

The 1944 Epizootic of Horsesickness in the Middle East.

By R. A. ALEXANDER, Section of Protozoology and Virus Diseases,
Onderstepoort.

Horsesickness is usually regarded as being confined in its distribution to the continent of Africa, including the island of Zanzibar, with the northern limit approximately at latitude 5° N except in the east, where it extends into Abyssinia, Eritrea and the Anglo-Egyptian Sudan. Outside Africa cases have been reported from Yemen along the southern Red Sea Coast of Arabia, but these have been regarded as local enzootics as a result of infection spreading either from Eritrea, or the neighbouring territory, under peculiarly favourable conditions and the outbreaks appear to have remained strictly isolated. Within the recognized area of distribution the annual incidence of enzootics or widespread epizootics are to be anticipated, apparently dependent upon the favourability of climatic and possibly other conditions to the insect vector. The reservoir of infection for this vector, which is believed to be one or more species of *Culicoides* (Du Toit 1944) is not known but several cases are on record of the prompt appearance of horsesickness amongst horses and mules imported into an area from which all equines had certainly been excluded for many years.

In Egypt a few cases were reported by Williams in a frontier squadron in 1913 but the first authentic record of an extensive epizootic of the disease, known locally as "nigma", was that described by Carpano (1931) following the diagnosis of a case at Komombo on July 30th, 1928. On that occasion infection spread slowly northwards and eventually reached Giurga. It died out during the ensuing cold winter months, the last case reported being on the 27th December, 1928. During that epizootic, in the three provinces of Aswan, Qena and Giurga, 26.3 per cent. of the horses out of a total population of 2782 contracted the disease and of these 88.7 per cent. died; of 631 mules 10.6 per cent. were diagnosed as being infected, with a mortality of 69.7 per cent.; data on the morbidity and mortality in donkeys could not be collected owing to the difficulty experienced in making definite diagnoses, but it was established that some deaths among donkeys did occur. According to all available information no further cases of horsesickness occurred for 15 years until a case was diagnosed on 9th July, 1943, again at Komombo. Again the infection travelled slowly northwards down the valley of the Nile until it reached Cairo on 8th February, 1944, but it soon died out and the last case reported was on the 10th February of that year. A striking feature of the epizootic was that although the number of equines in the affected areas was fairly large, all presumably

fully susceptible, the mortality was exceedingly low; out of 11,959 horses, 3,602 mules and 294,011 donkeys 727 (6.67 per cent.) horses, 75 (2.82 per cent.) mules and 801 (0.27 per cent.) donkeys were recorded as clinically affected. The respective mortality rate cannot be given because one of the measures of control that was enforced by the Egyptian veterinary authorities was not merely the immediate destruction of all clinical cases, but the immediate destruction of all equines in infected localities that showed a rise in temperature above 103° F together with a blood smear found negative on microscopic examination.

After February, 1944, it appeared as if the experience of 1928 was to be repeated and that infection would disappear during the winter. However, on 30th April, 1944, the disease reappeared at Aswan immediately north of Komombo and in spite of the reinstitution of vigorous control measures it continued its progress northwards until it had reached the outskirts of Cairo on 25th July. The following week cases were reported from Suez, Ismailia and the delta area north of Cairo. It will be seen, therefore, that in approximately 3 months the disease spread from the Sudan—Egyptian inter-territorial boundary down the entire length of the valley of the Nile to the sea and to adjacent populated areas. It is not possible to give any accurate figures of the morbidity and mortality because in the early stages of the epizootic even suspected cases were immediately destroyed, and, from the middle of June, an extensive immunization campaign was brought into operation. However, a report from Dr. Salem Bey, Director of Veterinary Services (personal communication) shows that in the 6 provinces of lower Egypt (Sharkia, Beheira, Dakahlia, Kalioubia, Gharbia and Menoufia) a total of 1,618 cases were diagnosed in a horse and mule population of 28,269. The relative numbers of horses and mules were practically equal but almost exactly 3 times as many cases were diagnosed in horses as in mules (1033 and 344 respectively). Amongst donkeys 241 cases were definitely recognized but no figures are available of the total number in the area.

In reviewing the history of horsesickness in Palestine the Chief Veterinary Officer (personal communication) reported that a Turkish translation of Friedberger and Frohner's Veterinary Pathology by Dr. Minas Bey, dated 1896, states that African horsesickness was prevalent in 1876 in Egypt and Syria, which then included Palestine, affecting horses, mules and donkeys. Kamel Eff. Taher, chief veterinary officer to the Emir Abdallah of Transjordan reported that he was informed by His Highness that outbreaks periodically occurred at intervals of 3 to 4 years in the Hedjaz at the end of the last and the beginning of the present century, being most serious in the coastal area. Bedouin horseowners knew the disease well and used to move their animals inland into the desert on its appearance, in order to escape infection. Ahmed Hamdi Bey, acting Director of Veterinary Services, Syria, advised that during the autumn of 1912 there was a serious outbreak which caused very high mortality in Turkish cavalry horses in the region of Aleppo, following the introduction of horses from the Hedjaz into the affected units. The disease was not diagnosed as horsesickness at the time but, after seeing several cases in Palestine, Hamdi Bey was convinced that the 1912 outbreak was horsesickness. The available information therefore indicates that although horsesickness has been the cause of heavy mortality from time to time as local enzootics outside the usually recognised area of distribution, it has never assumed

the epizootic proportions of the 1943 and 1944 outbreaks in Egypt. As soon as the Palestine authorities learned that the disease had reached the Nile delta area in 1944, and threatened the Suez Canal zone, they placed a complete embargo upon the movement of all equines from Egypt into Palestine. This embargo became effective from 5th July, yet, in spite of all precautions, the presence of horsesickness in Palestine was established at the end of August. It was first diagnosed with certainty in an Army unit at Sarafand in the Ramle Sub-district of Lydda on 30th August, immediately following which a report was received that a case of undiagnosed disease had occurred 6 days previously in a mule at Gaza, the symptoms of which greatly resembled horsesickness. In spite of the enforcement of vigorous control measures, which are discussed below, in an endeavour to limit the spread of infection both amongst the animals in infected localities, and from infected to new localities, the disease spread rapidly. In this respect it differed markedly from the experience in Egypt. The general direction of spread was northwards, almost all the earlier cases and the great majority of the total number of cases occurring in the low lying coastal plain where the warm humid climate, and the prevalence of vegetation such as orange groves, provided environmental conditions presumably favourable to the insect vector. It is worthy of note that in the dry desert climate of Beersheba, where there is virtually no open water and very little vegetation, no spread occurred within localities into which infection was introduced. For example, 12 cases of horsesickness were diagnosed in 12 different places, 7 of which in animals definitely established as having been illicitly moved from the heavily infected areas of Lydda and Gaza districts, and yet there was no local dissemination. Similarly the spread in the hilly areas of the Nablus and Jerusalem districts was considerably less than on the coast. Of 58 cases in 17 localities in the Nablus sub-district, 30 occurred in two places in the Jordan Valley. During the epizootic 656 horses, 166 mules and 14 donkeys died, while 443 horses, 227 mules and 8 donkeys were diagnosed as suffering from horsesickness and destroyed in 353 localities, which term covers Jewish settlements, Arab villages, and Bedouin encampments. According to the 1943 census the equine population of Palestine is given as 19,000 horses, 9,900 mules and 107,700 donkeys. Therefore horsesickness was responsible for the loss of 5.1 per cent. of the horses, 3.9 per cent. of the mules and only a negligible percentage of donkeys, but it is quite certain that the mortality would have been considerably higher if the immunization campaign had not been prosecuted with great vigour.

In addition to Palestine, cases of horsesickness were reported from Syria, Lebanon, and Transjordan, but no details are available of the mortality or any peculiarities of the epizootic. It is of interest to note that in Cyprus no report of horsesickness has been received up to the present, but bluetongue of sheep is prevalent and a strain of virulent virus was forwarded to Onderstepoort for identification.

NATURE OF THE DISEASE AND DIAGNOSIS.

1. *Egypt.*

There is no doubt whatever as to the correctness of the diagnosis. The symptomatology and pathology differed in no respect from that seen in South Africa as a result of infection with a comparatively mild or avirulent strain of virus, except that there was evidence to show that the period of incubation was particularly long, a fact which was confirmed

subsequently experimentally. Blood samples were collected from typical cases in horses, mules and donkeys in oxalate, carbol, glycerine as anti-coagulant and preservative, and were brought to Onderstepoort for investigation. One sample from a donkey was injected intravenously (dose 5 c.c.) into a known susceptible horse (384), and a horse (382) previously immunized against virus strain 0. The immune horse showed no reaction. In the susceptible horse a febrile reaction commenced after an incubation period of 16 days. The temperature reaction was mild, fluctuating between 104.5° and 105° for 5 days, when it returned to normal by crisis. Additional symptoms were slight icterus, marked oedema of the supraorbital fossae (dikkop), cardiac weakness as shown by a rapid thready pulse, cardiac dyspnoea, and slight pulmonary congestion and oedema. The horse made an uninterrupted recovery without any treatment other than good nursing and complete immobilization. Although the diagnosis of dikkop horsesickness was never in doubt, the prognosis at no stage was grave. Blood collected at the height of the febrile reaction was subinoculated into 2 donkeys whose sera at the time of injection were devoid of any specific neutralizing antibodies, and 2 horses previously immunized with routine neurotropic vaccine; no febrile or clinical reaction was produced. The infectivity of the blood used was controlled by neurotropic fixation in mice.

It is of interest to note that the horse which recovered from injection with the Egyptian donkey virus, was subsequently found to be solidly immune to a virulent strain of virus obtained from a horse in Palestine.

One strain of virus from each of the three species of equines in Egypt was fixed neurotropically in mice by serial intracerebral passage without difficulty. After fixation, *in vitro* serum virus neutralization tests were carried out against various antisera. Specific virus neutralization was demonstrated, and the results, shown in Table 1, are discussed below.

2. Palestine.

By the time the disease had spread to Palestine, the local veterinarians had obtained a sound knowledge of the clinical picture from study in Egypt. Consequently, the first cases were diagnosed promptly, and the Chief Veterinary Officer kindly forwarded several blood samples to Onderstepoort for differential investigation. It was possible to carry out a detailed examination of the virus contained in only one of these samples, referred to as virus 7577, collected from a horse on 11th September, 1944. In addition to being fixed neurotropically in mice for specific serum virus neutralization tests, (cf. *intra*), 5 c.c. of the blood was injected intravenously into a known susceptible horse (168) on 26th September, 1944. After an incubation period of only 5 days a marked febrile reaction commenced (maximum temperature 106.8° F.). Clinical symptoms of both dikkop and dunkop horsesickness developed, and the animal collapsed and died suddenly on the 4th day of fever. Blood collected on the day before death was subinoculated into 2 horses that had previously been immunized with routine vaccine and horse 384 that had recovered from infection with the Egyptian donkey strain of virus (cf. *supra*). No reaction was produced in either animal.

SERUM VIRUS NEUTRALIZATION TESTS.

The technique for the intracerebral protection test in mice has been described previously (Alexander 1935). For the tests, homologous antisera to the 7 virus strains incorporated in the routine vaccine being issued

at the time, were selected. In addition, two sera from horses immunized as a routine test for the efficacy of the vaccine were included. These sera are stored in desiccated form after dehydration by sublimation from the frozen state in vacuo over anhydrous calcium sulphate. Time did not permit the attenuation of the Palestine virus, by serial passage through mice, to a degree sufficient to ensure the survival of a fully susceptible horse, so the homologous antiserum was obtained from a donkey which failed to show any reaction to the virus, but nevertheless developed high titre antibodies. Antisera against the Egyptian virus were obtained from the horse which reacted to, and recovered from, infection with that virus, and from two donkeys which also failed to react. The latter sera had not been desiccated but were stored in tightly stoppered bottles in a refrigerator at 5° C. with "Merthiolate*" in a concentration of 1:10,000 as a preservative. Numerous trials (as yet unpublished) have shown that there is no decrease in specific antibody content of sera either after desiccation, or on storage either in liquid or dried form. The two virus strains designated L and 114 respectively had been isolated from horses in the field, whose immunity had been broken down on exposure to natural infection. These horses had been immunized with a vaccine containing a different combination of virus strains to that in use at present. These two strains were included in the tests merely for comparative purposes, to illustrate the marked difference between two antigenically dissimilar viruses. Unfortunately no antiserum against virus 114 was available to complete the series.

For the actual neutralization tests, the virus antigens were used after approximately 70 brain to brain passages through mice, and each emulsion was diluted in 10 per cent normal horse serum saline so that the LD 50 was 2.0. Each test was carried out in triplicate by two highly skilled technical assistants working independently, and with no knowledge of either the serum or antigen being studied at the time. The results agreed within very close limits, but, if any discrepancy did occur, suitable repetitions were made. The end points were calculated from the mean of not less than 6 titrations. The results are given in tabular form in Table 1.

Result.

Neutralization by the type anti-sera shows that there is a marked similarity if not complete identity between the Egyptian strains of virus no matter whether the origin was a horse, a mule, or a donkey. It is believed that the slight differences in titre, shown by the same sera against either of the three antigens, are within the limits of experimental error and of no significance. When the Palestine virus is taken into consideration as well, it is seen that all four virus strains from the Middle East show practically complete reciprocal crossneutralization to relatively high titre. This would indicate that the four strains are identical, particularly when it is noticed that, in addition, the titres against the two aberrant strains L and 114 are almost identical. The similarity is indeed very close but attention must be directed to two differences. Firstly anti-Vryheid serum shows well-marked neutralization of Palestine virus, but no trace of neutralization of either of the Egyptian strains. Secondly other minor differences in neutralizing titres are apparent e.g. OD and Vaalhartz antisera. Whether any significance can be attached to these discrepancies is a point on which adequate data have not been collected to warrant the expression of an opinion, but it is known that slight differences in antigenic structure may result from prolonged serial passage.

* "Merthiolate" = Sodium ethyl mercuri thiosalicylate, Eli Lilly & Co.

TABLE 1.

Serum Virus Neutralization of Virus Strains by type Anti Sera.

| Type. | IMMUNE SERA. | | | NEUROTROPIC VIRUS STRAINS. | | | |
|--------------------|----------------------|------------------|-----------------|----------------------------|------------|------|------|
| | Homologous Titre. | EGYPT. Horse. | EGYPT. Mule. | EGYPT. Donkey. | PALESTINE. | L. | 114. |
| 449..... | 2.25 | 0.18 | tr. | 0.34 | 0 | 0 | 0 |
| 1180..... | 1.20 | 0.43 | 0.30 | tr. | 0 | 0 | 0 |
| Vryheid..... | 2.08 | 0 | 0 | 0 | 1.08 | 0 | 0 |
| OD..... | 1.59 | 1.26 | 1.29 | 1.34 | 2.04 | 0 | 1.88 |
| KA..... | 1.88 | 0.30 | 0.61 | 0.48 | 0.60 | 1.51 | 0 |
| O..... | 1.69 | 0.30 | 0.65 | 0.30 | 1.15 | 0 | 2.18 |
| Vaalharz..... | 1.58 | 1.91 | 1.64 | 1.98 | 0.81 | .51 | 2.42 |
| Vaccine..... | — | 1.60 | 1.45 | 1.51 | 1.00 | .30 | 1.81 |
| Vaccine..... | — | 1.27 | 1.28 | 1.51 | 1.64 | .68 | 1.75 |
| Egypt, Donkey.... | — | 2.35 | 2.30 | 2.32 | 2.51 | .18 | 1.78 |
| Egypt, Donkey*.... | — | 2.22 | 2.26 | 2.00 | 2.23 | 0 | 1.70 |
| Egypt, Donkey*.... | — | 2.44 | 2.34 | 2.51 | 2.56 | tr. | 1.70 |
| Palestine*..... | — | 2.71 | 2.71 | 2.81 | 2.48 | 0 | 1.75 |
| L..... | 2.48 | 1.42 | 1.46 | 1.47 | 1.06 | 2.48 | 0 |

NOTE.—Titres calculated according to method of Reed and Muench and expressed as the logarithm of the 50 percent. end point.

tr. = survival of less than 50 percent of the mice with the highest concentration of antiserum.

* Sera obtained from donkeys. All other sera from horses.

Finally it is shown that the serum of horses, immunized with the routine vaccine, neutralizes all the virus strains. This would be anticipated from the finding that two of the constituent virus strains neutralize to titres nearly as high as the homologous Middle East antisera, and two other strains, KA and O, show low titre but nevertheless appreciable neutralization. Therefore the results of the *in vivo* immunity test, referred to previously, are confirmed by the *in vitro* tests which, in turn, are reflected in the results of the immunization campaign to be discussed later.

Comment.

The results of the laboratory experiments show that there is only one major difference between the Egyptian and the Palestine viruses, if it is accepted that the slight differences in antigenic structure are not significant. The Egyptian virus was found to be comparatively avirulent and characterized by an exceedingly long incubation period, whereas the Palestine virus, in these respects, is similar to many strains which have been isolated and studied in South Africa. Although the laboratory tests, of necessity, were carried out on a limited scale, these characteristics were confirmed by personal observations in Egypt, and by the comprehensive reports from the Palestine veterinary authorities. Incidentally, it should be borne in mind that the isolation of a virus from Egypt, with a similar abnormally prolonged incubation period, has been reported previously by Carpano (1931). This difference between the two viruses becomes of great interest when considering the progress of the epizootic, and the source of infection of the two countries. It is thought that a more detailed knowledge of the factors governing transmission by the insect vector might clarify the position.

One further point merits comment, and that is the incidence of and mortality from horsesickness in donkeys to which reference has been made. Since the disease is practically, if not completely, unknown in donkeys in Southern and Central Africa this might at first sight be taken to constitute a major difference in the virus. The fact that the three donkeys included in the transmission experiments failed to show any detectable reaction indicates that this is not the case. It is quite impossible to give any accurate estimate of the percentage of donkeys which were affected in the Middle East, since large numbers certainly show only a febrile reaction without the development of any of the pathognomonic clinical symptoms e.g. edema of the supraorbital fossae (dikkop), on which to base a diagnosis, and hence escape detection. However, a large number of donkeys showed all the classical symptoms but, even in these, mortality would probably not be higher than 4 per cent. On post mortem examination the lesions are identical but of lesser degree than those shown by horses and mules. In Egypt the common donkey is *Equus asinus* var *nubiensis* whereas, the Southern African variety is *somaliensis*. The Egyptian animal is, on the whole, somewhat smaller and lighter, the most common colour is light grey (white) the hairy coat is somewhat finer in texture and shorter, the head is relatively smaller and the ears shorter, he appears to be more intelligent and alert, and his gait is considerably faster. It is interesting that these easily apparent differences between the two varieties occur in animals with a marked difference in susceptibility to a virus, and that variety *somaliensis* normally is confined to those areas in which the disease persists in epizootic form..

THE ORIGIN AND SPREAD OF INFECTION.

A. Egypt.

When due consideration is given to all the known facts there appears to be no doubt that the 1944 outbreak was not a recrudescence of the infection introduced in 1943 but was a new introduction from the South.

The customs barrier between the Anglo-Egyptian Sudan and Egypt is situated at Wadi Halfa. To avoid this barrier, there is at least some traffic along the various caravan routes through the desert to the east and west by smugglers engaged in illicit trade. These caravan routes converge on Komombo or places in the immediate vicinity, where the first cases were diagnosed in each successive outbreak. In the absence of any definite proof, it is reasonable to assume that one or more animals in the early stages of the long incubation period of the disease crossed the inter-territorial border legitimately, or more probably, illegitimately and reached Komombo before the development of any clinical symptoms, thus setting up a local reservoir of infection for the insect vector to initiate the epizootic. Once the focus of infection was established, further progress of the disease is more easily explained by the movement of infected animals than by immigration of the vector. Infection spread slowly northwards in a series of bounds, in some cases the new focus being as much as 50 miles from the nearest infection to the south. The long period of incubation, and the movement of animals during that period, adequately explain those bounds. If the midge *Culicoides* is the chief natural transmitter, and it is present in myriads throughout the valley of the Nile, the progress of infection would be continuous, and not discontinuous, were migration of the vector, with its small range of flight, the factor of importance. It is not denied that

mechanical transport of infected vectors may have contributed to the spread, but it is believed that this method would have been of importance only in the vicinity of the large towns or settlements and not in the rural areas.

A peculiar feature of the epizootic was that infection continued to spread northwards without leaving smouldering foci of infection in the rear. Thus, the experience of two previous outbreaks, that infection continued to spread northwards until it died out with the advent of winter was repeated within the epizootic itself, in that no permanent reservoir of infection was left behind. In Southern Africa the disease annually makes its appearance simultaneously at widely scattered points over vast tracts of country, and there is no evidence of spread, other than purely local dissemination, from one such point to another. This appears to indicate that there exists a virus reservoir other than the equine, and that transmission from this reservoir to the susceptible equine takes place only when a particular set of circumstances become favourable, usually in the late summer months. Unfortunately, nothing is known of these circumstances except that, at that time, *Culicoides* trapped in the field are capable of transmitting infection (Du Toit 1945). Obviously, this natural reservoir is not present in Egypt, and it cannot be replaced by either the horse, the mule, or the donkey, so that each recrudescence of infection should be regarded as a reinfection from outside.

B. Palestine.

How horsesickness was introduced into Palestine has not been ascertained, and must always remain a matter of conjecture. When the first cases were diagnosed at the end of August, the nearest focus of infection was the Canal zone of Egypt, from which it was separated by the Sinai desert, and a complete embargo on the importation of all equines had been in operation for more than 6 weeks. It is possible that an infected carrier donkey may have been smuggled through with a camel caravan and that the introduction was completely on a par with that into Egypt. On the other hand it must be noted that the first cases occurred in the neighbourhood of the trans-desert motor road and the air-port. This suggests the possibility of mechanical transport of infected vectors by motor vehicles, though it is not known whether the delicate *Culicoides* would survive a journey over the desert by that means. Transport by motor is not considered likely, in view of the fact that horsesickness was not diagnosed in Southern Lebanon until nearly three months after the first Palestine cases, and during that period, motor vehicles were constantly entering the Lebanon after passing through the heavily infected coastal plain of Palestine. Under those conditions, one would have expected the transfer to the Lebanon to have taken place much more rapidly if mechanical transport by road was the important factor. Transport of vectors by air must not be lost sight of. Prior to the Palestine outbreak, the whole of the delta area of the Nile was infected. There was considerable movement of aircraft between the two countries, and, for military reasons, a great deal of the flying was done at night. The interiors of the fully illuminated aeroplanes at the time of loading would attract the heliotropically positive *Culicoides* and, in the absence of any antimosquito precautions, suitable enclosed planes would serve as ideal vehicles for the transport of infected midges to the airport less than an hour's flying time away. This appears to be the most probable explanation, but does not take into account the fact that the Palestine virus was found to differ markedly in respect of virulence and

period of incubation from that isolated in the vicinity of Cairo. Consequently, the very definite possibility exists that infected vectors were carried by air, not from Egypt, but in aeroplanes that touched down at night at some aerodrome where horsesickness is enzootic but outside the area where rigorous anti-malaria and anti-yellow fever precautions are enforced. It is on this assumption that the opinion was expressed that there existed a far greater danger of introducing horsesickness into India by air from the Middle East than from South Africa in the convoys by sea. This is an aspect which should receive attention with the increase in flying services after the war.

GENERAL MEASURES OF CONTROL.

Egypt.

As soon as it was apparent that the disease was spreading rapidly the Egyptian veterinary authorities enforced protective measures with commendable rapidity. A complete embargo was placed on the importation of all equines, goats, and dogs from the Sudan. In unaffected areas north of the outbreak, a system of thorough veterinary inspection particularly of transport animals was instituted. At selected strategic points for instance, at every bridge leading into Cairo, at suitable crossroads or at bridges over the canals, veterinary guards were stationed for the purpose of inspecting all equines passing in either direction. Simultaneously with the clinical inspection, the animals were sprayed with Flemmings solution (lime sulphur); it is doubtful whether this had the desired insecticidal effect but supplies of pyrethrum, D.D.T. or gammexane were not available. As soon as a case of horsesickness was diagnosed, the affected animal was destroyed with compensation to the owner, the carcass buried or disposed of under veterinary supervision, and a general stand-still order proclaimed. The history of the affected animal was traced and all in-contacts examined daily. Any animal showing an elevation of temperature was isolated and a blood smear taken for microscopical examination. If the blood smear was found to be negative for any of the protozoan diseases, the case was regarded as one of horsesickness and the animal immediately destroyed. Meanwhile every effort was made, with the limited amount of vaccine available, to immunize all in-contacts, preference naturally being given to horses and mules, and all animals so treated were branded for future identification. The standstill order was enforced for 6 weeks after the last diagnosed case, but this period was subsequently reduced to 21 days. As stated previously these measures failed to check the spread of infection, but nevertheless it is certain that they contributed very materially to limiting infection, and to the record of an extraordinarily low morbidity rate. Factors which contributed to the failure were:—

- (1) The great difficulty in making an early diagnosis of the first cases in a new focus of infection, particularly in donkeys, and the fact that the blood of equines is infective before detectable clinical symptoms appear.
- (2) Inadequately experienced veterinary staff and accessory personnel for inspection duties.
- (3) Lack of adequate supplies of a reliable insecticide.
- (4) Completely inadequate supplies of vaccine, to eliminate all susceptible hosts by mass immunization of a broad band at a selected strategic point north of the advancing infection.

- (5) The fact that economic considerations made it quite impossible to stop the transport of food, and particularly vegetables, at night when the pack and draught animals became exposed to the greatest danger of infection.
- (6) Lack of co-operation on the part of the peasants, as shown by the failure to report fresh cases, and the illicit movement of animals from infected to non-infected areas. For instance 26 horses, 10 mules, 978 donkeys and 8 dogs were seized by the Police in the act of contravening the regulations, and many carcasses of affected and unreported animals were found in the Nile, in the canals, and secreted in the fields and byways.

The veterinary authorities were harshly criticized in many quarters for the severity of the protective measures enforced, for the financial burden imposed upon the Ministry in paying compensation for approximately 1,000 animals destroyed, and for the interference with the normal flow of trade. It is certain, however, that the rate of advance of infection was slowed down very materially pending the importation of large supplies of vaccine.

Palestine.

The control measures enforced in Palestine were practically the same as those in Egypt; in addition, the sale of equines in animal markets was prohibited, in an attempt to limit movement. In a Gazette Extraordinary, dated the 15th September, the prohibition of movement rules were applied to the whole of the country, and the confinement of all horses, mules, and donkeys in their stables from sunset to sunrise was made compulsory. The imposition of these regulations caused great inconvenience and even hardship but with the co-operation of the fellahin the measures proved highly effective, pending the arrival of adequate supplies of vaccine.

Besides the compulsory stabling from sunset to sunrise, owners were strongly advised to keep alight in their stables smoke fires burning damp litter, dung etc., to drive off the insect vector, and where possible, to rub the animals down with an insect repellent. It is difficult to say to what extent these measures contributed to limiting infection, but several instances of their effectiveness, when carried out properly, may be quoted.

- (1) Probably the most heavily infected district was Lydda, where 730 cases of horsesickness occurred. Numerous deaths occurred daily, even amongst army remounts which were maintained in open smoked lines, yet amongst 100 Police horses in eight stables, only one death occurred. These horses never left the stables, which were heavily smoked day and night, until they had been immunized.
- (2) About 70 horses and mules were housed in a public stable in Jaffa-Tel Aviv, in an area where 160 animals were lost. This stable was divided into two sections by a partition and smoking of both was carefully carried out. In the one section, stabling 30 animals, no deaths occurred. In the other section 15 out of 40 died. It was subsequently learned that in spite of the regulation prohibiting movement before sunrise, the 40 animals left the stable daily before dawn on ice distributing rounds.

- (3) None of about 70 animals belonging to the Oil Companies, who ensured that the regulations were carried out conscientiously, became infected.

It must be conceded, therefore, that the precautionary measures, advised, and as far as possible enforced, by a staff augmented by the temporary employment of 2 veterinarians and 70 stock inspectors did limit infection to some extent, but it will be seen that immunization must be regarded as the only really effective control measure.

IMMUNIZATION.

No facilities were available for the preparation of horsesickness vaccine in either Egypt or Palestine on a scale sufficiently large to be of any material value, so that the whole of the Middle East was dependent upon supplies which could be imported by air from Onderstepoort and Kabete. Kabete supplied 4,600 doses to Palestine and an unknown, but larger quantity, to Egypt. Onderstepoort supplied 209,100 doses to the Egyptian Government, and 86,000 doses to other authorities including the British army, Palestine, Syria, Lebanon and Transjordan. By *in vitro* and *in vivo* laboratory tests it has been shown that this vaccine produces a satisfactory immunity against four strains of virus, isolated from different sources, that were used for the test. It remains to review the actual results which were obtained in the field.

Egypt.

Full details are not available of all the animals on which vaccine was used in Egypt, but the Director of Veterinary Services kindly supplied the following information for the period May 1st to September 30th, 1944, for the 6 provinces of Lower Egypt. Out of a total of 13,942 horses and mules treated, 209 subsequently died. Of these, 53 died within 3 days of injection, 148 died between the 4th and 10th day, 100 died between the 11th and 20th day, and 8 died thereafter. When the long incubation period of the virus is taken into consideration it is seen that at least 201 of the animals (53+148) must have been in an advanced stage of the disease when the vaccine was administered, and that no protection could have been expected. Thereafter the death rate decreased rapidly but it required about 3 weeks for an adequate immunity to develop.

Palestine.

More complete figures were obtained from Palestine. These figures are of particular value and interest because, unlike Egypt, there is no history of any recent epizootic of horsesickness, and consequently the equine population could be regarded as being completely susceptible. A total of 29,558 animals belonging to civilian owners was immunized, but the number of army animals has not been disclosed. Amongst the immunized animals 530 deaths occurred. The number of days after injection on which these deaths occurred are of sufficient importance to merit presentation in tabular form (see Table 2).

On the day that general immunization was carried out at any centre, all animals that were obviously suffering from horsesickness were destroyed, and actually 45 such animals were presented for treatment. These animals would undoubtedly have died within 24 or 48 hours. This accounts for

HORSESICKNESS IN THE MIDDLE EAST, 1944.

TABLE 2.
Post immunization mortality in 530 horses and mules throughout Palestine.

| District. | DEATHS. | | | | | | | | | | | | | | | | | | | | | | | Total Deaths. |
|----------------|--------------------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|-------|---------------|
| | DAYS AFTER IMMUNIZATION. | | | | | | | | | | | | | | | | | | | | | | | |
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23-33 | |
| Lydla..... | 1 | 5 | 14 | 22 | 6 | 11 | 16 | 7 | 20 | 12 | 6 | 18 | 1 | 10 | 5 | — | — | 4 | 2 | 2 | 3 | 5 | 1 | 171 |
| Haifa..... | — | 3 | 3 | 7 | 5 | 5 | 5 | 4 | 5 | 1 | 8 | 2 | 5 | 6 | 1 | 5 | — | 3 | 1 | — | — | — | 1 | 70 |
| Nablus..... | — | 8 | 6 | 1 | 10 | 2 | 5 | 7 | 5 | 5 | 10 | 5 | 4 | 11 | 5 | 1 | 3 | 2 | 1 | 3 | — | 1 | 1 | 96 |
| Gaza..... | — | 1 | 2 | — | 3 | 3 | 5 | — | 1 | — | 4 | — | 2 | 1 | 1 | — | 1 | — | — | — | — | — | 1 | 25 |
| Tiberias..... | 1 | — | — | 1 | 3 | 2 | 3 | 3 | 4 | 1 | 2 | 2 | 1 | — | 1 | 1 | 2 | — | — | — | — | 1 | 4 | 32 |
| Acre..... | — | 1 | — | — | — | 2 | — | — | 1 | — | 1 | 2 | — | — | 1 | — | — | — | — | — | 1 | — | 1 | 10 |
| Jerusalem..... | — | 2 | — | — | 1 | — | 1 | 1 | 1 | — | — | — | 1 | — | — | 1 | — | — | — | — | — | — | — | 8 |
| Army..... | 7 | 9 | 9 | 8 | 8 | 11 | 9 | 12 | 13 | 7 | 7 | 2 | 6 | 2 | 4 | 2 | 1 | 1 | — | — | — | — | — | 118 |
| TOTAL..... | 9 | 29 | 34 | 39 | 36 | 36 | 44 | 34 | 50 | 26 | 38 | 31 | 20 | 30 | 18 | 10 | 7 | 10 | 4 | 5 | 4 | 7 | 9 | 530 |

the decrease in the number of deaths on the 1st and 2nd day after immunization, and should not be construed as indicating something in the nature of an interference phenomenon such as has been reported between the neurotropic and pantropic viruses of yellow fever (Findlay and MacCallum 1937), a phenomenon which has been demonstrated also in horsesickness (unpublished experiments by author). After the injection of vaccine, deaths continued at a fairly constant rate until there was a sharp drop after the 14th or 15th day. Actually, of the 530 animals which died, 86 per cent. of deaths occurred 14 days or less after immunization, and 95 per cent. within 18 days. This indicates again that it takes approximately 21 days for an immunity, sufficient to protect against virulent natural infection, to develop, an observation which contrasts in striking manner with the slow appearance of antibodies in the serum of immunized horses, where the peak is reached only after a period of approximately 90 days. (Alexander 1935). There appears to be one possible explanation for at least some of the deaths which occurred after the 21st day. It must be remembered that by far the greater portion of the vaccine used was prepared at Onderstepoort in South Africa. When the vaccine was issued from that laboratory it was certainly bacterially sterile, and each dose contained at least 100 infecting doses of each virus strain; usually the infectivity was considerably in excess of this immune standard. The bottles were packed in fluted cardboard containers, and held in position in wooden boxes with liberal quantities of dry sawdust which also served as an insulator against heat. The cases were well cooled in refrigerator chambers before dispatch to the aerodrome to be loaded on military planes for transport to Cairo where they were transferred as expeditiously as possible, to other machines for transport to the main distributing depot in Palestine. A great deal of the vaccine was issued during the South African winter, i.e. during the excessively hot summer months of the Middle East, so that the vaccine before injection of necessity must have been exposed to wide variation of temperature. The essential portion of the vaccine is a living virus. Although this virus is characterised by remarkable stability, and unusual keeping qualities, it is rapidly inactivated by heat. It is certain, therefore, that in many cases there had occurred a considerable reduction in titre of the vaccine, if not complete inactivation, by the time it was possible for the injection to be carried out. At least some of the deaths after the 21st day must be attributed to the use of inactive vaccine, as a result of which the animals developed no immunity, or an immunity only to a surviving antigenically aberrant strain. It is indeed remarkable that the reported results were so good, and a great deal of credit is due to the expeditious manner in which the bulky vaccine (dose 10 c.c.) was handled after being issued.

Naturally it is quite impossible to hazard even a guess as to the number of animals which were saved by the vaccine, but the opinion has been expressed, that the number probably runs into hundreds if not thousands of horses and mules of great value and in the circumstances quite irreplaceable. The experience in Jaffa and Tel Aviv which are regarded as one locality affords an excellent example. Horsesickness was first diagnosed there on the 7th of September. Due to the early limited supply of vaccine it was decided by the authorities to give priority to animals used for agricultural purposes, rather than to urban animals which could probably be replaced by motor vehicles if the majority were lost. Consequently there was a lag of 26 days before general vaccination was carried out on the 3rd to 5th of October. During that period 118 died or were destroyed, and actually 14

were in an advanced stage of the disease when presented for injection. During the next 10 days, 32 additional deaths occurred, and a further 10 during the following 10 day period, after which mortality ceased.

This experience of an extensive epizootic of horsesickness in a fully susceptible equine population indicates that control measures, having as their aim, the limitation of infection amongst the minute night flying vector and the prevention of the infective insect vector gaining access to the host, if carried out to a degree which results in almost complete immobilization of the animals, may reduce the incidence of the disease very considerably. Active immunization of all susceptibles, however, is the only effective measure of control and, if the neurotropic attenuated virus vaccine is used, it can be expected that an adequate immunity will be produced approximately 3 weeks after injection. This period of three weeks corresponds to the period of rest after injection that is advised, because it must be borne in mind that the development of an active immunity is dependent upon actual multiplication of the virus within the body. Although the reaction is very mild a systemic reaction certainly occurs in fully susceptible animals between the 8th and 12th day, during which exercise or work is not advisable. No period of rest is necessary for the immune or partially immune animal on subsequent reinjection.

THE FUTURE OF HORSESICKNESS IN THE MIDDLE EAST.

Up to the present it has merely been shown that certain species of *Culicoides* harbour the virus of horsesickness, and that at certain seasons of the year they are capable of transmitting infection by bite (Du Toit 1945). Any details of the conditions essential for this natural transmission, as well as the identity of the virus reservoir, await elucidation. In the Middle East, *Culicoides* are present in swarms, but obviously at least one condition for continued dissemination of infection is lacking, because annual epizootics do not occur as they do throughout the recognized area of distribution of the disease in Africa. The most probable explanation is that the natural virus reservoir is absent and that in itself is a point of the greatest importance because it supports the contention that the equines do not constitute that reservoir. The epizootic in the Middle East was controlled by mass immunization. It will be interesting to see whether the disease reappears during the following summer months. If not, it behoves the responsible authorities to ensure that a reservoir of infection to initiate an epizootic is not again introduced during a time when the unknown conditions for rapid dissemination of infection are again favourable i.e. during the late summer months. In the case of Egypt the first consideration should be the control of the movement of all equines to and fro across the Egypt-Sudan border. Any such movement should be restricted to animals which had been immunized not less than 21 days, and not more than 12 months, previously. To serve as an additional control against the illicit introduction of a virus reservoir of infection, all horses, mules, and donkeys in a suitable strategic area around Komombo should be immunized annually. All immunized animals should be suitably marked by brand or tattoo to ensure that a completely immune population is maintained. During the period from the beginning of June to December additional veterinary and inspecting staff should be drafted into the area to ensure that the regulations are carried out. In addition, strict anti-insect measures should be applied to all aircraft arriving at an Egyptian aerodrome from the South.

In the case of Palestine there appears to be far less danger of importing the disease in equines, but the application of anti-insect measures to aircraft, particularly those taking off and landing at night, should be rigidly enforced.

In one or other of the countries arrangements should be made for the establishment of an adequately staffed and equipped laboratory for the production of the requisite amount of vaccine at short notice. It is probable that the large laboratories in the South would continue to be able to meet the demand, but the cost of transport by air would be so high under normal circumstances as to make the cost of a mass immunization campaign almost prohibitive. Alternately consideration should be given to the possibility of keeping on hand stocks of concentrated virus preparations, imported in the desiccated state, for reconstitution and dilution when required.

SUMMARY.

- (1) The history of horsesickness in Egypt and Palestine is traced.
- (2) It is believed that the 1944 epizootic was started in Egypt by the introduction of one or more infected equines into the Komombo area from the South and that it was not a recrudescence of the infection introduced the previous year.
- (3) The chief characteristics of the epizootic are described and figures are quoted to show the morbidity and mortality in horses, mules, and donkeys.
- (4) The manner in which infection was introduced into Palestine remains obscure, and the various factors involved are discussed. The possibility that infected insect vectors were carried by aircraft, not only from Egypt, but from some other focus is discussed.
- (5) The great similarity but not complete identity between the Egyptian and Palestine strains of virus, as determined by *in vitro* and *in vivo* laboratory experiments, is reported. The chief point of resemblance is the similarity of antigenic structure; the chief points of difference are the period of incubation in horses and the virulence.
- (6) Attention is directed to the susceptibility of the donkey.
- (7) The general measures of control and their relative effectiveness are described.
- (8) Mass immunization is shown to be the only effective measure of control, and figures are given to indicate the rate of development of immunity.
- (9) The future of horsesickness in the Middle East and the measures necessary to prevent reinfection are discussed.

ACKNOWLEDGMENTS.

The receipt of a number of reports from Dr. Fahmy Salem Bey, the Director of Veterinary Services, Egypt, on the progress of the epizootic after the return of the author from a tour of inspection of the Delta area of the Nile on the invitation of the Egyptian Government is gratefully acknowledged. Details of the Palestine epizootic were obtained from a full

HORSESICKNESS IN THE MIDDLE EAST, 1944.

report by Dr. Binns, Acting Director of Veterinary Services Palestine, forwarded as a personal communication. Permission for the use of the data supplied was readily granted and the liberal quotations made from the report are acknowledged. It is to be hoped that that valuable report will be published *in extenso* as it contains a mass of data of local interest which it was not possible to incorporate in this article. All concerned must acknowledge with a sense of deep gratitude the part played by the South African Air Force in transporting all the vaccine to Cairo without mishap.

REFERENCES.

- ALEXANDER, R. A. (1935). Studies on the neurotropic virus of horsesickness III. The intracerebral protection test and its application to the study of immunity. *Onderstepoort Jnl.*, Vol. 4, No. 2, pp. 349-378.
- CARPANO, M. (1931). African horsesickness as observed particularly in Egypt and Eritrea. *Ministry of Agric. Tech. and Science Service (Vet. Service) Bulletin* 115. Government Press, Cairo. (Translated from Italian by E. Talariwitch).
- DU TOIT, R. (1944). The transmission of bluetongue and horsesickness by *Culicoides*. *Onderstepoort Jnl.*, Vol. 19, Nos. 1 and 2, pp. 7-16.
- FINDLAY, G. M. MacCALLUM (1937). An interference phenomenon in relation to Yellow Fever and other viruses. *Journal of Path. and Bac.*, Vol. 44, No. 2, pp. 405-424.