (par. 43). According to par. 44, destruction must be ordered if the official veterinary declares the outbreak of the disease as probable or if other legal measures would not enforce effective protection; it may further be ordered if the speedy suppression of the disease is in the public interest. Par. 45 specifies that the cadavers of glanders-infected animals must be immediately and harmlessly removed and must be stored carefully in the meantime, they may not be skinned. According to par. 46 the police are required to make a written report to the military authorities and the pertinent federal stud farm on every serious epizootic outbreak and suspicion as well as on the course and termination of the disease. Par. 62 to 65 establish for livestock and slaughter yards, inclusive of public slaughter houses, that at the outbreak or suspicion of a disease the involved animals are to be taken into police custody immediately; prohibition of driving-off may be imposed (par. 64). Par. 66 to 73 deal with the question of compensation. This must be paid for animals destroyed on police orders or which owing to police orders died of the disease which prompted the police order; for animals felled by glanders or pleuropneumonia after a prompt report had been made, if

the preliminary conditions existed under which a legal order destruction is required; in addition, for animals presumed to have died du- an inoculation ordered by the police (par. 66). The regulations governing the raising of funds for compensations and its determination are left to the states; however, compensation must be paid in full if the animals were not infected with the disease on which their destruction was based. According to par. 68, compensation is based on the animal's mean value; with respect to glanders-infected animals, this amounts to 3/4 of their value; the insurance liability payable from private agreements is calculated to 3/4 of this sum. Par. 70 specifies that no compensation will be paid for animals belonging to the nation, the states or the provincial stud farms, or for animals which, in the case of glanders, are imported at least 90 days prior to the confirmation of the epizootic, if no proof is submitted that they were infected after importation into the country. According to par. 72 the claim will not be honored if the owner or otherwise responsible person intentionally or negligently fails to make a report or delays it for more than 24 hours; he must remain unpunished, however, if another responsible person makes the report in time; in addition, no compensation is due if the owner has obtained one of the animals in an infected condition and he was cognizant of its disease; also, if the owner or his representative did not follow the regulations or trespassed them, or if he allowed the animals to run around in forbidden locations, resulting in their death. The established punishments are prison terms up to 2 years or fines of 15 to 3,000 Marks in the following cases: 1. Intentional contrary action to the regulations contained in par. 6,32-34,36-38,41,43 subpar. 2, 45,51 subpar. 2, 56,57,61 subpar. 3,4; intentional failure to report, or delay by more than 24 hours, if another responsible person has not made the report in time, also: Failure to adequately quarantine the sick and suspected animals; this punishment pertains to persons who intentionally counteract the orders of the competent authority or the official veterinary based on par. 7 subpar. 1, 11 subpar. 1,2,19-23,26-28,35,39,40,43 subpar. 1,47, 48,58,59,61 subpar.2,63,64 and 78; who intentionally removes signs officially affixed to houses, etc., for the purpose of preventing contagion, finally: who intentionally excavates cadavers or parts of cadavers which were buried on police orders, or whoever illegally gives such to others. In addition to the prison term, a fine of up to 1,500 Marks may be levied. Negligence in these cases is punishable by fines of 10-150 Marks (par. 75). Confinement may also be imposed. In addition to the punishment, confiscation of all illegally imported animals, cadavers etc. may be ordered, regardless of whether or not they belong to the convicted person. This also happens if no particular person can be held responsible (par. 77). Par. 78-92 contain terminal rules.

The Prussian export law of the Federal epizootic law of 26 June 1909, dating from 25 July 1911.

The first part, par. 1-4, deals with methods and authorities; it may be mentioned that in case of complaint against orders pursuant to the legal regulations, no recourse to civil suits against the government is permitted, only complaints to the local police and, as a last resort, to the Secretary are allowed. Par. 5-8 deal with the question of compensation; par. 9 specifies that total compensation is to be granted by the provincial agricultural organizations in case of animals killed on police orders owing to rabies, glanders or pleuropneumonia, and for animals who have died of these diseases, also: for animals that died of these diseases subsequent to police orders, also: for

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animals that died of glanders or pleuropneumonia after a timely report, if the preliminary conditions existed under which police-ordered destruction is mandatory. The cost of compensation, administration, etc. may levied within the agricultural organizations from the involved owners. Par. 24-28 deal with expenses. Expenses arising from the proclamation, administration and supervision of measures and the conduct of police-ordered veterinary procedures are generally borne by the state, those arising from the execution of the regulations are borne by the communities, independent rural areas, and the owners and managers.

Thus the control of animal glanders is regulated by law; on the other hand, human glanders is not included among the diseases covered by the Federal law of 30 June 1900 concerning the control of diseases dangerous to the commonwealth.

The prevention of transmission of glanders from person to person also starts with the diagnosis. The clinical course is as follows:

Acute glanders in man, following incubation of 2-3 days, commonly begins either with local symptoms, especially after injuries to the extremities, or with generalized symptoms, fever may be absent at first, chills are rare; soon irregular elevations, pains in the extremities, muscles, joints; at times one assumes typhus or influenza; then small ecchymoses, in which pustules erupt, abscesses in joints and muscles. The nose, if it becomes involved at all, usually is attacked only shortly before death, as evidenced very clearly by the cases studied by me. Duration 6 to 32 days at the most, before death.

Chronic human glanders is similar to that of the horse, here too "worm-like" manifestations appear under the skin, but lesions resembling erysipelas also are encountered at times, also swelling of joints. Nasal symptoms may be absent, temperature may be normal at times; the duration may range from months to years. In acute cases the diagnosis may soon be made from the examination of pustule contents, otherwise by agglutination. In humans, isolation is one of the most important measures, in addition to the most thorough disinfection of all items which the patient touches. Therapeutically, in addition to the necessary general and surgical measures, X-ray treatment (Zieler 155) is applicable. The nursing staff and in operations, the assistants must be made aware of the great danger of infection through the smallest wound.

The legal measures for the control of human glanders are left to the states.

For Prussia, the law concerning the control of contagious diseases of 28 August 1905 is applicable.

It makes every case of sickness or death due to glanders reportable, and this within 24 hours after detection. The report is made to the police. Change in apartments or communities by the sick person must also be reported after 24 hours at the latest (par. 1). Responsibility for the report rests, in sequence, with the physician, the head of the family, every person otherwise active in the treatment and care of the patient, the owner in whose apartment the disease or death occurred, and finally the coroner (par.2). In public

hospitals or similar establishments the director or his deputy are responsible for the report (par.3). According to par.4 the report may be made verbally or in writing or by mail. The stipulations of par. 6-10 of the Federal law, concerning the control of diseases endangering the commonwealth of 30 July 1900, are also applicable to sickness, suspicion and death of glanders, according to par. 6. Certain limitations exist, however, regarding the visit by the official physician, but he may ask the police to order an autopsy is glanders is suspected. Par. 12 specifies that in cases of glanders, certain measures may be taken under the purview of par. 12,14,19 and 21 of the above Federal law, for the observation of sick persons, for their isolation, disinfection and with respect to corpses. The local police are the competent authority, the county commissioner may in some cases assume their responsibilities. The state police do not become involved thereby. Legal recourse against police orders is administered according to the State administrative law, but a complaint does not have a staying effect, (par.12). Par. 14-24 deal with claims for indemnity for items lost to the owner owing to police measures (destruction, disinfection). Compensation is paid only upon application. Par. 25-33 regulate the question of funds. Par. 34-36 deal with punishment under this law; prison sentences are given to persons who use or release infected items or items suspected of contagion prior to official disinfection, thus opening up paths for the spread of the infectious disease; fines up to 150 Marks or confinement are imposed on persons who fail to report, bars entrance to the official physician or intentionally gives false information to the official physician or the authorities; the same punishment is meted out to persons who counteract officially imposed measures. Par. 37 and 38 contain terminal rules. Of the executory regulations to this law it should be mentioned that post-mortem examinations may be ordered in communities that do not have such an ordinance, if cases of glanders have occurred. Annexes 1-4 include report and diagnostic forms, annex 5 contains detailed instructions for disinfection.

Mecklenburg-Schwerin is covered by a regulation concerning the reporting of epidemic diseases, contained in the Government Bulletin for the Great-Dukedom Mecklenburg-Schwerin of 30 October 1893, No. 18.

I. According to par. 4, chapter III of the medical regulations, the physician must immediately report to the mayor and the competent county physician, the outbreak of an epidemic disease.

In the future, in addition to diseases seldom met in this country .... glanders.....is to be included among the epidemic diseases within the meaning of this law.

II. The report does not become compulsory solely after the disease has developed into an epidemic, but physicians must without delay report all cases of the epidemic diseases listed under I. treated by them...

Action to be taken after a report is listed in the "New medical regulations of 15 February 1830." Par. 4 specifies that the county medical officer, after receiving the report, is to betake himself to the location at once, and together with the authorities (and a surgeon or veterinary) should undertake the necessary examinations of the nature and cause and danger of dissemination, and should "issue tentative orders for the prevention and suppression

of the disease." Execution of the measures is the responsibility of the local authorities. In all cases the county medical officer must make a report to the government.

The Braunschweig law of 29 June 1904 progresses even further and specifies compulsory reporting in cases of suspected glanders, otherwise it is practically identical with the Prussian.

Mecklenburg-Strelitz has also issued new regulations — High Order of 27 April 1905 (official bulletin, p. 111); here the report is the duty of the physician, as in Mecklenburg-Schwerin.

Human glanders cases are not subject to compulsory reporting in Sachsen, Wurttemberg, Baden, Sachsen-Coburg-Gotha, Schwarzburg-Sonderhausen, Reuss a.L., Elsas-Lothringen; conditionally reportable in Hessen and Sachsen-Weimar.

The measures for the prevention of glanders transmission to humans must first prevent the dissemination of the disease among horses; by clinical observation, but principally by means of the mallein eye test and serologic methods, diagnosis has experienced such excellent simplification that regulated utilization of these methods must result in the reduction of dissemination to a minimum. By way of proper training and corresponding caution on the part of persons coming in contact with glanders, human infections may be avoided almost completely. The strictest isolation of all diseased animals and persons and immediate destruction of all glanders-infected animals are of fundamental importance. The excellent results of immunization against glande represent a mighty step forward in the control of this disease.