EUROPEAN COMMISSION FOR THE CONTROL

OF FOOT-AND-MOUTH DISEASE

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REVIEW

OF

EPIZOOTIOLOGY AND CONTROL OF

FOOT-AND-MOUTH DISEASE IN EUROPE

from 1937 to 1961

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by

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INTRODUCTION

This review has been prepared in accordance with the request made at the Eighth Session of the Commission.

The last 25 years have been of the greatest interest from points of view of both the epizootiology and control of foot-and-mouth disease. During this period there were two extensive European epizootics: in 1937-39 and 1951-52. Since the war there have also been a number of regional epizootics: in northern Italy in 1945-48; in Greece, Turkey and Yugoslavia in 1951; in France and the Federal Republic of Germany in 1956-58; in Spain and Portugal in 1958-59; in Turkey in 1957; in eastern Europe in 1959-60; and in Greece in 1960-61. There was also the epizootic in Israel in 1959-60. It has been possible to follow many of these epizootics closely and several of them are of particular interest.

During this period, also, it has become possible to control foot-and-mouth disease in continental Europe by the suitable application of vaccine. During this period the complement fixation technique was developed and so, much assistance has been given in typing the virus. After the war, there was a marked advance in foot-and-mouth disease research and much knowledge has been gained, e.g. cultivation of virus in tongue epithelium and in kidney tissue cultures, susceptibility of unweaned mice, modification of virus, etc., much of which has already found practical application.

In this review there is some statistical data. They have been taken from the Bulletins of the O.I.E., the Report of the U.K. Departmental Committee on Foot-and-Mouth Disease, 1952-54, and Reports of the Sessions of the European Commission for the Control of Foot-and-Mouth Disease.

EPIZOOTIOLOGY OF FOOT-AND-MOUTH DISEASE IN EUROPE

A. Pattern of Foot-and-Mouth Disease in Europe

Until 1920, the pattern of foot-and-mouth disease epizootics in Europe seemed quite clear: new extensive epizootics swept across continental Europe from the East and moved westwards and southwards. German records show that, on many occasions, as in 1892, 1899 and 1910, epizootics entered Europe across the eastern German borders from Russia. It is also known that some epizootics entered Europe from Asia Minor through the Balkan countries. In 1920, there was a change in the epizootiology of the disease in Europe, for an epizootic originated in France and moved over Europe from the south and west of the Continent towards the north and east. A similar occurrence took place in 1937 when infection entered France from North Africa. The epizootic of 1951-52 was first recognised in the middle of Europe and spread to practically all European countries. The regional epizootic of 1956-58 also began in the middle of the Continent and spread to a limited extent to some European countries.

Since 1910, up to 1959, no invasion is known to have taken place from Russia. In 1959, however, outbreaks again appeared in some countries west of Russia - Rumania, Poland and Finland - undoubtedly as a result of invasion from Russia. This invasion seems to have been limited and the control measures taken in the invaded countries to have been very strict. Probably for these reasons no wide-spread epizootic occurred.

The European Epizootic of 1937-39

Just before the extensive epizootic in 1937-39, the foot-and-mouth disease situation in Europe was very satisfactory. During 1935 and 1936, the number of outbreaks steadily decreased and in the spring of 1937, it looked as if the disease was about to die out in Europe. Only France, Italy and the Netherlands had some few outbreaks of a mild character. In April, the number of outbreaks in these four countries was 6, 3, 79 and 26 respectively. All other countries were reportedly free.

In May 1937, however, France was invaded from North Africa. In the beginning of 1937 an epizootic moved across North Africa from west to east, through Morocco and Algeria. Sheep and pigs mainly were affected and the disease was generally mild in character. The transmission of this infection from Africa to France could not be avoided. Each spring a large number of sheep and pigs were being imported into France from North Africa and this took place also in 1937. These animals were, in fact, intended for immediate slaughter, but part of the consignments was sold in markets and disseminated throughout the country. During May, sheep from Morocco, which had been imported into Marseilles, caused several outbreaks of foot-and-mouth disease in regions east and west of that city, and during June the disease spread rapidly throughout southern France. At about the same time, a new focus of infection appeared in the western part of France, caused by pigs from Morocco imported into Bordeaux, and also in June the disease appeared near Paris caused by sheep from southern France. During July northern France became

infected along the Channel coast, and the disease crossed the Franco-Belgian border of Flanders. Luxembourg and the Netherlands were also invaded. From the eastern part of France the disease spread to Switzerland and to the German border at the Rhine. In August there was spread in all directions in France and Belgium, and the first cases appeared in western Germany.

The spread continued during September and October and in the latter half of October the disease crossed the Franco-Italian border and also spread within Switzerland. In November, there was rapid extension towards the east and north in Germany. In the late summer and autumn cases began to appear in Denmark. In November also, the first outbreaks appeared in Yugoslavia.

At the end of December, the first outbreaks appeared in Poland and in Czechoslovakia.

During early 1938, foot-and-mouth disease spread in all directions in Central Europe, while in France, Belgium and Holland the disease had practically disappeared. In the middle of the year the disease reached its peak in Germany with an overwhelming number of outbreaks in northern Germany. The number of outbreaks in Denmark also increased rapidly. During the second half of 1938 practically all other European countries became infected. The disease spread from Denmark to Sweden, and some few outbreaks occurred also in Norway. The epizootic continued eastward through Poland to Russia. Austria became infected from Germany at the beginning of 1938 and spread into Yugoslavia. Hungary became infected in May 1938 from Czechoslovakia. In Rumania the first outbreaks appeared in August 1938, probably as a result of invasions from both Hungary and

Yugoslavia. In October the infection reached Bulgaria from Yugoslavia. Greece also became infected in October 1938 and Albania in January 1939. There was spread in Italy, and the first cases appeared in Spain and Portugal. Some few outbreaks also occurred in Finland.

The virus which caused this extensive wave of foot-and-mouth disease was identified in several countries as of the O type. It was unusually infectious especially in 1937, when France, Belgium and the Netherlands were overrun within a few months. In 1938 spread was considerably slower and at the end of the year the epizootic had only reached as far east as the Russian border. This O virus which, in northern Africa had caused a benign disease mainly among sheep and pigs, caused an epizootic of hitherto unknown severity among the highly susceptible livestock population in Europe.

In 1938, when the first wave of infection had ceased in France, Belgium and the Netherlands, and had continued its way towards the north, east and south-east in Europe, new epizootics appeared in each of these three countries. In France and Holland these new epizootics, which were caused by virus of type A, reached about the same intensity as the earlier ones. Later on, epizootics caused by type A appeared in several other European countries but were not generally so severe as the first wave of infection. Later, during the epizootic, some sporadic outbreaks were caused by virus of type C.

In table I the number of outbreaks in most of the European countries is given. It should be noted that for a number of countries the epizootic was still in progress when the last reports were made. However, in countries like Poland, Czechoslovakia and Austria the epizootic was in regression (1, 2*).

*) These reference numbers refer to the bibliographie which will be attached to the final issue of this document.

Table I

Outbreaks during the 1937-39 Epizootic

France (1937-38)	Poland (1938 - 1 March '39)
378,703	234,506
Belgium (1937-38)	Czechoslovakia (1938 - 1 March '39)
102,763	240,118
Luxembourg (1937-38)	Austria (1938 - 1 March '39)
5,089	38,474
Netherlands (1937-39)	Yugoslavia (1938 only)
265,113	17,588
Germany (1937-39)	Hungary (1938 only)
703,602	5,151
Denmark (1938-39)	Rumania (1938 - 1 March '39)
105,910	20,961
Sweden (1938-39)	Bulgaria (1938 - 1 February '39)
7,253	244
Switzerland (1938-39)	Italy (1938-39)
19,134	31,696

Great Britain also became involved in this extensive continental European epizootic. In October 1937 a series of outbreaks started and continued until March 1938 during which time there were in all 265 outbreaks.

They were in the south-eastern, southern and south-western parts of the country, and it was thought migrating birds played some part in the transmission of the virus from the Continent.

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Between the two large European epizootics of 1937-39 and of 1951-52 the foot-and-mouth disease situation in Europe was comparatively quiet. The disease was enzootic in most European countries and the types of virus found were mainly O and A.

During that period, however, there were two regional epizootics of much interest, one in northern Italy in 1945-1948 and the other in Greece, Turkey and Yugoslavia in 1950-51.

The Epizootic in Northern Italy in 1945-48

At the end of the Second World War northern Italy was reportedly free from foot-and-mouth disease. However, as soon as importation of livestock was restored, the Po Valley became infected. The first outbreaks were caused by virus of type O of low virulence. At the end of 1945, however, a very pathogenic virus of the C type appeared in that area. While the O virus disappeared, the C virus spread all over the Po Valley where it dominated for three years and then suddenly disappeared. The disease caused by the virus of the type C was extremely severe and there was a high mortality even among adult cattle.

This epizootic is of special interest because it is the first time that foot-and-mouth disease caused by a virus of the C type is known to have spread throughout an area and caused an epizootic.(3).

The Epizootic in Greece, Yugoslavia and Turkey in 1951-52

In 1950-51 there was a regional epizootic in Greece, Yugoslavia and Turkey and probably Syria and Iraq were also included. In table II is given the number of monthly outbreaks during 1951 in Greece, Yugoslavia and Turkey, as well as monthly numbers of diseased animals in Iraq in 1951 and the number of diseased animals in Syria in the whole of 1951 and 1952.

Table II

	Greece	Yugoslavia	Turkey	Iraq	Syria
1951					
January	36	0	4	733	
February	65	0	5	325	
March	131	0	7	3,233	
April	4,404	0	0	4,530	
May	17,647	277	8	6,251	106,818 (for the whole of 1951)
June	24,568	230	192	2,498	
July	7,444	632	512	1,535	
August	828	1,183	1,271	574	
September	474	659	896	37	
October	477	212	480	289	
November	191	226	453	158	
December	301	61	352	217	
1952					124 (for the whole of 1952)

The table shows that there was a flare-up of the disease in all five countries in 1951. There is good reason to believe that there was a regional epizootic in these five countries.

In Greece the epizootic started in 1950 in the district of Attika. Vaccination was carried out with a bivalent vaccine. However, a month after vaccination there were some ruptures of immunity. After virus of type C had been demonstrated a trivalent vaccine O, A and C was used for vaccination with good results. In the beginning of the epizootic, virus material had been sent to a German foot-and-mouth disease laboratory where it was typed as A and finally identified as the varient A5. A vaccine produced with this virus was then used, with favourable results. However, in the beginning of 1951, foot-and-mouth disease spread beyond the district of Attika and with great rapidity, invaded large parts of Greece. From table II it will be seen that the peak of the epizootic was in June (4, 5).

Yugoslavia was free from foot-and-mouth disease from July 1950 until the last day of April 1951 when the southern part of the country, Macedonia, was invaded from Greece. Bivalent vaccine O-A was used against this invasion but the immunity ruptured within a short time after vaccination. The invading virus was shown to be of the A type and later was identified as the variant A5. From this virus a Vallée-Schmidt-Waldmann vaccine was produced locally and gave good results. With the help of this vaccine, combined with the application of strict veterinary measures, the invasion from Greece was brought under control (6, 7).

In May 1951, the disease spread from Greece into Bulgaria. There is reason to believe that virus from Greece also invaded Albania.

In Turkey there was also an epizootic of foot-and-mouth disease in 1951. The disease is enzootic in Turkey with some few hundred reported outbreaks (infected villages) annually. The number of outbreaks in 1950, 1951, 1952 and 1953 were 71, 2,891, 1419 and 284 respectively (8). The situation through 1951 will be seen in table II: it will be seen that the epizootic had its peak in August 1951. In the beginning of 1952 samples of virus from different parts of Turkey were typed (9) and virus of the types O, A_4, A_5 and C were identified.

It is impossible to ascertain the true origin of this regional epizootic. It would appear, however, that the infection possibly originated, as so often previously, in some eastern countries. It is remarkable that this epizootic was arrested in south-eastern Europe so that no movement northwards into western Europe took place.

The European Epizootic of 1951-52

During 1950 and the beginning of 1951 the foot-and-mouth disease situation in western European countries remained fairly steady compared with previous years. The numbers of outbreaks in 1950 in France, Belgium and the Netherlands and the Federal Republic of Germany were 8,094; 408; 2,485 and 583, respectively. During the spring of 1951 there were some outbreaks in the Federal Republic of Germany caused by the virus types O and A_4 (10). In May/June several outbreaks occurred around Hannover caused by virus of type A_5. It was found that this new type was the same type as that which had caused outbreaks in Greece. The German authorities thought that this new A_5 strain was

probably of local origin and a variant of an A type inside Germany. Virus of type C was also demonstrated in northern Germany at this time. Thus, simultaneously there were in Germany the following four types: O, A_4, A_5 and C.

The new variant A_5, however, dominated the picture. It was extremely contagious and spread rapidly in West Germany. It also spread northward to Denmark, Sweden and Norway, westward to Belgium, Netherlands, Luxembourg and France, from France into Spain, and from Spain into Portugal. Switzerland, Italy and Austria were invaded and spread took place into Eastern Germany from where the disease entered Poland and finally Russia. Later, the disease entered Finland.

Of the countries in the Eastern part of Europe, Hungary probably remained free from the infection. No information is available concerning Czechoslovakia and Rumania. The position in Greece, Yugoslavia, Bulgaria and Turkey during 1951 has already been referred to.

From the Continent the virus spread to Great Britain where, between November 1951 and November 1952, it caused 583 outbreaks.

As stated above, virus of the C type was also demonstrated in the northern part of the Federal Republic of Germany in May 1951. It also showed a tendency to spread, although more slowly than A_5, and invaded a number of countries in which it appeared 2 - 4 months after the A_5 invasion. Thus, as occurred in Italy in 1945, C virus assumed an epizootic character and spread over a wide area. The spread of these viruses (A_5 and C) is of considerable interest. Examples from some countries may be quoted.

The first country to be invaded from Germany was Denmark, where there were, in all, some 27,000 outbreaks. Of these, some 500 outbreaks were probably caused by virus type C.

Belgium was invaded by A_5 virus from Germany at the beginning of September, 1951 and by C virus in January, 1952, probably from the Netherlands. In all, some 59,000 herds were infected.

The Netherlands was invaded by A_5 virus from Germany at the beginning of September 1951 and by C virus during the second half of December. Here two waves of infection could well be demonstrated. During the first wave of infection caused by A_5 virus some 20,000 herds were infected; during the second wave some 7,000 herds.

France was invaded by A_5 virus at the end of 1951, and in the beginning of 1952, C virus was demonstrated. The total number of outbreaks was some 320,000.

The situation in Switzerland and Sweden during the 1951-52 epizootic is of special interest. Switzerland became infected with A_5 virus at the beginning of October, 1951 when foot-and-mouth disease was found among cattle imported from Denmark. Later on, outbreaks were found along the railway line of the St. Gottard caused by Danish and Dutch cattle in transit to Italy. In other regions outbreaks were caused by imported agricultural products. From October, 1951 until the end of the year there were, in all, 181 outbreaks, and in 1952, 109.

Sweden became infected from Denmark in the latter half of September 1951. From September until March 1952, when the epizootic ended there was a total of 840 outbreaks in Sweden, all of which were caused by virus of A_5 type except 6 of which C type was the cause (11).

Table III

Number of outbreaks in the 1951-52 epizootic in some European countries

Portugal (1952-53)	Switzerland (1951-52)
15,045	426
Spain (1952-53)	Italy (1951-52)
11,031	43,690
France (1951-52)	Finland (1952-53)
330,056	121
Belgium (1951-52)	Poland (1951-53)
59,302	106,800
Luxembourg (1951-52)	Austria (1951-52)
1,329	12,607
Netherlands (1951-52)	Hungary (1951-52)
27,805	-
Germany (1951-52)	Greece (1950-51)
204,300	56,652
Denmark (1951-52)	Yugoslavia (1951-52)
27,769	3,657
Sweden (1951-52)	Bulgaria (1951-52)
833	32
	Turkey (1950-51)
	4,222

The European foot-and-mouth disease epizootic of 1951-52 was certainly violent and caused a large number of outbreaks in different countries. However, a comparison of the figures in tables I and III shows that the epizootic of 1937-39 was still more violent. The position in the group of countries of France, Belgium, Luxembourg, the Netherlands, the Federal Republic of Germany and Denmark is that the total number of outbreaks during the 1937-39 epizootic was about $1\frac{1}{2}$ million while in the 1951-52 epizootic there were less than half of that number. It should also be noted that in countries like Switzerland and Sweden the incidence in the latter epizootic was almost negligible.

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It has already been mentioned that the foot-and-mouth disease virus of the A_5 variant which appeared in the Federal Republic of Germany in June 1951 was considered as being of German origin. However, Ubertini (12) has cast some doubt on this assumption. At the beginning of 1951 he had examined virus harvested in Greece in the autumn of 1950, and identified it as type A without any distinction of variant. In 1953 a more precise determination of this virus from Greece was made by Ubertini. He came to the conclusion that the Greek strain was of the A_5 type and was identical with the strain isolated some months later, first in Germany and then in many other European countries. Thus, the virus of type A_5 had appeared in Greece in 1950 and in Germany in 1951 and the two strains were shown to be identical from both a serological and a clinical point of view. In Ubertini's opinion it is, therefore, highly probable that the extensive European epizootic of 1951-52 had its origin in Greece and not in Germany.

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There has been no major epizootic in Europe since that of 1951-52. However, the disease has occurred as minor epizootics in some regions: France and the Federal Republic of Germany 1956-58; Spain and Portugal, 1958-59; Turkey 1957; Russia and eastern European countries 1959-60; Greece, 1960-61. There was also the epizootic in Israel in 1959-60 which was of great interest for Europe.

The Epizootic in France and the Federal Republic of Germany 1956-58

The foot-and-mouth disease situation in western Europe, during the first half of 1956 was very quiet. Some countries were completely free from the disease and in others there was only a very limited number of outbreaks. The Federal Republic of Germany was, in fact, free during April and May.

In the middle of the year, however, the disease flared up in France and the Federal Republic of Germany and soon assumed an epizootic character. The number of outbreaks in France were: in 1956 - 6,800; in 1957 - 99,424 and in 1958 - 14,127, respectively. The number of outbreaks in the Federal Republic of Germany were: in 1956 - 1,401; in 1957 - 6,383; and in 1958 - 1,265, respectively. In both countries the number of outbreaks during this regional epizootic was low as compared with former epizootics. In both countries the three classical types of the virus O, A and C were present during the epizootic.

The spread of the infection from France and the Federal Republic of Germany into neighbouring countries could not be avoided. The disease spread into Belgium, Luxembourg, Switzerland, Spain and Portugal as well as into Denmark, Czechoslovakia and Austria. Some of the more eastern countries such as Poland, Hungary and Rumania, also had outbreaks which were attributed to invasion from western Europe. The infection also spread to England causing outbreaks along the Channel coast.

Most of these countries were only slightly infected. There were probably two reasons for this: the measures taken in France and the Federal Republic of Germany made infection less heavy than in former epizootics; measures taken in the invaded countries.

In table IV the numbers of outbreaks during this limited epizootic are shown:

Table IV

Number of outbreaks in invaded countries

Belgium	1,589	Czechoslovakia	301
Luxembourg	20	Austria	145
Switzerland	285	Poland	26
Spain	3,313	Hungary	16
Portugal	5,454	Rumania	37
Denmark	62		

It will be seen from table IV that the number of outbreaks in most of the countries, except Spain and Portugal, was limited compared with the two former epizootics.

The epizootic in Spain and Portugal in 1958-59

When foot-and-mouth disease occurs in Spain it is usually found first in the North of the country where there are common grazings with France. Early in 1957 some small outbreaks caused by virus type A_5 occurred first in the north and later in the center of the country (13). In June-July of the same year some outbreaks caused by virus of type C occurred in the Pyrenean region near France. During 1958 an epizootic developed and during 1957-58-59 and '60 there were 161, 1887, 1265 and 244 outbreaks, respectively. In addition to the types A and C, type O was also identified during the epizootic. Since March 1961 no outbreaks have been reported from Spain. It should be noted that some outbreaks, especially in pigs, may have had their origin in imported infected meat.

Foot-and-mouth disease has occurred fairly frequently in Portugal; invasion as a general rule having taken place from Spain. The overall position in Portugal is not considered to be serious and the disease has shown a tendency to die out (14). In May 1958, an epizootic started in Portugal as a result of invasion from Spain of virus type A. During 1958-59 and '60 there were 3,912, 1,489 and 53 outbreaks, respectively. The last outbreak in Portugal was reported in December 1960. It should be noted that also in Portugal imported meat constitutes a potential source of infection.

The epizootic in Turkey, 1957

Independently of the flare-up of foot-and-mouth disease in western Europe, a severe epizootic occurred in Turkey in 1957. The foot-and-mouth disease situation in Turkey is of special interest to Europe,

because that country is a link between the continents of Asia and Europe. Foot-and-mouth disease is enzootic in Turkey and, as a rule, of a very mild character. An outbreak in Turkey refers to an infected village, and in Turkey there are some 50,000 villages. The normal foot-and-mouth disease picture is 300-800 outbreaks annually with a flare-up every 3-4 years. There has never been an epizootic in the European sense of the word in Turkey, as far as is known. The 1957 epizootic started in May in the eastern part of the country, probably as the result of invasion from Iraq where there was a flare-up at that period. (The number of animals affected in Iraq was 2,073 in 1956, 898,941 in 1957 and 3,683 in 1958).

The disease spread from east to west in Turkey and soon reached the European part of the country. The epizootic lasted from May to December, reaching its peak in July with 3,390 outbreaks: in all there were some 8,000 outbreaks. The epizootic was caused by virus of type O: it was very serious and caused a high mortality (15).

From European Turkey the disease spread also into the neighbouring countries of Greece and Bulgaria, where further spread was arrested.

Foot-and-Mouth disease in Russia and eastern European Countries

Earlier foot-and-mouth disease in Russia was of much importance to the rest of Europe. Until the epizootic of 1920, extensive European epizootics always moved across the continent from east to west as a result of infection from Russia and in some cases also from Asia Minor. The last extensive epizootic invading Europe from Russia was in 1910. From 1910 to 1959 no spread of foot-and-mouth disease originating in

Russia is known to have taken place to her western neighbouring countries. During 1 9 5 9, however, there was undoubtedly again a spread of the disease from Russia westward, although it seems to have been on a limited scale.

Some information on the epizootiology of the disease in Russia was given by Gribanov in 1958 (16) and by Bôiko in 1960 (17). During 1955 and 1956 many samples of virus from many places in Russia were examined. Of these 30.2 percent were of the O type, 64.6 percent of the A type and 5.1 percent of the C type. The A type was demonstrated in the central part of European Russia, in White Russia and in the Ukraine and it was this virus which invaded Russia from the west in 1952. The viruses O and C were demonstrated in the Republics of Central Asia and types O and A in the Republic of Georgia.

For a number of years no information was available about the number of outbreaks of the disease in Russia. However, from the beginning of 1961, Russia has reported the monthly number to the OIE: January, 75, February 43, March, 25, April, 22, May, 39, and June, 44. The number of outbreaks must be regarded as extremely limited in so huge an area.

In 1959 it was reported from Russia that virus of type O was present in the Ukraine and the Petrograd district. It was from here that spread westward took place.

Rumania was the first country to be invaded. The country had been free during 1958 until December when the first outbreaks occurred. During 1959 the disease spread throughout the country. In April, 1960 the country was again free and has remained so since that time. The

casual virus was of type O. The number of outbreaks were: 1958 - 5, 1959 - 419, and 1960 - 24. From Rumania the infection spread to the neighbouring countries of Bulgaria, Yugoslavia and Hungary.

Bulgaria was free from foot-and-mouth disease in 1959 until April when it was invaded from Rumania. In August 1960 the country was again free and no outbreaks have been reported since that time. The number of outbreaks were 1959 - 70, and 1960 - 4. The casual virus was, as in Rumania, of type O.

Yugoslavia was invaded from Rumania in November 1959, before which the country had been free for five years except for one outbreak in February 1959. Yugoslavia was again declared free in April 1961. The number of outbreaks were: 1959 - 50, 1960 - 41 and the first half of 1961 - 10. There were, in fact, three groups of outbreaks in Yugoslavia: near the Rumanian border in November 1959; near the Bulgarian border in June 1960; and near the Hungarian border in November 1960. In all three groups virus of type O was identified.

Hungary was free from foot-and-mouth disease during 1958. In 1959 there were some few outbreaks in March. In November of the same year, outbreaks occurred near the Rumanian border. Since February 1961, Hungary has again been free of the disease. The number of outbreaks were: 1959 -21, 1960 - 22 and the first half of 1961 - 2. The cause of infection in November 1959 was as in the outher countries, virus of type O.

It is not known if there was an invasion into Czechoslovakia from Russia in 1959. It seems, however, as if infection appeared in a district in the center of the country in the autumn of 1959 causing a

considerable number of outbreaks. Four other districts became infected. All three types of the virus O, A and C were demonstrated. The number of outbreaks were: 1959 - 143, 1960 - 85 and the first half of 1961 - 48. Czechoslovakia has recently been declared free of foot-and-mouth disease

Poland was free during 1958 and also during 1959 until October/ December, when a number of outbreaks occurred, first near the Czechoslovakian border and later near the Russian border. Virus of types A_5 and O were identified. The number of outbreaks were: 1959 - 393, 1960 - 373 and the first half of 1961 - 15.

In Finland some outbreaks occurred in November, 1959 near the Russian border. The casual virus was typed as O. The number of outbreaks were: 1959 - 41 and January 1960 - 1. Since January 1960 up to the middle of 1961 no further outbreaks have occurred. There is some doubt whether all the reported cases were actually foot-and-mouth disease.

Austria was free from foot-and-mouth disease for more than two years when some outbreaks occurred in October, 1959 near the Czechoslovakian border. In October, November and December, 1959, there were 4, 1 and 1 outbreaks respectively. Virus type O was diagnosed. During 1960 Austria was again free from the disease until December when the disease was identified in slaughtered animals imported from Hungary. The infected animals were found in the central cattle market in Vienna and virus type O was identified, this was the same type that had caused the recent outbreaks in Hungary. During the first half of 1961 no outbreaks occurred in Austria.

It will be noted that the number of outbreaks in the above countries was very limited compared with former days.

The epizootic in Greece 1960-61

Since the extensive foot-and-mouth disease epizootic in 1951 until 1960 there were only a limited number of outbreaks in Greece. They seem to have been caused mainly by invasion from Turkey and by infected frozen meat imported from South America. Virus of types O and A were demonstrated. In 1960 and 1961, however, a new dangerous situation developed in the country. Greece was free during 1960 until September, when the disease was demonstrated near the Turkish border and the casual virus was typed as O. Also in September, foot-and-mouth disease occurred in a piggery in northern Greece where the pigs had been fed with swill from infected frozen meat imported from South America. Virus of type C was demonstrated. In February, 1961, the disease broke out in another piggery also in northern Greece where the pigs again had been fed with similar swill. The type of virus demonstrated was A. During the rest of 1960 and in 1961 until July a number of outbreaks occurred mainly in the northern part of the country but there were also some in the central part and near Athens. The total number of outbreaks during the epizootic was 297.

In September the country was again declared free from foot-and mouth disease (18).

The epizootic in Israel, 1959 - 60

An epizootic of much interest to Europe occurred in Israel in 1959-60. Israel is under constant threat of invasion of foot-and-mouth disease from her neighbours, Lebanon, Syria and Jordan, where the disease occurrs and where effective control measures are difficult to carry out.

During the past few years Israel has had some outbreaks: 1953 - 2; 1954 - 1; 1935 - 9; 1956 - 94; 1957 - 34. An outbreak in Israel refers to an infected farming community: there are 950 such communities in the country. In 1958 the first outbreaks of the disease in Israel were in March, undoubtedly as a result of invasion from Syria. There were some difficulties in typing the causal virus and it was not until September of that year that it was finally typed as Asia I, a type which had been demonstrated earlier in many parts of Asia, in Hongkong, Thailand, Burma, India, Pakistan, Afghanistan, Iran, and more recently, in Syria and Lebanon. From Mardh 1958 to 1 January 1959 in all there were 13 outbreaks of the disease in Israel, of which12 were caused by virus of type Asia I and one by virus of type O. The Asia I outbreaks were of a somewhat mild character and the virus showed little tendency to spread. During 1959 there were outbreaks in Israel caused by virus of type O. Then in the middle of October, virus of the Asian type was again found. On this occasion, the disease started with a serious outbreak in a farming community near the Lebanese border and soon spread to other parts of the country. It was quite serious and showed considerable tendency to spread, causing 100 outbreaks in 1959 and 193 in 1960.

This epizootic is of special interest to Europe because it occurred so near to Turkey, which is the link between the Near East and Europe. The Asian virus has, as already mentioned, been demonstrated in Iran and Syria and may possibly appear in Turkey on some future occasion. If foot-and-mouth disease caused by the Asian type of virus developed into an epizootic in Turkey of a severity similar to that of the epizootic in 1957, the situation would be very dangerous for Europe (19, 20).

Epizootiology of Foot-and-Mouth disease in the United Kingdom

The epizootiology of foot-and-mouth disease in the United Kingdom has special characteristics. A true slaughter policy has been operated there for many years and vaccination has never been applied. The livestock, therefore, is highly susceptible to the infection. The United Kingdom is invaded from time to time by foot-and-mouth disease and during many years there have been outbreaks each year. As already mentioned, the European epizootics of 1937-40, 1951-53 and 1956-58 also spread to the United Kingdom. Imported meat from South America is also another source of infection.

The pattern of each of these twokinds of infection is clear.

When the continent of Europe is heavily infected along the Channel and the North Sea coasts, infection is conveyed to the United Kingdom by indirect means and outbreaks occur in the southern, south-eastern and eastern coastal areas of England. This was clearly shown during the epizootics of 1937-38 and 1951-52. During the epizootic of 1956-58 in France when the number of outbreaks was negligible in Denmark and the Netherlands, and limited in Belgium, nearly all the invasion from the Continent was found in the south and south-western coastal areas - opposite France.

On the other hand, primary outbreaks, the source of which is considered to be imported meat from South America occur in any part of the country in which such meat is distributed. In 1958, for example, there were 29 primary outbreaks in the United Kingdom, of which it was concluded that 17 were due to invasions from the Continent, probably northern France and in 10, the virus was introduced into the country with infected meat.

Over the years all three types of virus have been demonstrated in the United Kingdom.

Epizootiology of foot-and-mouth disease in the Netherlands

The foot-and-mouth disease situation in the Netherlands has been very satisfactory since 1953 when systematic vaccination of practically the whole cattle population was introduced and this procedure was combined with slaughter of infected and susceptible animals. The number of outbreaks has been: 1954 - 34; 1955 - 48; 1956 - 47; 1957 - 40; 1958 - 11; 1959 - 6; 1960 - 3 and during the first half of 1961 - 2. It should be noted that most of the outbreaks have been among pigs which are not vaccinated and among calves. Over the years all three types of the virus have been present in the Netherlands.

Recent outbreaks in Europe

Since the epizootic of 1951 - 52 the foot-and-mouth disease situation in Belgium has been very satisfactory, undoubtedly due to extensive vaccination. The number of outbreaks, mostly in pigs which are not vaccinated and in young stock are: 1954 - 700; 1955 - 195; 1956 - 693; 1957 - 328; 1958 - 568; 1959 - 57; 1960 - 180. All three types of virus, O, A and C have been identified.

In November 1960 there was a flare-up of the disease caused by virus type C, which spread from some important markets to many parts of the country. Compulsory vaccination was extended throughout the country and the results were highly satisfactory as the disease was rapidly brought under control.

After the small epizootic in the Federal Republic of Germany in 1956-58 there were only 118 outbreaks during 1959. However, during 1960 and 1961 there was a flare-up with 1,395 outbreaks in 1960 and 2,763 in the first half of 1961. It is understood that most of the outbreaks were in pigs which were not vaccinated and that they were caused by virus of type C.

It was mentioned above that the situation in Eastern Germany during the 1951-52 epizootic was very satisfactory because systematic vaccination had been introduced. It is understood that this vaccination has been continued and that the results have remained satisfactory. However, as in the Federal Republic of Germany there was a flare-up caused by virus type C during 1960 and 1961 and the disease being confined largely to pigs. The number of reported outbreaks were: in 1960 - 189 and in the first half of 1961 - 342.

Probably in connection with the flare-up in Germany there were also some few outbreaks in Denmark and Sweden.

Because of its central position in Europe Switzerland is much exposed to the infection when the disease is prevalent in neighbouring countries. In 1960-61 the situation in Germany and Italy was reflected by the incidence of the disease in Switzerland. In 1960 there were 96 outbreaks and 131 during the first half of 1961. In 1961, mainly virus of the C type was demonstrated.

Since the epizootic of 1951-52 until the autumn of 1960 the disease was enzootic in Italy with numbers of annual outbreaks varying from some 7,000 to some 13,000. All three types of virus, O, A and C in different proportions, have been present. In 1960-61 a flare-up

mainly caused by virus of type C occurred. This epizootic started during the last months of 1960 and the number of outbreaks in October, November and December 1960, were - 572, 928 and 1,810 respectively. An increase in the number of outbreaks used to be normal in these months; on this occasion, however, the virus of type C showed much tendency to spread and had a marked affinity for pigs.

The epizootic reached its peak with 4,795 outbreaks in March 1961 and then began to regress and in August only 274 outbreaks were reported.

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With the virulent epizootic of 1937-40 the foot-and-mouth disease situation in Europe became more and more serious for the number of infected herds steadily rose and the disease spread in a severe form to more and more countries. The position in Germany and its neighbouring country, Denmark, illustrates this point. In Germany the numbers of outbreaks during five epizootics which occurred between 1896 and 1940 were 350,000, 240,000, 800,000, 240,000 and 940,000 respectively; in Denmark during five epizootics which occurred between 1911 and 1940 the numbers of outbreaks were 1,300, 7,000, 8,000, 160,000 and 100,000 respectively. This position is probably related to the steady up-grading of cattle in Europe, the growing traffic in livestock and perhaps increase of the virulence of the virus. There are recent examples of this increased virulence. Foot-and-mouth disease in Turkey is enzootic and usually of a mild character. In 1957, however, O virus invaded Turkey and caused an epizootic of a hitherto unknown high virulence. There is also the example in Israel where the virus of the Asia I type had invaded the country in 1958 without showing any tendency to spread. In 1959, however, a new invasion of the same type of virus caused a

real epizootic. A further example concerns the epizootiological change which type C has undergone. Until 1945, virus of type C is known to have caused only sporadic outbreaks in Europe and had shown no tendency to spread. In 1945, however, virus C appeared in Italy and caused a real epizootic, mainly in the North. Also, during the epizootic of 1951-52 virus of type C caused the second wave of infection which spread from the Federal Republic of Germany to many European countries. Since then C virus has been present in several European countries where it has not been previously demonstrated. It has repeatedly shown some tendency to spread.

At the end of 1961 most countries in Europe were free from the disease and in those in which the disease was present the incidence was low. However, the situation is in some ways dangerous because the cattle population in many of the countries is highly susceptible to the disease since there has been a low incidince for a number of years and only a limited vaccination has been carried out.

There are probably five main sources of infection for Europe.

(1) The existing centers of infection within Europe may flare up and the disease may spread to many countries.

(2) Russia, which in former days was a source of infection and from which again in 1959 infection was introduced.

(3) The Near East through European Turkey; the existence of virus of the Asian type in this region is of special importance.

(4) Africa, from where the European epizootic of 1937-40 started. From Africa there is also the threat of the introduction of three South African types of the virus.

(5) Imported meat from South American countries is a source of infection for importing countries.

These sources concern foot-and-mouth disease in Europe. It must not be forgotten, however, that the infection in Europe is a source of the disease for other regions in the world. Russia, for example, was invaded from Europe in 1938 and in 1952, respectively, by virus type O and virus type A_5. It is also known that the disease has been introduced into North Africa from Europe.

Incidence of Foot-and-Mouth

	1950	1951	1952	1953	1954
Portugal	191	15	11.503	3.521	3
Spain (*)	200.993	12.105	1.524.514	35.260	5.189
France	8.094	10.040	320.016	5.513	838
Belgium	408	50.358	8.487	2.551	700
Luxembourg	0	190	382	6	4
Netherlands	2.485	20.750	7.654	308	34
Fed. Rep. of Germany	583	154.478	54.572	2.012	481
Switzerland	21	317	109	14	5
Italy	11.193	10.802	32.888	6.750	6.450
Austria	40	171	12.439	221	0
Yugoslavia	0	3.480	177	1.438	416
Greece	-	56.566	954	4	25
Turkey	72	2.891	1.419	284	648
Bulgaria	0	30	2	23	5
Rumania	?	?	?	?	?
Hungary	0	0	0	0	0
Czechoslovakia	?	?	?	?	?
Poland	0	1.018	87.227	18.555	5.634
Finland	0	0	112	9	0
Ireland	0	0	0	0	0
U.K.	20	116	495	40	12
Denmark	8	23.492	4.277	210	43
Sweden	0	459	374	1	1
Norway	0	2	2	0	0

sease in Europe from 1950 to 1960

1955	1956	1957	1958	1959	1960
0	41	37	3.912	1.489	53
924	9.254	17.839	226.597	89.191	11.259
2.451	6.800	99.424	14.127	6.188	7.382
195	693	328	568	57	180
0	18	2	0	0	0
48	47	40	11	6	3
257	1.401	6.383	1.265	118	1.395
3	121	111	53	13	96
12.635	5.890	7.394	6.453	11.764	11.547
0	37	108	0	6	1
42	0	0	0	65	41
8	17	4	7	22	169
471	1.345	8.630	189	299	543
0	0	35	1	70	4
?	0	37	5	419	24
0	2	14	0	21	22
?	0	145	13	143	85
?	23	26	0	393	373
0	0	3	3	41	1
0	0	0	0	0	0
9	159	184	116	43	298
43	6	45	11	1	1
0	0	0	0	0	2
0	0	0	0	0	0

MODES OF TRANSMISSION OF FOOT-AND-MOUTH DISEASE

Many investigations have been carried out at different times on problems concerned with the mode of transmission of foot-and-mouth disease. From time to time, the results of surveys have been published: examples are the articles by Trautwein in 1929 (22) and by Waldmann and Nagel in 1939 (23), the Report of the United Kingdom Departmental Committee (1952-54) (24). Sven Andersen and the writer also studied this problem in Denmark in 1940 (25).

The infected animal, which excretes virus is the source of the infection: the excretion occurs in the acute stage of the disease and possibly in some cases, periodically, after recovery from the disease.

The course of the disease and the highly infectious nature of the virus are of importance in the rapid and wide spread of foot-and-mouth disease. In this connection it may be recalled that the virus is present at first in the specific primary lesion where it multiplies greatly and from where it enters the blood and so invades all parts of the body. It is excreted in the saliva even before the appearance of mouth lesions with a very large increase in amount when the lesions burst. Following invasion of the blood, the virus is excreted in the milk, urine and dung. Because of its high infectivity, only very small amounts of the virus are required to set up the disease and because of its high resistance in the dry state, the virus may remain infective for relatively long periods and may be carried for long distances.

The direct and indirect methods of spread from the infected animal on infected premises are well known: movement of animals, through infected markets, by contaminated vehicles, etc. Such

methods are not considered in detail in this review. Some further information, however, has been obtained during the past 25 years on some modes of transmission and they will now be described: transmission by human beings, by milk, by meat and offal, by wind, by birds, by fodder and vegetables and by escapes of virus from laboratories, The subject of excretors of virus will also be considered.

Transmission of Foot-and-Mouth Disease by Human Beings

It is generally accepted that foot-and-mouth disease is a typical example of a disease spread by an intermediate carrier, and that man is regarded as the most important carrier. This conviction is based on circumstantial evidence which, in many cases, is overwhelming. This question was studied also by Sven Andersen and the writer. It is not always easy to trace the movements of people from farm to farm and much cross-examination may be required to extract detailed information. It is always best to ascertain the movement of the people at the beginning of the epizootic when there are only very few outbreaks. Of the several examples of spread by human beings during epizootics in Denmark, two are now given as illustrations.

Denmark had been completely free of foot-and-mouth disease during 1935 except for one outbreak in November on a large island where all the animals in the infected herd were slaughtered. In December 1935 and January 1936 there was a small epizootic on another island with a total of 11 outbreaks and where all the infected herds also were slaughtered. The origin of the primary outbreak was not known. Throughout the district there were a further 10 outbreaks, spread over a fairly wide area, separated by distances up to many

kilometers. It was ascertained that in one of the outbreaks there had been direct contact by movement of infected animals: in 7 of the 10 outbreaks movement of people was involved, while in another, this was suspected. In only one of the outbreaks could no origin be determined. No other explanation for the transmission of the virus could be found.

The other was in December 1937 and concerned the occurrence of the disease on another large Danish island which had been free for about a year when seven outbreaks occurred on 10, 17, 22, 23, 25, 28 and 30 December, respectively. The origin of the primary outbreak was not known and no connection was found between it and the first of the secondary outbreaks. The last five outbreaks, however, had direct connection with the second outbreak. A person visited this farm on 16 December, the day before the disease was diagnosed, and he then visited the other five farms between 16 and 18 December and foot-and-mouth disease appeared in them between 22 and 30 December. In three of the five outbreaks the person was in close contact with the animals in which the disease was first demonstrated. In one case he was only in the horse stable. No other explanation for the transmission of the virus to the five farms could be found.

In Norway there is an interesting example of spread by man which seems to indicate that it may be possible to introduce the virus into a stable after walking across infected ground (26). During the Second World War when the Oslo Fjord was blocked by ice and when the country was free from foot-and-mouth disease a shipment of pigs was sent from Denmark to a southern port in Norway and from there by rail

to Oslo. The vans which conveyed the pigs were not waterproof. When the pigs arrived in Oslo they were found to be infected with foot-and-mouth disease. Ten outbreaks occurred on farms situated along the railway line from the southern port to Oslo, some on the western and some on the eastern side. All the outbreaks had the following in common: each infected farm was within 100 yards or less from the railway tracks; in each the disease appeared about a week after the infected animals had passed; the people of each of the farms had to cross the railway tracks to reach the highway. It has also to be noted that no farm became infected where people did not have to cross the railway line. No explanation could be found other than that the inhabitants from the farms which became infected, had to cross the presumably infected track and brought virus on their boots into the stables.

The outbreaks in Norway have much similarity to those in Switzerland in 1956 when pigs in transit caused five primary outbreaks between Basel and Chiasso on the Italian border (27).

Two examples will illustrate spread over long distances by human beings. The first was during the European epizootic which started in France in the spring of 1937 (28). During the summer, France became heavily infected and the disease began to appear in its neighbouring countries to the north and east. On 1 November a group of workers from Yugoslavia returned to their country from France where they had been employed during the summer. At that time Yugoslavia was free of foot-and-mouth disease. The first two outbreaks in Yugoslavia appeared in the herds of two of the returned workers, in two different communities.

The other example is the outbreak in Canada in 1952 (29). There is a great possibility that the virus was taken from Germany to Canada by a German worker, who had left a farm in Germany while foot-and-mouth disease was present there. He went direct to a herd in Saskatchewan and 17 days after he had left the infected herd in Germany he was working with susceptible animals. He admitted that he had not cleaned his working clothes or his working boots before leaving Germany or before starting work in Canada. Pigs on the Canadian farm in question showed the first symptoms of foot-and-mouth disease 10-12 days after the arrival of the immigrant at the farm. The virus was of type A which was also the predominant virus in Germany at that time. No other explanation of the introduction of the virus into Canada could be found, so there is every reason to believe that it was conveyed by the immigrant.

Following an epizootiological study in 1938, Waldmann and Hirschfelder (30) stated that rats, wild animals, birds and insects play little part in the spread of foot-and-mouth disease. The most important intermediate carrier of the infection is man, who comes into close contact with cloven-footed animals, and who enjoys greatest freedom of movement.

It would seem that the above-mentioned examples emphasise this statement.

Spread of Foot-and-Mouth Disease by Infected Milk

Milk and skim milk can be very dangerous sources of infection. If milk is not sufficiently heated at a dairy, all farms belonging to the dairy may be contaminated. A striking example comes from Norway (31). In 1926, milk from an infected farm was sent to a dairy and this resulted

in the spread of the disease to over 100 farms. Since pasteurization of milk has been controlled in Norway, however, there has been no further evidence of spread of infection through this medium. When foot-and-mouth disease appears or when the country is threatened from the disease the temperature of pasteurization of milk is raised by 5°C. throughout a wide area.

From Denmark many cases of spread of the disease, partly by infected milk, partly because of insufficient disinfection of milk-cans, waggons, etc. are known. There are examples where almost all the herds in a single district have contracted foot-and-mouth disease shortly after the first outbreak within the cooperative had been recorded. The following is a striking example of the consequences of neglecting the heat treatment of milk. During an epizootic in 1914-16 it happened that the machinery at a certain dairy broke down so that part of the milk could not be pasteurized. In accordance with the regulations the dairy informed the farmers concerned that the returned skim milk was untreated and should be boiled. These instructions were ignored by 27 of the farmers and all their herds contracted foot-and-mouth disease, which appeared first among calves and pigs. The infected milk originated from a herd where foot-and-mouth disease had not yet been diagnosed. Many occurrences are known where single milk routes within a dairy district have become infected because of insufficient disinfection of milk-cans, etc. An example during the epizootic in 1920 should be mentioned. A dairy had three milk routes and in two of them $3/4 - 4/5$ of the herds became infected, while all herds belonging to the third milk route remained completely free.

In the Report of the Departmental Committee on Foot-and-Mouth Disease milk as a carrier of the infection is also dealt with. It is stated that collection of milk from infected premises is prohibited but that it continues from other farms in the infected area. There is, therefore, a danger that some of it may come from cows in the incubating stage of the disease at a farm where no symptoms of the disease have been demonstrated. Thus, the feeding of infected milk to calves in transit at Crewe was the cause of the disease being spread to Scotland during the 1951-52 epizootic; also infected milk from another source that was fed to calves was responsible for the disease being spread from Cheshire to Derbyshire.

Transmission of Foot-and-Mouth Disease by infected Meat and Offal

Meat and offal infected with foot-and-mouth disease virus have, for many years, been considered as a source of infection for susceptible animals. Chilled and frozen meat and offal from South American countries where foot-and-mouth disease is prevalent is exported on a large scale to some European countries and is considered to have caused many outbreaks in them. There is overwhelming circumstantial evidence to this effect, mainly from Great Britain.

A considerable amount of research on the subject has been carried out in the laboratory and in one single instance it was possible to demonstrate foot-and-mouth disease virus in imported frozen meat.

Laboratory experiments were carried out first by the British Foot-and-Mouth Disease Commission in 1927 and in 1931 (32, 33). The results showed that the virus of foot-and-mouth disease can survive for long periods in bone marrow and in blood at temperatures ordinarily used

in the meat trade. Since the war the subject has been investigated by several authors using modern methods, and the results have been in keeping with those formerly obtained (see Appendix I).

It was Moosbrugger (34) who succeeded in demonstrating virus in imported frozen meat. An outbreak occurred in Switzerland which probably could be attributed to imported frozen pork. Lymph nodes were removed from six hams of the suspected meat, and after injection of extracts into cattle tongues, two of the nodes were shown to contain virus of type A. Thus, it has been possible for the first time to demonstrate virus in frozen meat from the ordinary trade and as far as it is known, this has not been repeated.

The epizootiological importance of infection from meat has clearly been shown in the United Kingdom and Greece.

In the United Kingdom (35) chilled and frozen meat imported from infected South American countries is thought to be responsible for more primary outbreaks of foot-and-mouth disease than any other single cause. For instance, during the years between 1939 and 1950 there were, in all, 355 primary outbreaks in Great Britain, of which 243 were attributed to imported meat. In the United Kingdom (36) it is considered that there are two sources of infection: from the continent of Europe, especially at certain times of the year, e.g. when large migrations of birds are occurring, and from imported infected meat and meat products. The patterns of the infection from these sources are clear. Since the disease has now been well controlled, largely by vaccination in most western European countries, invasion from the Continent is now found only in the south and south-eastern coastal areas of Great Britain.

On the other hand primary outbreaks, the source of which is considered to be imported meat, occur in any part of the country in which imported meat is distributed.

The total number of outbreaks in the United Kingdom in 1957, for instance, was 184 of which 43 were considered as primary and 141 as secondary outbreaks. The probable origins of infection in the 43 primary outbreaks were:

Continental 17

Imported meat from South American countries 23

Continental and imported meat equally possible . . 3

In Greece (37) a number of outbreaks have also occurred which have been attributed to imported infected South American meat. During the 1960-61 epizootic (38) there was clear evidence that such outbreaks had taken place. This epizootic started with some outbreaks in September near the Greek/Turkish frontier and were caused by virus of type O. Also in September, 1960, outbreaks occurred in a region in northern Greece in a piggery where the pigs were fed on waste material from frozen meat; on this occasion the outbreaks were caused by virus of type C. Later, similar outbreaks, caused by virus of type A appeared in another region in piggeries in which the pigs had also been fed on waste material from frozen meat.

Possible Transmission of Foot-and-Mouth Disease by Wind

The possibility of transmission of foot-and-mouth disease virus by air has been studied in the field and in two well-controlled laboratory experiments. The southern Scandinavian region is the part of Europe where this question seems to have most importance and it is

here that the field studies have mainly been carried out. Veterinary authorities in the Scandinavian countries are strongly of opinion that air-borne transmission of the virus accounts for the occurrence of primary outbreaks: this in fact is the only feasible explanation for the origin of several of the primary outbreaks on some isolated farms in these countries. Together with Sven Andersen the writer (39) studied this subject in Denmark and he also obtained information from the Danish veterinary authorities (40) and the views of the veterinary authorities in Sweden (41) and in Norway (42).

When northern Germany is infected, primary outbreaks of foot-and-mouth disease appear on the Danish Islands opposite Germany. These outbreaks have occurred far from the usual routes of commerce and travel and at times when no migration of birds was taking place. Primary outbreaks on the islands have usually been found when there were strong southern and south-western winds. A study of the distribution of outbreaks in Denmark shows that infection from Germany finds its way across the sea to the islands more often than across the land to Jutland.

In the study mentioned above the extension of foot-and-mouth disease in northern Germany and the direction of the wind during the last 14 days before a number of outbreaks occurred in Denmark was investigated for the period 1910-1938. It was found that, in the 14 days preceding the primary outbreaks in Denmark, south-western, southern and south-eastern winds blowing from northern Germany over the Danish islands had been prevalent. The distance from northern Germany to the Danish islands is 40-60 Km.

When foot-and-mouth disease has reached a certain extension in Denmark, Sweden becomes infected. Studies in Sweden (43), which were carried out when all infected herds were being slaughtered, have shown that there is a close relationship between the numbers of outbreaks in Sweden, the extension of the disease in Denmark and the direction and strength of the wind. The distance between eastern Denmark and Sweden is some 5 - 30 Km. and between Jutland and Sweden, some 100 Km.

Primary outbreaks of foot-and-mouth disease in Norway have always occurred in the late autumn, and only when the infection has been present in the most northern part of Denmark. They have been found on both sides of the Oslo Fjord and on the east coast down to the southern tip of the country, and often in very isolated farms near the coast. It should be noted that it is the practice to slaughter all infected herds in Norway.

The question of air-borne transmission has, as mentioned above, also been investigated by laboratory experiments.

Traub and Wittman (44) carried out two experiments in which susceptible calves and piglets were exposed to a current of air from a shed harbouring infected animals. Under the experimental conditions chosen, outgoing air from the sheds harbouring infected cattle did not produce foot-and-mouth disease in exposed susceptible animals.

Malmquist, Osteen, Johnson and the writer (45), in the collaboration between the Danish Veterinary Institute for Virus Research and the United States Department of Agriculture, carried out four laboratory experiments at the Danish Institute. In them air was blown from a box in which there were infected cattle to a box in which there were normal

susceptible cattle. The distance between the boxes was about 10 meters. In each experiment five cattle were infected by intradermo-lingual inoculation of virus and five were used as control animals. All the 40 cattle used in the experiments were proved to be highly susceptible to foot and mouth disease.

In the first experiment the five donor animals were inoculated with the Mexican Pueblo strain of type A virus; the five control animals did not become infected.

In the second experiment, the donor animals were inoculated with virus of type O; the control animals contracted foot-and-mouth disease.

In the third and fourth experiments some changes were made in the experimental conditions: the muzzles and tongues of the control animals were scarified to increase their susceptibility, and 48 hours after the inoculation of the five donor cattle, a cloud of sterile hay dust was introduced into the box as a possible mechanical carrier of the virus. In these experiments the donor cattle were inoculated with the Mexican strain and with virus of type O, respectively. In both experiments the control animals contracted foot-and-mouth disease.

These laboratory experiments showed that the virus of foot-and-mouth disease can be transmitted by air, under certain conditions. Although the distance over which the transmission occurred was only some 10 meters, it would appear possible that the virus can be air-borne over considerably longer distances under certain circumstances. Favourable conditions seem to exist in the northern German and Scandinavian areas which are divided by sea and where hight winds are prevalent during the dark period of the year in late autumn and winter.

Transmission of Foot-and-Mouth Disease by Birds

For many years it has been considered highly probable that foot-and-mouth disease can be spread by birds. In the United Kingdom it is believed that "apart from infected imported meat, birds are the most likely cause of primary outbreaks that occur in this country" (46).

Dijkstra in the Netherlands (47) also studied this problem and came to the conclusion that meadow birds and water birds play a great part in carrying the virus. In Denmark, also, it is believed that birds moving from northern Germany to the Danish islands can transmit the virus. It is, however, mainly in the United Kingdom that this question has been the subject of study. In connection with the many invasions of foot-and-mouth disease in Great Britain in 1937-1938 Eccles carried out some laboratory experiments (48). The results did not show much evidence in favour of the hypothesis that birds were of importance as virus carriers in nature, but, on the other hand, the theory was not excluded.

In connection with the many invasions of Great Britain during the 1951-52 epizootic the subject was examined by Wilson and Matheson (49). They concluded that "Available evidence is adequate to establish a prima facie case against birds and especially starlings on migration, as a means whereby foot-and-mouth disease is introduced into Britain; further, that the frequency of its introduction is dependent on the extent of the disease in certain coastal areas of the Low Countries and north-east France at the season of bird migration".

In the spring and summer of 1952 many outbreaks occurred in the southern coastal counties of England. At the same time there was much infection in the northern coastal counties of France. The evidence

suggests "that in 1952 for the first time the spring migration may have been responsible for introducing infection into this country".

Transmission of Foot-and-Mouth Disease by Fodder and Vegetables

This subject has been investigated mainly by Moosbrugger who reported on it on three occasions - at the 14th International Veterinary Congress in London, 1949 (50); at the 22nd Session of the O.I.E. in 1954 (51); and at the Symposium on Vesicular Diseases at Plum Island in 1956 (52). In several instances he found virus in fodder and vegetables imported into districts in Switzerland which had hitherto been free from foot-and-mouth disease. The epizootiological importance of infected fodder and vegetables is obvious. For instance, 11 primary outbreaks were reported from 1947 to 1953 in Switzerland in which there were present all the conditions that prove the transmission of foot-and-mouth disease virus by plants. These 11 outbreaks caused several secondary outbreaks which, in the most severe instance, totalled 92 in a single canton.

Foot-and-Mouth Disease Institutes as sources of infection

During recent years there have been official reports that foot-and-mouth disease virus has escaped from foot-and-mouth disease institutes in the following countries: Yugoslavia in 1959 (53), the United Kingdom in 1960 (54) and the Netherlands in 1960 (55).

In Yugoslavia in February 1959 an outbreak caused by virus of type O occurred on a farm some 24 kilometers from the Subotica Institute. All the animals had been vaccinated eight days previously. It was thought that the infection was brought to the farm from the Institute by an Institute worker who had failed to observe the necessary precautions.

In the United Kingdom in January 1960 an outbreak caused by virus of the SAT II type occurred on a farm within about a mile of the Pirbright Institute. It was accepted that this outbreak arose from an escape of this type of virus from the Pirbright Institute. There was no evidence of any direct contact but it seems possible that the virus escaped through ventilators in a barn containing cattle infected with the virus and was conveyed to the infected farm by pigeons which were prevalent in a green crop near the institute.

In the Netherlands in February 1960 three outbreaks appeared 30 - 40 kilometers from Amsterdam, in each of which virus of type O was identified. From careful enquiries it seemed highly probable that all three outbreaks were associated with the escape of virus from the foot-and-mouth institute in Amsterdam through the Amsterdam abbatoir, part of which is reserved for accommodating cattle used in testing vaccines.

It is highly probable that such escapes of virus have taken place in the past also from other foot-and-mouth disease institutes in Europe. However, in countries where foot-and-mouth disease is enzootic, such outbreaks might not be thought to be connected with the institutes and therefore have not been investigated. Foot-and-mouth disease institutes certainly constitute a latent danger of infection. It is for this reason that a joint meeting of representatives of the European Commission and the Foot-and-Mouth Disease Commission of the OIE was held in January 1960 when it was strongly recommended that no European institute should engage in the preparation of vaccine from exotic types of foot-and-mouth disease virus without approval (56, 57).

Transmission of Foot-and-Mouth Disease by Virus Carriers

The question of virus carriers is of the greatest epizootiological importance, and has, therefore, been under investigation for many years and subject to much discussion and differences of opinion.

Ever since the study of foot-and-mouth disease was inititated outbreaks have been observed in the field in which animals recovered from foot-and-mouth disease were brought together with susceptible animals. Outbreaks have been observed when recovered animals were brought into clean herds, as well as when susceptible animals were introduced into herds where previously there had been foot-and-mouth disease. In many such outbreaks it was believed that the infection was caused by the recovered animals, either by simple transmission of the virus or by its excretion.

However, it must be pointed out that, in studying the question of carriers, only outbreaks caused by recovered animals introduced into susceptible herds in clean stables or in pastures can be accepted and only occurring under circumstances in which there is no other possible source of infection. In stables where there has been foot-and-mouth disease previously it is impossible to exclude the presence of virus, and in countries where foot-and-mouth disease is enzootic the possibility of infection from sources other than recovered animals cannot be entirely excluded.

Over the years, many well-controlled observations and investigations have been made, so it should now be possible to form a clear opinion on the importance of virus carriers. Some of the observations will now be referred to, beginning with those made in Sweden and the United Kingdom, at times when they were completely or practically free from foot-and-mouth disease.

From Sweden, Forssman (58) reported an outbreak in 1897 and another in 1898, both at times when the country was completely free from foot-and-mouth disease. In 1897, a bull was imported from the Netherlands and was introduced into a herd in which the disease appeared two weeks later. In 1898, another bull was imported from the Netherlands and introduced into a herd in which foot-and-mouth disease was found five months later. It seems likely that these two animals brought the infection from the Netherlands to Sweden.

In the United Kingdom during the epizootic of 1922-24, when there were over 4,000 outbreaks, the traditional slaughter policy was partly given up and 105 diseased herds were dealt with by isolation. From these herds later on, animals were sold and introduced into herds in which there had never been foot-and-mouth disease. Outbreaks occurred in four of these herds and are reported as possibly having been caused by virus carriers; in three of them details are given (59).

In the first case foot-and-mouth disease occurred in a herd in November 1923 and from it a bull and a heifer were sold in July 1924 and introduced into another herd in which foot-and-mouth disease broke out 33 days later, i.e. about eight months after the two animals had recovered from foot-and-mouth disease.

In the second case, the disease was present in a herd in November 1923. In July 1924, a bull and a cow were sold to a herd where foot-and-mouth disease broke out about eight months after the introduction of these two animals, i.e. 15 months after they had recovered from foot- and-mouth disease.

The third case concerns a herd in which there was foot-and-mouth disease in November, 1923, and from which a bull and a heifer were sold to another herd also in July, 1924. About eight months after foot-and-mouth disease broke out in the herd into which they had been introduced, i.e. also about 15 months after the two introduced animals had recovered from foot-and-mouth disease.

Observations were made in Switzerland in 1927 by Bürgi (60) in a report on the general measures of control of foot-and-mouth disease, in which he expressed his opinion on the epizootiological importance of virus carriers. His opinion was that foot-and-mouth disease virus can persist in the organism of the recovered animal. He believed that virus can live for some months in the hoofs before it is eliminated, a theory first presented by Zschokke (61). According to experience collected over a number of years, Bürgi estimated that about 3 percent of recovered animals remain virus carriers and excrete virus intermittently. Most infections from them usually take place five to six months after the original infection, but cases are described in which they occur much later. Such infections were observed under the following conditions:

1. When recovered animals are mixed with animals which had never had the disease.
2. When susceptible animals are introduced into a recovered or an apparently recovered herd.
3. Among calves born from cows which have had the disease and which have remained in the same stable; in this case the infection occurs only when other animals from outside which have also had the disease are introduced into the herd.

4. When animals are brought together in a herd in which the disease occurred at different periods.

In considering these observations, however, only outbreaks occurring when recovered animals are introduced into clean stables (herds) should be accepted as being probably caused by virus carriers. Of Bürgi's four conditions only number 1 probably fulfils this requirement. It applies to only five of the 16 examples quoted by Bürgi.

In 1928, Olitsky, Traum and Schoening (62) reported on experiments carried out with 20 cattle from the field selected by Bürgi as suspected of being virus carriers and also with animals which had recovered from experimental foot-and-mouth disease.

The following is a summary of the first group of experiments:- "20 specially selected recovered cattle, from 58 to 234 days after infection with foot-and-mouth disease, did not transmit the disease when placed in contact with 35 cattle and 4 hogs. The periods of contact in these cases were from 56 to 87 days.

The bile from 13 of the recovered cases was injected subcutaneously into 16 cattle. Material from the foot lesions of 10 recovered cases was injected into the mucous membrane of the lips of six cattle. All these injections failed to infect.

32 of 33 cattle and the 4 hogs were proved to be susceptible to type O virus, and 11 of 13 of the same cattle and the 4 hogs were infected with type A virus one month after exposure to type O virus."

In the experiments with animals which had recovered from experimental foot-and-mouth disease, 21 cattle and one pig were used. They were slaughtered from 20 to 186 days after the infection and material was

taken from the foot lesions and injected intradermally into the posterior pads of 68 guineapigs. Foot-and-mouth disease occurred in one guineapig which had been inoculated with material taken from a heifer 34 days after infection. The authors state:- "The question arises in this instance whether there is a remote possibility that virus may have contaminated foreign material which entered the space between the old and new horn where it was retained and was later included in the inoculum. The hoofs, however, were washed, scrubbed, and were otherwise carefully controlled against contamination with outside virus, but since the latter may be active in a dilution of 1 : 10,000,000, the question as to whether such contamination occurred in this single instance must remain unanswered at present".

In 1928, Brandt (63) carried out nine series of experiments in Germany for the purpose of demonstrating virus in the hoofs of animals recovered from foot-and-mouth disease. The material to be tested for virulence was taken from 103 recovered cattle (12 to 159 days after infection) and nine pigs (5 to 123 days after infection). The material was inoculated into guineapigs and swine. In only one case was virus found and as there was some possibility of accidental infection this occurrence has no decisive value. Brandt states that it is possible that animals in very rare cases, can become virus carriers but that their number is much smaller than that believed by the Swiss authorities.

The fact that animals recovered from foot-and-mouth disease can excrete virus over a period of several months has, however, been proved by some laboratory experiments.

The first experiments were carried out by Waldmann (64) and by Waldmann, Trautwein and Pyl in 1931 (65) and resulted in the demonstration of foot-and-mouth disease virus in the bodies of recovered animals after the material had been concentrated according to the method of Pyl (66) by which virus can be demonstrated in apparently non-infective doses after concentration up to 1,000 times. These workers used a large number of guineapigs and cattle which had recovered from foot-and-mouth disease. In experiments with guineapigs, virus was demonstrated in some cases in kidney, bladder, blood and urine some time after infection. In experiments with 500 recovered cattle, virus was demonstrated from time to time in blood of 13 cattle (2.6 percent) from 7 to 158 days after infection. In a second experiment, 44 cattle were slaughtered and virus was found in the urine in three cases, the last case being 33 days after infection. In a third experiment, urine was taken from eight cattle over a period of many weeks and examined for the presence of virus. Virus could be demonstrated in urine from six of the cattle at different intervals from 18 to 246 days after infection.

The authors made the following comments on their experiments: the cattle which had been used in the experiments had previously been used for the production of hyperimmune serum; they had, therefore, been exposed to from 2 to 6 infections of different virus strains in quick succession and they had, furthermore, been injected with extra doses of virus.

However, Waldmann states that the experiments show in an incontestable manner that there exists in foot-and-mouth disease real permanent excreters of virus and that the virus is excreted through the urine. The experiments do not permit any conclusion as regards the number of permanent excreters under natural conditions.

In 1937 Galloway (67) carried out similar types of experiments in the United Kingdom, using guineapigs; however, all were negative.

In 1958 Michelsen (68) in Denmark reported on some experiments similar to those of Waldmann, Trautwein and Pyl. He investigated 321 recovered guineapigs and 44 recovered cattle, using Pyl's method of concentration of virus. In extracts from different organs of the guineapigs he found virus in two cases 22 and 30 days respectively, after infection. The cattle were investigated for the presence of virus in the urine from 10 to 50 days after infection, but all the samples of urine were negative.

In connection with the epizootic in Denmark of 1951-52 Michelsen (69) investigated 25 cattle from the field which were suspected of being virus carriers. Samples of urine were taken during a period of 10 to 14 days and examined for the presence of virus, after concentration according to Pyl's method: in no case could virus be demonstrated.

The following field observation reported by Michelsen in 1951 (70) may also be mentioned: a herd which was vaccinated with a bivalent OA vaccine contracted foot-and-mouth disease six weeks after vaccination. Virus material from two of the infected cows was shown to contain both O and A virus. As there was no epizootic in Denmark at that time it seems likely that the vaccines had contained free virus which had multiplied in the animals and caused foot-and-mouth disease.

In 1959, van Bekkum, Frenkel, Frederiks and Frenkel (71) found that a large proportion of cattle which had recovered from foot-and-mouth disease excreted virus in the saliva over a period of several

months. The virus could be demonstrated in material collected from the oesophagus by inoculation into unweaned mice or into the tongues of susceptible cattle. After contact with clinical cases of foot-and-mouth disease, vaccinated animals could develop a similar carrier stage without having shown symptoms of the disease. However, susceptible cattle kept in contact with such excretors remained unaffected, even if the oral cavity was swabbed with infected saliva. No cases of foot-and-mouth disease occurred in vaccinated or unvaccinated cattle or in unvaccinated pigs when introduced into a herd known to contain such carriers or if kept on the same premises with such cattle.

Some experiments which included very large numbers of recovered animals have been carried out and observations have been made in the field in different countries.

In this connection Olitsky, Traum and Schoening (72) in their report referred to a report by Mohler (73) about an experiment made during the 1914 and 1915 outbreaks of foot-and-mouth disease in the United States. They state:-

"In the early part of November 1914, foot-and-mouth disease appeared among 747 cattle on exhibition at the National Dairy Show in Chicago. Special permission was granted by the Secretary of Agriculture to retain these cattle under absolute quarantine until they had fully recovered, and by test proved not to be disseminators of the virus. On 26 December 1914, arrangements had been made to remove all but seven cattle to Cicero, Ill. These seven cows were slaughtered. Five had persistent mastitis and two reacted positively to tuberculin. The other 740 cattle were sprayed and scrubbed with

3 percent cresol solution, were taken through a foot bath and placed overnight in cleaned and disinfected quarters, and were then placed in box cars and transported to Cicero, Ill. On 25 March 1915, 50 head of young cattle were placed in contact with the recovered cases. In addition to this contact exposure, injections of saliva, faeces, urine, vaginal discharge and scrapings from the interdigital spaces were made into the susceptible animals. On 8 April, 50 hogs were added to extend the test. They were fed on milk from the recovered cows and were also allowed to consume the leavings and droppings from the cattle. Until 30 May no cases of foot-and-mouth disease had developed and the animals were released from quarantine."

Thus, in this particular group of 740 animals which had recovered from foot-and-mouth disease no carriers were fount.

In 1931 Forssman (74) reported on some field observations in Sweden in connection with epizootics during 1924-27, mainly in the south of the country. There were two waves of infection, the first caused by virus of type O, the second mainly by virus of type A. During the first wave in 1924/25, 4,849 farms became infected, of which 3,896 were situated in the district of Malmö, an area in the extreme south-west of Sweden facing the Danish island of Zealand. During the second wave in 1926-27, 6,512 farms became infected, of which 4,665 were situated in the district of Malmö. Among the farms infected during the first wave, some 32 percent became reinfected during the second wave. On 1 July 1927, the district of Malmö was declared free of foot-and-mouth disease. After this there was one new outbreak in December 1927, one in February 1928 and one in April

1928, and in each of them the infected herds were slaughtered. On 15 May 1928, the district was again declared free of foot-and-mouth disease. After that date the whole of Sweden remained free until 4 December 1929, when a new outbreak appeared in the district of Malmö, on this occasion caused by virus of type O. Thus the district of Malmö had been free from foot-and-mouth disease for 1½ years, or 2½ years except for the three outbreaks mentioned above.

During the two waves of infection, 205,136 cattle in the Malmö district had been infected. However, 28,944 of these animals had been infected twice, 9,855 had been slaughtered and 8,312 had died, which reduced the number to 158,025, representing 65.5 percent of the total number of cattle in the district. Among this considerable number of recovered cattle, there was a possibility that virus carriers could be present.

When the disease was over, the decimated herds in the Malmö district, in which there had been a total loss of some 18,000 cattle, were gradually renewed, the replacement beginning one month after the end of the disease and continuing for about two years. Important parts of the replacement were the introduction of susceptible cattle from outside, and by breeding in the herds. Apart from the three outbreaks mentioned above, no outbreaks took place in the Malmö district during 2½ years (there is no information as to whether the three outbreaks were in recovered herds).

Furthermore, when the epizootic of foot-and-mouth disease was over in Malmö this district was again opened for normal trade in cattle on 1 July 1927 and from then onward, about 100 cattle were sold monthly to

other, mainly central, parts of Sweden, where the whole cattle population was highly susceptible to foot-and-mouth disease. Thus, during $2\frac{1}{2}$ years some 2,500 cattle, of which some 65.5 percent had recovered from foot-and-mouth disease were placed in susceptible herds: not a single outbreak of foot-and-mouth disease was reported.

This was a practical epizootiological experiment on a large scale: 1) normal susceptible animals were placed in recovered herds, and 2) recovered animals were placed in susceptible herds. What is reported here proves that the chronic virus carriers did not play any part in the spread of foot-and-mouth disease in Sweden during the period mentioned. It should, however, be noted that the purchase of animals did not begin until one month after recovery and that no sale was permitted until 20 days after freedom from the disease. The conclusion therefore, bears no reference to the period within about two months after infection. Furthermore, the conclusion is valid for virus of type A and for virus of type O if it is excreted after $1\frac{1}{2}$ years following infection.

In 1951 Schang (75) reported from Argentina that he had worked with problems of virus carriers for many years and that he does not deny their existence, but only in exceptional cases. In 1926 he made the following observations: in a group of 600 cattle all had had foot-and-mouth disease and 20 days after their recovery, 50 susceptible cattle were put together with them by mistake and remained with them on the same pasture for several months. No foot-and-mouth disease was observed among the 50 susceptible animals so there could not have been any carriers among the 600. Similar types of experiments were reported over 20 years

at different breeding farms of cattle and pigs. In one of the farms, experiments were carried out every time there had been an outbreak of foot-and-mouth disease; in six cases with diseased cattle and in nine, with diseased pigs. Always, after a period of 10-15 days after the last case of the disease, the animals were considered to have recovered and were permitted free movement and mixing within the breeding station. These mixings had never caused any outbreaks of foot-and-mouth disease. These experiments were carried out with groups varying from 100 to 800 cattle and from 10,000 to 18,000 pigs. In 1959 Schang (76) reported that there is no evidence of the existence of virus carriers in Argentina.

In connection with the foot-and-mouth disease epizootic in Denmark in 1938-39 the importance of virus carriers was studied by Sven Andersen and the writer. The position in Denmark up to the epizootic of 1938-39 was that from November 1929 until September 1933 there had been a limited epizootic which had caused some 19,000 outbreaks. After October 1933 all infected herds in Denmark had been slaughtered. The large European epizootic of 1938-39 started in Denmark in the autumn of 1937 and until the beginning of July 1938 all infected herds were slaughtered. In July 1938 when general slaughter was abandoned, the 200,000 herds in Denmark posessed, therefore, a high degree of susceptibility to foot-and-mouth disease. The disease had also a very severe course. The number of monthly outbreaks from 1 July 1938 until 31 December 1939 is given in the following table. During July/October 1938 slaughter was continued on a limited scale and in all, 312 herds were slaughtered.

T A B L E

Monthly numbers of outbreaks

1 9 3 8

July	August	September	October	November	December
880	5,113	6,035	19,924	44,112	22,262

1 9 3 9

January	February	March	April	May	June
5,415	887	478	270	142	55
July	August	September	October	November	December
30	25	9	30	83	270

From the table it will be seen that the epizootic had its peak in November 1938, with about 44,000 outbreaks, that it had a normal course and that it was practically over by the middle of 1939. Some 105,000 herds were infected during that period, or a little more than 50 percent of the total number of the herds in Denmark. Practically all outbreaks during the epizootic were caused by virus of type O. From November, 1938, some few reinfections caused by virus of type A occurred and up to 1 April 1939 this type was demonstrated in 126 cases. From the table it will also be seen that there was an increase in the number of outbreaks in the last months of 1939. This was the beginning of a new epizootic caused by virus of type A which lasted until the middle of 1940 with some 4,500 outbreaks.

As this epizootic, due to virus type A could be predicted, the development of the foot-and-mouth disease situation was closely observed between 1 July 1939, and 31 December 1939. Questionnaires

were sent to the veterinary practitioners in order to obtain as much information as possible on the nature of the 447 outbreaks during the period and particularly on the number of outbreaks caused by virus of type A. The data collected also gave some information on the role played by possible virus carriers in the spread of foot-and-mouth disease. Satisfactory information was received about 352 of the outbreaks, which could be classified into four different groups.

1. In 86 outbreaks none of the animals had had the disease during the large, earlier epizootic, nor were any of them in the region where there were reinfections caused by virus of type A. The 86 outbreaks were, therefore, considered as being part of the large O epizootic. Most of these outbreaks had occurred in districts which were infected last and least heavily in the summer and autumn of 1938 and the winter and spring of 1939.
2. In 111 outbreaks the herds had been infected during the large epizootic and the animals which were sick at the time the report was made had either been purchased or had been born in the herd since the last outbreak. These outbreaks were distributed fairly evenly throughout the country.
3. In 44 outbreaks the herds had not had foot-and-mouth disease previously and animals which had recovered from the disease had been introduced into the herds sometime before the outbreak. During the outbreak the introduced recovered animals did not as a rule show any symptoms of the disease: in some few cases, however, they were mildly affected. These 44 outbreaks occurred in the same districts as the 86 mentioned under 1. It is, therefore, very questionable whether these outbreaks were caused by the introduced recovered animals or by circulating virus.

4. In 111 outbreaks the herds had been affected in the autumn of 1938 or in the winter of 1939 and now had foot-and-mouth disease caused by virus of type A.

Of the four groups only 3 is of special interest from the point of view of carriers: the outbreaks occurred in herds which never had had the disease and to which recovered animals were introduced. However, these 44 outbreaks appeared in regions where, at the same time, 86 other new outbreaks occurred. Introduction of virus by other means than the introduced recovered animals can, therefore, not be excluded.

As already mentioned, Bürgi stated in 1927 that, according to observations made in Switzerland of animals recovered from foot-and-mouth disease, about 3 percent became virus carriers. During the Danish epizootic from July 1938 to July 1939 some 105,000 herds out of a total of 200,000 became infected. That means that about 50 percent or some 1,500,000 cattle had foot-and-mouth disease during the epizootic; that would again mean that there would be some 45,000 possible virus carriers distributed in the Danish herds by 1 July 1939; thousands of recovered herds would thus contain one or more such carriers. It is obvious that this large number of carriers would cause a large number of outbreaks in different ways: in the recovered herds among introduced animals, or among susceptible calves born into the herd after the first outbreak, or on being introduced into some of the 50 percent of the susceptible herds. According to Bürgi the great proportion of outbreaks caused by virus carriers should occur 5 to 6 months after the first outbreak. If this were true for Denmark, as the large number of first

outbreaks occurred in October/December 1938, when, in all, some 86,000 herds were infected, a large number of secondary outbreaks would probably occur during March/June 1939. The table gives no indication of such an increase in the number of outbreaks: on the contrary, it will be seen that the epizootic had a normal course and that from 1 February 1939, the number of outbreaks rapidly decreased. It must be noted that no records about reinfections after 1 February until 1 July 1939 are available.

CONTROL OF FOOT-AND-MOUTH DISEASE

Different Methods of Control

For many years the control of foot-and-mouth disease has been a problem of much economic importance in most European countries. The methods have varied in different countries but the objectives have been similar: to prevent outbreaks and, when they occur, to eradicate the source of infection and try to arrest spread. The prevention of invasion by such measures as quarantine of animals and control of importations of animals and products of animal origin is, of course, an important objective.

During the period dealt with in this review the following main methods of control have been used: stamping-out, isolation of infected herds, use of hyperimmune or convalescent serum, vaccination in different forms, i.e. mass vaccination, ring vaccination, border vaccination and vaccination combined with slaughter of infected herds and the application of strict veterinary measures.

The Stamping-out (Slaughter) Policy

By the stamping-out policy in the control of foot-and-mouth disease is meant slaughter of infected herds combined with the application of strict veterinary measures without vaccination or serum treatment. Only a few European countries with especially favourable geographical positions have successfully applied this method over a number of years: the United Kingdom, Ireland and Norway.

The stamping-out or slaughter policy was introduced in Great Britain in 1892 (77). It was partly abandoned during a serious epizootic in 1922-24 and isolation of some infected herds was permitted. Since then, however, a stamping-out policy has been strictly maintained.

Every year since the 1922-24 epizootic some outbreaks ranging from 8 to 670 have occurred. The livestock in the country are highly susceptible to the disease because no vaccination or serum treatment is used. This, together with the heavy concentration of animals and the amount of movement of both livestock and people, increases the risk of spread of the disease following its introduction into the country. Much experience has now been gained in the United Kingdom in the application of a stamping-out (slaughter) policy and all the problems relating to it.

The policy and its problems have been discussed at several of the Sessions of the European Commission for the Control of Foot-and-Mouth Disease; and the experiences were very valuable in formulating the Commission's overall plan of control in 1957 (78). It is stressed in the plan that the following points are essential for a stamping-out policy:-

1) Early notification of a suspicion of the presence of the disease must be available.

2) A very meticulous system of dealing with such reports must be in force and must be readily put into effect - the system must include rapid diagnosis, immediate control of movement of stock over an area, immediate quarantine of the suspected or infected farm, tracing of all contact animals and slaughter of direct contacts on other farms, e.g. animals recently moved off the infected place and animals handled by the owner of the infected place or his veterinary surgeon after contact with infection.

3) There must be rapid means of slaughter and disposal of carcases on the infected place.

4) It is essential to have an organization capable of dealing with all the detailed tracing of stock which is necessary.

5) A system of recording movements of stock must be permanently in force and enforced to allow of easy tracing of animals.

6) Visits to examine stock in the vicinity of outbreaks must be made to discover secondary outbreaks as early as possible and also to discover whether the first reported case is, in fact, the primary one.

7) There must be considerable elasticity in financial arrangements to allow of vigorous pursuit of the policy.

8) The farming community must be willing to cooperate in every aspect of the work.

When the Commission's overall plan of control of foot-and-mouth disease was drawn up it was considered that in most European countries a stamping-out policy, not supplemented by vaccination, was impracticable, but should be the ultimate objective.

Some further details of the stamping-out (slaughter) policy as operated in Great Britain were explained at the Eighth Session of the Commission (79) in 1961. The following extract is taken from the Report of that Session:-

"The procedure followed in Great Britain during outbreaks of foot-and-mouth disease is well recognized and the "infected area" procedure is adopted. This inv[illegible]e stopping of all movements of animals in an area of 10 miles radius around the outbreak. This is maintained until 14 days have elapsed since the last outbreak occurred; then the area is reduced to five miles and this, in turn, is maintained for a further seven days. Infected and in-contact animals are slaughtered

and destroyed by burial or burning, and disinfection of the infected premises is carried out. The movement of animals onto and from infected farms is traced. In the two-mile radius around the infected farm all the premises are visited and the stock inspected. This is done to ensure that all the animals in that area are free from disease and that the farmers are alerted to the need of reporting any suspicious case as soon as it comes to their notice. This procedure of inspecting farms in the two-mile area is also of considerable assistance in cases where no specific origin has been found for the original case and, occasionally, the source of infection is discovered during these inspections.

When markets have been involved and there is danger of widespread distribution of stock, the controlled area procedure is adopted; this arrests the movements of animals over wide areas and enables the veterinary staff to carry out an inspection of these animals until movement restrictions on individual farms have been imposed. When this is accomplished the controlled area restriction is withdrawn. This controlled area restriction is sometimes used where there is widespread distribution of cases throughout the country and in order to prevent the possibility of infected animals entering markets. This control area is maintained until the incidence of disease has been considerably reduced.

Isolation of Infected Herds

In former days isolation of infected premises was the most essential part of control of foot-and-mouth disease in many countries. The value of this method as compared with the stamping-out policy was studied by Forssman (80) in connection with epizootics in Denmark and Sweden in 1929-33. These epizootics, caused by virus of O type started almost simultaneously on the southern Danish islands and in southern Sweden and were a result of invasions from northern Germany. In Denmark infected herds were isolated; in Sweden they were slaughtered. Throughout Denmark there were some 20,000 outbreaks, of which the largest part occurred on the Danish islands. In Sweden there were in all 216 outbreaks, mainly in the southern part of the country. On the Danish island of Zealand, with an area of some 7,500 sq. km., and which is opposite the southern tip of Sweden, there were some 10,000 outbreaks. In the district of Sweden facing Zealand, with an area of some 4,700 sq. km., there were 146 outbreaks. Agricultural conditions in these two parts are very similar. Forssman concludes that the reason for the great difference between the course of the two epizootics in these areas must be the methods of control which were applied; in Denmark, isolation; in Sweden, slaughter; the value of isolation seeming to be doubtful, while the stamping-out policy giving brilliant results.

Although the results of Forssman's study indicate that under the given circumstances, the stamping-out policy was much superior to isolation of infected herds, the following points should also be noted. In Denmark during the 1929-33 epizootic there were only some 20,000 outbreaks compared with some 160,000 during the epizootic in 1924-27 and some

105,000 during that in 1938-39. While Sweden also applied slaughter of infected herds during the epizootic of 1938-39, this policy did not prevent invasion and some 7,000 herds became infected. The reason for the success of the stamping-out policy in Sweden in 1929-33 is probably that Swedish cattle were less susceptible to the infection because of the epizootic in 1924-27 and also the invading O virus was probably of low virulence.

PASSIVE IMMUNIZATION WITH HYPERIMMUNE AND CONVALESCENT SERUM

During the serious foot-and-mouth disease epizootics in the twenties, treatment of animals with hyperimmune or convalescent serum was introduced on a large scale in several countries. Trautwein (81) described the results of this method in Germany. When it was first introduced the animals were injected with hyperimmune serum at their home farms just before they were sent to shows and the results were very satisfactory. Even during periods in which there was widespread foot-and-mouth disease, outbreaks never appeared at such shows. Animals arriving at large markets were also treated with serum and outbreaks at markets became very rare. When they did occur, as a rule they were mild in character and did not spread. This was a great improvement because before this serum treatment was introduced, shows and markets played an important role in the epizootiology of foot-and-mouth disease and often caused explosive spread. Serum was also used in the field in different ways: directly, in infected herds for the protection of non-infected animals, in surrounding districts near infected herds and also strategically. All the results were very good.

During the violent epizootic of 1937-40 hyperimmune serum and convalescent serum were also used on a small scale. Serum thus became an important weapon in the control of foot-and-mouth disease. The passive immunity, however, lasted for only a relatively short time and serum is expensive to produce; this method of protection, therefore, could never find general application in the control of the disease.

CONTROL MEASURES DURING THE EUROPEAN EPIZOOTIC OF 1937-40

The measures taken to control the severe European epizootic of 1937-40 varied in the different countries. Three countries with especially favourable geographical positions succeeded in controlling the invasion by operating a slaughter policy: the United Kingdom, Norway and Finland. The United Kingdom was somewhat heavily invaded and from October 1937 to March 1938 had 275 outbreaks. Norway and Finland became only slightly affected at the end of 1938, with 21 and 6 outbreaks, respectively.

Several other countries on the Continent applied slaughter of infected herds: Switzerland, Poland, Denmark and Sweden. Although this slaughter was undoubtedly of some value it could not prevent the disease from penetrating into the countries and causing regular epizootics, although it seemed to limit the spread.

Switzerland was invaded from France at the beginning of September 1937 and although slaughter of infected herds was practised until the the epizootic was over, the disease gained a foot-hold and spread to a considerable extent throughout the country. From September 1937 to 26 February 1939 a total of 2,025 herds were slaughtered, while, during the epizootic there were some 19,400 outbreaks.

Poland was invaded from Germany in December 1937 and an attempt was made to follow the example of Switzerland. However, the pressure of the disease on the frontier soon became so intensive that the slaughter policy had to be abandoned except under special circumstances. In all, 411 herds were slaughtered. Some 11 percent of cattle in Poland were affected.

During the epizootic Denmark was first invaded in August 1937 and until July 1938 all infected herds, some 300, were slaughtered. In July 1938, however the intensity of the disease in northern Germany was overwhelming and the number of outbreaks in Denmark became so large that it was impossible to continue slaughter of all the infected herds. However, until November 1938, when the peak of the epizootic was reached, slaughter was continued and in all, 670 herds were slaughtered. During the epizootic some 105,000 or somewhat more than 50 percent of all herds in Denmark were infected.

Sweden was invaded from Denmark at the beginning of October 1938 and until 7 November all infected herds were slaughtered. Then, also Sweden had to abaondon the slaughter policy and limit it to sporadic outbreaks. In all, 801 herds were slaughtered. In southern Sweden some 7,000 or 20 percent of herds were infected but the continued slaughter policy prevented the disease from spreading much to the north.

In Norway there were 21 outbreaks, 10 in November 1938 and 11 in December, all of which were dealt with by slaughter.

In Finland all the six herds infected in December were slaughtered.

Thus, only two continental countries, with exceptional geographical positions, Norway and Finland, and with very limited numbers of outbreaks were able to carry through a slaughter policy to final success. The other countries had to abandon this policy because the invasion of the virus became too great.

In other countries the control of the disease was based on the application of veterinary police measures, but it is difficult to see how much this method influenced the course of the epizootic.

VACCINATION

The Vallée-Schmidt-Waldmann Vaccine

During this severe epizootic of 1937-40 an event of the greatest importance in the history of foot-and-mouth disease took place: an effective vaccine against the disease appeared and stood its first trial. The principles of the vaccine are based on experiments carried out with diphtheria toxin, by Ramon (82), who in 1923 reported that he had treated diphtheria toxin with formalin and heat and that the toxin had lost its virulence completely but had preserved its immunising effect. Ramon applied the term "anatoxin" to this inactivated diphtheria toxin. In 1925-26 Vallée, Carré and Rinjard (83, 84) inspired by the work of Ramon, carried out experiments in which they inactivated foot-and-mouth disease virus; this "anavirus" had a certain immunising effect. In 1927 Bedson, Maitland and Burbury (85) and in 1931 Gibbs (86) investigated also the effect of formalin on foot-and-mouth disease virus by the vaccination of guineapigs. They demonstrated that a virus suspension could be inactivated by formalin and thereby lose its virulence completely, but retained considerable immunising value: however, the immunity was of a short duration.

Soon after this, a new principle proposed by Sven Schmidt for immunisation against foot-and-mouth disease was worked out in Denmark - immunisation with virus adsorbed onto aluminium hydroxide. Schmidt had already initiated some work with Ramon's diphtheria anatoxin. Together with Linderstrøm-Lang (87) he purified the anatoxin by adsorption onto aluminium hydroxide followed by elution and so obtained a very concentrated antigen. Schmidt et al (88) also showed that following the addition of 10 percent aluminium hydroxide to a purified and concentrated anatoxin, very small doses could induce a strong immunity. During his work with diphtheria anatoxin Schmidt realized that the experience gained could be used in virus research. In 1934, Schmidt initiated collaboration with the Foot-and-Mouth Disease Institute on the island of Lindholm, Denmark. During this collaboration between Schmidt, Hansen and the Director of the Lindholm Institute, Schmit-Jensen (89), a number of experiments were carried out in which guinea pigs were vaccinated with foot-and-mouth disease virus adsorbed onto aluminium hydroxide. The present writer had the very interesting experience in the summer of 1935 of seeing these experiments brought to a conclusion. The results were brilliant and there could be no doubt that this new principle opened up new possibilities for vaccination against foot-and-mouth disease. Later on, Schmidt (90) investigated the vaccinating effect of virus adsorbates attenuated by heat, and also the vaccinating effect of virus attenuated by formalin and then adsorbed onto aluminium hydroxide. Furthermore, he demonstrated that culture virus could be used in a vaccine produced according to the new principle with good results, provided that the virus titre was sufficiently high.

The next step was to investigate the immunising effect of such vaccines on naturally susceptible animals, first of all, cattle. The investigations were started on Lindholm in 1936 and, at the same time, contact was made with some foreign foot-and-mouth disease institutes for the purpose of accelerating the investigations. The large German institute on the island of Riems took up the new problem, where a number of laboratory experiments were carried out on cattle by Waldmann and Köbe (91). In the spring of 1938 the experiments were so advanced that the vaccine could be tested out by a large field trial and the first results were reported at the Twelfth Session of the O.I.E. (92).

Waldmann and Köbe (93) also published details of the experiments which led up to the preparation of the new vaccine: Strodthoff (93) gave further information on the results of the field trial. A description of the method of preparation of the vaccine was given by Waldmann (94).

The position was, therefore, that following the results of work in France, England, Denmark and Germany, the Vallée-Schmidt-Waldmann vaccine became a reality.

Results of the use of the Vallée-Schmidt-Waldmann Vaccine

The Vallée-Schmidt-Waldmann vaccine appeared in the middle of the 1937-40 intensive European foot-and-mouth disease epizootic, and so could have no influence on the general course of the epizootic, partly also because of the very limited available amount. The epizootic, however, afforded an exceptionally good opportunity to test its value in the field. This was done first in Germany and soon afterwards in

Denmark. At the first large field trial in Germany some 40,000 cattle were vaccinated. The first results were summarised as follows (95):

1) The vaccine was shown to be innocuous: no infection was caused by the vaccine and no local reaction of any importance was observed under the field conditions.

2) An active immunity against field infection developed within 12 to 14 days: after that time the disease did not appear in any premises, and already after 5 to 6 days there was a marked degree of protection. In premises where the disease appeared 5 to 6 days after vaccination only some of the animals became infected.

3) In heavily infected localities so far the immunity lasted 2 to 3 months.

Later, Waldmann (96) reported that the vaccine creates almost 100 percent protection of a duration which is at least 4 to 5 months, in the presence of an epizootic.

A further report by Waldmann at the O.I.E. Session in 1939 (97) stated that vaccinated cattle were protected against infection for 8 to 10 months. He described the field use of the vaccine in the German province of East Prussia in 1938-39. In this province there were some 136,000 herds. The infection entered East Prussia from the west and south-west and vaccination was, therefore, first of all carried out along the western and south-western borders of the province. It should be noted that very severe sanitary measures were applied during the vaccination campaign. Although the amount of available vaccine was

limited the result of the campaign was that only 2 percent of the herds in East Prussia became infected, while the neighbouring regions to the west and south-west, where conditions were similar but where no vaccination was carried out, 30 to 40 percent of herds became infected.

Without any doubt the vaccination along the border was of the greatest importance for the whole of the province. The result of this vaccination led to the opinion that it would be possible to obtain total protection by total vaccination.

At the same O.I.E. Session Petersen (98) described the results of the use of the vaccine in Denmark, where large-scale production began in November, 1938. From the middle of November until the end of December 1938, some 74,000 cattle in 4,170 herds were vaccinated with a vaccine of type O. At this time the epizootic had reached its peak in Denmark and, therefore, the danger of infection was very great. Following the vaccination campaign, 431 of the vaccinated herds became infected: 192 during the first six days after vaccination, 142 from 10 to 12 days after vaccination and seven after more than 14 days. In most, the disease was reported as being moderate. The results of the vaccine must be considered as highly satisfactory as it was carried out in heavily infected regions.

At this session of the O.I.E. (99), the importance of the new vaccine was thoroughly discussed when the following statement was made: "O.I.E. recognises that control of foot-and-mouth disease has undergone a radical change by the use of active immunisation and that in the future the protection of a country can be envisaged and an epizootic can be eradicated even if it is widespread".

In 1942, Waldmann (100), in reporting on the use of the vaccine between February 1938 and April 1942, stated that 4,601,880 animals in some 460,000 herds had been vaccinated and that the immunity lasted for at least six months and, in general, eight months, the number of breakdowns in herds which had been vaccinated less than six months previously being 0.177 percent. The vaccines were prepared against virus of both O and A types.

Petersen (101) also reported that in Denmark between the middle of November 1938 and the end of April, 1942, 1,765,547 cattle in some 88,000 herds had been vaccinated: some 122,000 with O vaccine, some 263,000 with A vaccine and some 1,380,000 with bivalent OA vaccine. The results were excellent.

In 1948, in discussing modern control of foot-and-mouth disease, Flückiger (102) stated that vaccination against foot-and-mouth disease is most effective when combined with slaughter of infected herds. The following system of control was practised in Switzerland:

1) Immediate slaughter of infected animals;

2) Vaccination of exposed cattle;

3) Immediate disinfection of the infected and exposed farms;

4) Quarantine measures.

Soon after its appearance in 1938 several countries took steps to produce the new vaccine on a large scale and within a few years, vaccine was produced in Italy, the Netherlands and Switzerland, in addition to Germany and Denmark. After the war, and mainly after the large epizootic of 1951-52 foot-and-mouth disease institutes have been established throughout Europe and existing institutes were expanded.

Results of Vaccination during the European Epizootic of 1951-52

The control of the extensive European epizootic in 1951-52 was based mainly on vaccination in most European countries. However, the sudden appearances of the new variant of foot-and-mouth disease virus A_5 and of virus of the C type in the middle of Europe took the countries by surprise and complicated the control measures enormously. In addition, the facilities for the production of vaccine at that time were not nearly adequate to deal with the situation.

The 1951-52 epizootic started in the Federal Republic of Germany. It was found that animals vaccinated with vaccines containing the ordinary A types of the virus were not satisfactorily protected against the new A_5 variant; vaccines produced with that variant, on the other hand, had a very satisfactory effect, and their use in the Federal Republic of Germany, although limited, was undoubtedly of considerable importance in the control of the disease. In this connection, comparison between the epizootic of 1937-38 and that of 1951-52 shows that in 1937-38 there were some 703,000 outbreaks in Germany, while in 1951-52 the number in the Federal Republic of Germany was some 204,000.

Denmark was the first country to be invaded from the Federal Republic of Germany and here the control of the epizootic was based on isolation and vaccination. At the beginning of the epizootic there was a considerable amount of bivalent vaccine OA ready for use, and it proved to have some immunising value against the invading virus A_5. Large-scale production of A_5 vaccine was begun and the control of the disease became a race between the spread of A_5 virus and production of A_5 vaccine. Undoubtedly, the vaccination limited the losses to a

marked extent. In many of the infected herds the disease was extremely mild because of previous vaccination and often only some few of the animals were infected. It is highly probable that without vaccination against A_5 virus there would have been a repetition of the severity of the disease as in the 1938-39 epizootic, when some 100,000 herds became seriously infected. When the epizootic caused by C virus started in Denmark a considerable amount of vaccine against this type was available and it was possible to vaccinate on a large scale with the result that the number of outbreaks caused by C virus was limited to a few hundred.

There was a marked shortage of vaccine in Belgium against A_5 virus when the country was invaded from Germany and the epizootic extended widely. As in Denmark, however, a considerable amount of vaccine against the C type was available, and following the invasion of this type its spread was controlled. Generally speaking, vaccination in Belgium was valuable as shown by the number of outbreaks in the 1937-39 and 1951-52 epizootics: in the former there were some 100,000 and in the latter, some 59,000.

In the Netherlands the epizootic caused by A_5 virus was not very serious. A large proportion of the cattle had been vaccinated at the beginning of each year with bivalent vaccine OA and the A factor in the vaccine protected fairly well against virus A_5. C virus had never been demonstrated previously in the Netherlands with the result that the cattle had no immunity against this type. Vaccine against it was prepared and its use in the field gave very satisfactory results. The effect of vaccination in the Netherlands is reflected by the incidence of the disease during the 1937-39 and the 1951-52 epizootics: in the former there were some 265,000 outbreaks and in the latter some 27,000.

Also in Luxembourg foot-and-mouth disease was controlled mainly by vaccination, but it was impossible to obtain a sufficient supply of vaccine. Nevertheless, there was only 1,329 outbreaks in 1951-52 as compared with some 5,000 in 1937-38.

When France was invaded by A_5 virus at the end of 1951 there was a marked shortage of vaccine. The effect of vaccination was not very obvious in France, for the total number of outbreaks during the 1951-52 epizootic was some 320,000 and during that of 1937-38 some 378,000.

Austria was invaded in November 1951. Here, also, control was based on the application of veterinary sanitary measures and vaccine had to be imported and this resulted in a marked shortage of supplies. As in the other countries in which vaccination was practised, however, there was a marked difference between the situation in 1937-38 and in 1951-52 in Austria. During the former there were some 38,500 outbreaks and some 12,600 during the latter. The measures taken also prevented the spread of the disease from Austria into the two neighbouring countries, Yugoslavia and Hungary.

Italy was invaded in October 1951 and about 2,000,000 of Italy's 8,000,000 - 9,000,000 cattle were vaccinated. A comparison between the incidence of the infection in the two large epizootics shows that during that of 1938-39 there were some 31,700 outbreaks in Italy, while during that of 1951-52 the number was 43,700.

From the Federal Republic of Germany, foot-and-mouth disease spread also eastwards to East Germany. In this part of Germany, however, systematic vaccination of the cattle population was being

carried out before the epizootic began. This followed experiences over several years of the Instituto on the island of Riems, where there is a large potential for vaccine production. Practically all the cattle population, except those kept for virus production, are vaccinated annually.

The result of this vaccination in East Germany was that the epizootic caused only very slight losses where from January 1951 until January 1952 only 1 percent of all herds became infected, while in the Federal Republic of Germany during the same period, the disease infected 11 percent of herds. The results in East Germany were an excellent example of the results of vaccination.

The situation in Switzerland and Sweden during the 1951-52 epizootic is of special interest. Switzerland became infected by A_5 virus at the beginning of October 1951 and until the end of the year there were 181 outbreaks as well as 109 in 1952. All the outbreaks in Switzerland were dealt with by immediate slaughter, ring vaccination and the application of strict veterinary police measures and the invasion was completely controlled. A comparison between this epizootic and that of 1937-39 shows that during the former (from 1 September 1937 until 26 February 1939) 2,225 infected herds were slaughtered, but that this extensive slaughter, although of much importance in limiting the spread of the disease could not arrest the infection, for there were some 19,400 outbreaks. In the 1951-52 epizootic, the outbreaks were limited to 290. Sweden became infected in September 1951, and until March 1952, when the epizootic ended there were, in all, 840 outbreaks. In 818 of them slaughter was practised; the remaining

22 were not slaughtered, 11 because of high breeding value and 11 because of previous vaccination. The slaughter policy in Sweden was combined with extensive vaccination, 1,000,000 cattle being vaccinated. Thus Sweden, like Switzerland avoided an extensive epizootic, due, undoubtedly also, to the combination of vaccination and the slaughter of infected herds. During the epizootic of 1938-39 801 infected herds were slaughtered in Sweden but the invasion continued and some 7,000 herds became infected. It is highly probable that the extensive vaccination carried out in Denmark was of some considerable importance in limiting the spread of infection from Denmark to Sweden.

Although Yugoslavia did not become infected during the general 1951-52 European epizootic it was invaded from Greece in April, 1951, and the causal virus was typed as A_5. As in some other countries, vaccine prepared with the ordinary A strains of the virus did not produce any satisfactory immunity. It was only when vaccine was prepared in Yugoslavia using the local strain A_5 that good results were obtained. By the combination of strict veterinary measures and vaccination the invasion from Greece was brought under control.

During the extensive European epizootic of 1951-52 it became evident that there was too little vaccine available in Europe and that it had been used too late. Many of the European countries have appreciated this position and existing foot-and-mouth disease institutes have been expanded and new institutes have been established. Foot-and-mouth disease vaccine is now being produced in Austria, Belgium, Czechoslovakia, Denmark, France, the Federal Republic of Germany, East Germany, Greece, Italy, the Netherlands, Poland, Russia, Spain, Switzerland, Turkey and Yugoslavia.

Results of Vaccination during the 1956-58 Epizootic

During the flare-up of foot-and-mouth disease in France and Germany in 1956-58 vaccine was used on a large scale in these countries. In France, some 4,000,000 cattle were vaccinated in 1956, some 5,200,000 in 1957 and some 6,000,000 in 1958. This last figure represented about one-third of the total cattle population in France.

In the control of foot-and-mouth disease in the Federal Republic of Germany a considerable number of herds were slaughtered at the beginning of the epizootic. However, the control was first of all based on vaccination: ring and mass vaccination. Between July 1956 and August 1958 about 70 percent of the cattle in the Federal Republic of Germany were vaccinated and in some of the Länder the entire cattle population was included.

Spread of the disease from infected France and Germany to neighbouring countries could, of course, not be prevented. Because of precautions taken in these two countries, however, the spread was limited to a considerable extent, compared with previous epizootics. In the invaded countries strong control measures including vaccination were also applied. In countries such as Denmark, Switzerland and Austria slaughter of infected herds combined with vaccination was carried out on a limited scale: ring and border vaccination.

In Denmark the slaughter policy was again introduced in 1953. The number of outbreaks in 1956-57-58, were 6, 45 and 11 respectively.

Switzerland, because of its geographical position, is very much exposed to invasion when its neighbouring countries are infected and also because of the considerable transit of animals. The number of outbreaks were in 1956, 121, in 1957, 111 and in 1958, 53. Switzerland has continued its usual policy of control: a combination of slaughter of infected herds, vaccination and the application of strict veterinary measures, which has been called the "Swiss system of control", and in which the different factors are considered to be of equal importance and supplementary to each other. The Swiss method is very flexible and the local conditions are always taken into consideration in applying the measures of control.

Austria was free from foot-and-mouth disease in 1956 until the last months of the year (103). At this time the disease had spread to southern Germany and it was decided to vaccinate in Austria along the German border. Vaccination was actually carried out in Austria in a depth of 5-10 km. along the border from Switzerland to Czechoslovakia, beginning in December 1956. Some invasion, however, took place from Germany and between 10 December 1956 to the end of February 1958, there were, in all, 149 outbreaks. The country was then free from the disease until September 1957 when there were two outbreaks. Control in Austria was based on slaughter of infected herds, vaccination and the application of strict veterinary measures. Control in Austria was effected with much perseverance and was of the greatest importance not only for Austria but also for further spread of the disease to her eastern and south-eastern neighbours. There was no spread, for example, in Yugoslavia. It is of much interest from both epizootiological and control points

of view that when the first wave of infection was over, Austria remained free from the disease. Vaccination in zones along the borders of both Austria and Germany (Bavaria) apparently kept Austria free from further invasion.

As shown in table V the infection in Bavaria only reached its peak when the invasion of Austria was over.

Table V

Number of outbreaks in Bavaria and Austria

Period	Bavaria	Austria
1 - 15 Dec. 1956	37	13
		6 *
16 - 31 Dec. 1956	64	28
		27 *
1 - 15 Jan. 1957	39	42
		19 *
16 - 31 Jan. 1957	86	7
1 - 15 Feb. 1957	151	5
16 - 28 Feb. 1957	155	0
1 - 15 Mar. 1957	217	0
16 - 31 Mar. 1957	166	0
1 - 15 April 1957	107	0
16 - 30 April 1957	135	0
1 - 15 May 1957	208	0
16 - 31 May 1957	152	0

* Weekly outbreaks

The control of foot-and-mouth disease in Belgium is based on mass vaccination, using trivalent vaccine O-A-C, which was begun in 1955 when some 1,230,000 cattle were vaccinated. In 1956, some 850,000 cattle were vaccinated and in the following years about 50 percent of cattle in Belgium have been vaccinated annually. Because of this mass vaccination foot-and-mouth disease has lost its economic importance in Belgium to a considerable extent. The position now is that the few outbreaks are confined to calves and pigs. The Belgian veterinary authorities are convinced that only because of this mass vaccination has Belgium avoided an extensive epizootic in 1956-57 (104).

Luxembourg was free from foot-and-mouth disease during 1956 but was invaded in December of that year. The first infected herds were slaughtered but when the disease spread very rapidly it was decided to abandon slaughter and to vaccinate all the cattle, sheep and goats in the country, some 130,000 animals. In December 1956 and January 1957, there were 20 outbreaks, and since then Luxembourg has been free of foot-and-mouth disease. Thus, mass vaccination was able to bring foot-and-mouth disease completely under control in Luxembourg.

The foot-and-mouth disease situation in the Netherlands is of special interest (105). Through the years 1947-52 vaccination was increasingly applied and in 1951, when the last epizootic started more than 50 percent of the cattle had been vaccinated with a bivalent O-A vaccine. The invasions by the two virus types, A_5 and C, were well controlled by the use of the appropriate vaccines. The veterinary authorities and the farmers were well satisfied with the results and the authorities were of the opinion that it would be possible to control

foot-and-mouth disease in the future by a combination of vaccination and slaughter of infected animals. Slaughter of infected animals was begun in 1952. Between 1 February and 15 April, 1953, the first vaccination of practically the whole cattle population was carried out and annual vaccination has been continued, using trivalent vaccine. As an additional control measure, it has also been decided that all transport of non-vaccinated animals should be prohibited in the Netherlands. It was systematic vaccination in the Netherlands that made possible the application of a slaughter policy. It seems as if the economic problem of foot-and-mouth disease is solved in the Netherlands as far as cattle are concerned. The country suffered very heavy losses from the disease during previous epizootics, but since the first systematic vaccination in 1953, losses have been reduced to a minimum.

There have been a number of outbreaks in Greece since the epizootic of 1951. By the application of mass vaccination combined with strict veterinary measures, however, the disease had been brought under control on each occasion. A very dangerous situation developed in 1960-61 when outbreaks, caused by virus of types O, A and C occurred simultaneously. The application of the usual measures was again followed by successful results. It is of interest to note that the vaccine used in this campaign was a kidney tissue culture vaccine, produced at the new Greek foot-and-mouth disease laboratory (106,107).

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For some years the Swiss system of controlling foot-and-mouth disease, which consists of a combination of slaughter, vaccination and the application of strict veterinary measures has been applied in Austria, Denmark, Switzerland and Yugoslavia, and so far, has succeeded in keeping foot-and-mouth disease under control in them.

No exact information is available on the control measures adopted in eastern European countries, but it is understood that vaccination is used, together with the application of strict veterinary measures. The foot-and-mouth disease situation in most of these countries has been satisfactory for a number of years, as no large epizootics have developed in the region.

In Russia, also, the situation is satisfactory. It is understood that extensive vaccination plays an important role in bringing the disease under control. The vaccine used in Russia is produced from virus cultivated in young rabbits and adsorbed on aluminium hydroxide (108).

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An overall plan for the control of foot-and-mouth disease in Europe, put forward by the Commission's Standing Technical Committee, was approved and adopted at the Fourth Session of the Commission. The following statement is taken from the Report of that Session:- "The Committee was satisfied that vaccination had been shown to be valuable in the control of foot-and-mouth disease and was applicable in most European countries. It should be considered as a means of bringing the disease sufficiently under control so that, eventually, a stamping-out policy might be adopted. It is, therefore, recommended that in

those countries where a heavy weight of infection is present or where there is continued threat of infection the policy should be systematic vaccination. The system may vary in accordance with the circumstances in the particular country; it may be possible, for example, to adopt annual vaccination of all cattle stock in the country or vaccination may be done around foci of infection or in threatened areas. When the number of outbreaks has been sufficiently reduced, vaccination may be supplemented by slaughter of animals on infected premises. Later, there may be a reduction in routine vaccination and the stamping-out policy may be adopted as the main method of control. This stage may not be reached in a particular country until its neighbours and countries from which imports, particularly of livestock, are made, have reached a similar position. Only after this stage will it be possible to rely entirely on a stamping-out policy. It is obvious that sufficient supplied of trustworthy vaccine must be available and that there is a staff capable of organising and carrying out vaccination. It must be realised that, whatever the policy, it is essential to control the movement of stock, to dispose of infected material and to carry out effective disinfection. The Committee was impressed by the success of the vaccination policy in those countries where it has been systematically applied. Not only has the number of outbreaks been reduced but the weight of infection has been minimised because, as a general rule, only young cattle and pigs have succumbed to infection."

"In most European countries a stamping-out policy not supplemented by vaccination is impracticable, but the Committee regards a stamping-out policy as the ultimate objective."

A study of the results of the vaccination in France in 1956 was carried out by Lucam, Mackow and Magat (109) in which vaccinated animals were observed over a period of five months. A trivalent vaccine was used during a period of extension of the epizootic. Vaccination was carried out in the immediate neighbourhood of infected premises, thus the probability of vaccinated animals becoming exposed to the infection was great.

In general the results were very satisfactory: the study showed that about 99 percent of the vaccinated herds were protected during the five months.

A further study of the results of the vaccination in France in 1957 was carried out by Lucam (110) in 1957, when some 100,000 herds in some 80 departments were infected. Only vaccination carried out with trivalent vaccines and around foci of infection in the form of ring vaccination are taken into account in this study. The study comprised 56,440 herds and foot-and-mouth disease appeared in 146 of them (0.25 percent); thus 99.75 percent of vaccinated herds were protected. This study also showed that the immunity lasted for at least five months. These very satisfactory results show that in a country like France where foot-and-mouth disease has been enzootic for about 50 years, vaccination is the best weapon for its control.

The conclusion from this study was that control of foot-and-mouth disease in France must be based on a combination of two fundamental factors: generalised compulsory vaccination and slaughter of infected herds.

Early in 1961 (111) it was reported that the number of cattle vaccinated in France had increased from about one-third in 1959 to about half the cattle population in 1960, and that slaughter of infected and in-contact animals was being carried out in 18 departments in the eastern part of the country, including frontier areas between France and Switzerland and France and Germany.

During the latter part of 1961 slaughter of infected herds was extended in France and was practised in practically all the departments.

At the International Symposium on Virology in Lyons in 1958 (112) at which practically all workers on foot-and-mouth disease in Europe were present, reports were presented on the results of vaccination throughout Europe and the subject was again thoroughly discussed. It was appreciated that vaccination was of great value in the control of foot-and-mouth disease but it was obviously necessary to combine it with the application of strict veterinary measures including slaughter of infected herds. It was stated that vaccination should be carried out systematically and that it was advisable to use trivalent O-A-C vaccine. It was stated, further, that control of foot-and-mouth disease would be impossible in Europe without the use of vaccine, correctly applied.

Vaccination of Sheep and Goats

While the immunising value of the Vallée-Schmidt-Waldmann vaccine in cattle is generally recognised, there is little available official information on the effect of the vaccine in sheep and goats. It appears, however, that the results of vaccination of these animals is as satisfactory as in cattle.

In Italy, vaccination of small ruminants has been practised for several years; in 1955-59, for instance, a total of some 5,850,000 sheep and some 316,000 goats were vaccinated and the results were considered to be good (113).

In Greece, also, where a large proportion of the ruminants are sheep and goats, for many years they have been vaccinated, as well as the cattle. As already mentioned, Greece has succeeded in keeping foot-and-mouth disease well under control by mass vaccination combined with the application of strict veterinary measures. During the epizootic of 1960-61, for instance, some 275,000 cattle and some 800,000 sheep and goats were vaccinated: there was an incidence of about 1.1 percent of breakdowns in immunity in the vaccinated cattle, and about half that figure in sheep and goats (114).

In Cyprus, where there are some 35,000 cattle, some 500,000 sheep and goats and some 35,000 pigs, systematic vaccination of all susceptible animals was initiated just over five years ago. Virus of types O and A have been demonstrated in Cyprus, and, therefore, a bivalent vaccine is used. The vaccination campaign starts early in March and lasts six to seven weeks. The results may be considered as very satisfactory. For some $3\frac{1}{2}$ years no serious outbreaks have been recorded amongst the cattle. Each year, however, there are a few cases in young dairy cattle which are brought under control by ring vaccination.

Good immunity is obtained in sheep and goats but it does not last for more than six to eight months. Most of the outbreaks occur from November onwards, when new-born lambs are infected and the disease then spreads to the adult animals. The disease runs a very mild

course in the adult animals, affecting no more than 10 percent of the total number in the flocks. Even in infected areas the total number of flocks which become infected does not exceed 5 percent. These observations indicate that the vaccine produced satisfactory immunity, which is excellent for the first six to eight months but then becomes weaker and weaker (115).

Vaccination of Pigs

While vaccination of cattle, sheep and goats has resulted in inducing a satisfactory immunity, vaccination of pigs has been much less effective. Over the years, many laboratory experiments have been carried out with pigs and new methods of vaccination have been studied. Different vaccines have produced either a low degree of immunity or no immunity. On the other hand, notwithstanding the poor results of the laboratory experiments, the vaccine has been used in pigs in the field and, apparently, with some good results, in some cases. There is an interesting example from Belgium (116). Some years ago an epizootic caused by virus of type C occurred among pigs. A highly potent monovalent vaccine produced from cattle virus of C type was used for the pigs, following which the epizootic was arrested.

In 1960 (117) some field experiments were carried out in France, in which pigs were vaccinated, intradermally, with the ordinary vaccine. The results were reported as being very satisfactory: it was stated that immunity was established almost immediately and lasted for some three to four months.

During recent years foot-and-mouth disease virus, mainly of type C has shown a tendency to spread among pigs. It has therefore, become necessary to develop a vaccine with a good immunising effect in pigs.

EVOLUTION OF VACCINES

The first Vallée-Schmidt-Waldmann vaccine which appeared in 1938 was a monovalent vaccine prepared from virus of type O, and the source of virus was natural virus material produced on cattle tongues (epithelium and lymph). It was obvious from the beginning that virus produced artificially on cattle tongues was an expensive source of virus and that in countries where foot-and-mouth disease is widespread, there was difficulty in producing the required large amounts.

Other sources of virus have, therefore, been sought. Since the end of the Second World War much research work has been carried out and some remarkable results have been obtained. In 1950, culture virus grown in explanted cattle tongue epithelium was introduced in the Netherlands as a source of virus for the preparation of the Vallée-Schmidt-Waldmann vaccine.

In more recent years, another kind of culture virus is being used in the preparation of the vaccines: virus grown in kidney tissue cultures.

A third source of virus is the vaccino-foot-and-mouth disease virus complex grown on cattle skin; this kind of vaccine has found considerable application in France.

The monovalent vaccine of 1938 was used in a dose of 60 ml for adult cattle. This amount was very large and impractical for use in the field and many experiments have, therefore, been carried out to lower the dose.

The inactivated vaccine using natural or culture virus, is complicated to produce, is relatively expensive, and produces a relatively short-lasting immunity. It was, therefore, thought that a modified virus,

multiplying in the treated animal and producing a long-lasting immunity, would be the ideal vaccine and could probably be effective in small doses. Foot-and-mouth disease virus has been modified by its passage through embryonated eggs and through rabbits and such modified virus has had some application in the field as a vaccine against the diseass.

Cultivation of Foot-and-Mouth Disease Virus in explanted Tongue Epithelium

In 1947, Frenkel reported for the first time on the cultivation of foot-and-mouth disease virus in explanted cattle tongue epithelium and that virus had been cultivated through 12 successive passages (118). At that time the cultivation of virus was still being carried out on a laboratory scale. However, the method was rapidly developed and in 1950 the virus was grown on a large scale and was used as the source of virus in the Vallée-Schmidt-Waldmann-vaccine. A full description of the large-scale cultivation was given by Frenkel in 1951 (119). Frenkel's method has now been in use for more than 10 years in the Netherlands. All the three types of the virus, O, A and C have been cultivated and vaccines have been produced from them. It is this trivalent culture virus vaccine that is now being used with so much success in the systematic vaccination of cattle in the Netherlands.

Frenkel's method has been introduced in a number of other countries in Europe and in other parts of the world, and has been of the greatest importance for the control of foot-and-mouth disease. However, the method has some limitations because, in some countries, it is difficult to obtain a sufficient number of cattle tongues for cultivation of the virus.

Cultivation of Foot-and-Mouth Disease Virus in Kidney Monolayer Tissue Cultures

In 1955, Sellers (120) and Bachrach, Hess and Callis (121) reported, independently, that they had cultivated foot-and-mouth disease virus in kidney monolayer tissue cultures produced from pig and bovine kidneys. Sellers cultivated virus of types O and C and passed them through four passages; Bachrach et al. passed virus of type A through 14 passages. Experiments on this subject were also carried out by Wesslén and Dinter (122) and by Mazzaracchio et al. (123). Both groups of workers cultivated virus of types O, A and C.

This new culture virus was first used as a source of virus in the vaccine by Mazzaracchio, Zavagli et al. (124). They prepared a vaccine containing O and A culture virus and this vaccine produced an excellent immunity in cattle when challenged 22 days after vaccination. In 1960 Zavagli (125) reported on some experiments on duration of immunity. A large number of cattle had been vaccinated in the field with culture virus vaccines produced from kidney tissue culture virus of type C. Tests showed that there was complete immunity in cows up to 13 months after vaccination, and that, after 14 months, a certain decrease occurred. The number of animals used in the experiments and the serological tests gave clear evidence on the efficacy of the vaccine used in the experiments.

This type of culture virus was used as a source of virus for vaccine production in Israel during the epizootic in 1959-60. caused by virus of Asia I type (126). The vaccine was prepared in the

classical way by adsorption of the virus to aluminium hydroxide and then inactivation by formalin. Some 77,000 cattle were vaccinated with this vaccine and the results were apparently satisfactory. (see also p. 99)

Kidney tissue culture virus-vaccine was also used in the field in Greece during the epizootic of 1960-61 when three types of the virus, O, A and C were causing outbreaks. The vaccines were prepared as monovalent vaccines. The vaccine of type O was used in five departments on a total of some 100,000 cattle and some 316,000 sheep, goats, and pigs. Because virus type C also appeared in one of the five departments, vaccination was carried out there with a mixture of types O and C vaccines. There was a breakdown in immunity in 0.8 percent of the cattle and 0.4 percent of the sheep, goats and pigs. Vaccination with type A vaccine was carried out in three departments on some 24,000 cattle and some 73,000 sheep, goats and pigs. No breakdown of immunity was observed. Vaccine of type C was used in nine departments where some 151,000 cattle and some 436,000 sheep, goats and pigs were vaccinated. In one of the departments the disease re-appeared four months after vaccination was carried out. Following re-vaccination in the area no further cases occurred. There were, in all, about 1.4 percent breakdowns in immunity among cattle. It is evident that the results of the vaccinations were very satisfactory for foot-and-mouth disease was brought completely under control.

This new method is now in full development in many countries and in Italy, for instance, kidney tissue culture virus is being produced on a large scale in several foot-and-mouth disease laboratories.

Production of Vaccino-Foot-and-Mouth Disease Virus Complex

This method was first suggested some 35 years ago by M. Belin. Its principle is the following. Adult cattle, which have never had foot-and-mouth disease, nor have been vaccinated are shaved and cleaned all over the body. The skin is then scarified and infected with vaccinia virus. Immediately afterwards, the animal is injected in the tongue with foot-and-mouth disease virus. The vaccinia virus multiplies in the skin and the foot-and-mouth disease virus multiplies in the tongue and enters the bloodstream, so reaching the skin tissue. Foot-and-mouth disease virus has no affinity to normal hairy skin, but in some way this tissue has now become susceptible through the presence of the vaccinia virus. About four days after infection, when the temperature reaches a certain level, the animals are slaughtered. At that time a yellow coagulated exudate covers the skin. The crust which contains a mixture of vaccinia and foot-and-mouth disease virus, is harvested with the help of a sharp spoon, and the average yield is 700-800 g. The titre of the vaccinia virus is much lower than that of normal vaccinia virus harvested from cattle. The titre of the foot-and-mouth disease virus in the mixture is as high as that of a normal natural virus produced on living cattle tongues. The mixed virus material is extracted in water, centrifuged and filtered in the same way as the tongue virus, and from the sterilized virus extract, a vaccine is prepared in the usual way: adsorption to aluminium hydroxide and inactivation by formalin and heat.

C. Belin has reported on this method recently (127, 128) on several occasions. The vaccine prepared with this virus complex is now being controlled by the French Government and has found considerable application in France.

Concentration of Vaccine

The monovalent vaccine produced from virus of type O, which appeared in 1938 contained 0.7 percent of natural virus material and 50 percent aluminium hydroxide. The dose of the vaccine was, for adult cattle, 60 ml. and the amount of virus per dose was, therefore 0.42 g. There was, however, a considerable problem to produce sufficient amounts of virus on living cattle tongues. In 1941, Waldmann et al. (129) published a new formula for the vaccine in which the amount of virus was considerably reduced. A monovalent vaccine now contained 0.24 percent virus, a bivalent vaccine, 0.40 percent. The dose was still 60 ml. for both a monovalent and a bivalent vaccine. With the intention of standardising the production of vaccine in different countries, an O.I.E. meeting was convened in Berne in 1947 (130), and it was recommended that the vaccine should be produced as a bivalent vaccine containing the virus types O and A. It should contain at least 0.2 g of virus per dose of vaccine for adult cattle.

When the vaccine came to be used in the field in Denmark, the large volume of 60 ml. to be injected was found to be quite inconvenient. Some tests were, therefore, undertaken with vaccines in smaller doses but containing a largerpercentage of virus. The 1938/39 epizootic in Denmark provided an opportunity to make field experiments with such vaccines, and they were carried out by the writer in collaboration with

Harbo (131). Vaccines were produced which contained 4 percent virus, the dose being 6 ml. Two injections were given and satisfactory immunity was produced.

In 1940, Altara and Serra (132) reported that they had continued the Danish experiments and had obtained very good results with concentrated vaccines. In 1947, Altara (133) reported on the use of 1,000,000 doses of bivalent concentrated vaccine containing 5.4 percent of virus material. The dose was 10 ml. for adult cattle and the immunity lasted for about four months.

In 1947, Rosenbusch, Decamps and Gelormini (134) reported on a concentrated vaccine containing 5.0 percent virus. Its use intradermally, in a dose of 2.0 ml. gave good results in Argentina.

Camargo and Mott (135) in 1949 reported on a year's production and use in Mexico of 12,000,000 doses of a concentrated monovalent vaccine containing 6 percent of virus and injected intradermally in a dose of 2 ml. for adult cattle and 1.0 ml. for small animals. During the campaign in Mexico some 60,000,000 vaccinations were carried out with this vaccine with, generally, good results.

Thus, several successful vaccines of various concentrations of virus have been produced, but controlled large-scale experiments, comparing vaccines of different concentrations for duration of immunity, had not been carried out.

However, in the cooperative work of the Danish Veterinary Institute for Virus Research and the U.S. Bureau of Animal Industry, two large experiments on this subject were conducted by the writer in collaboration with Malmquist, Osteen and Johnson (136).

The first experiment with 160 cattle involved a series of vaccines in which the virus content was varied and the aluminium hydroxide content was kept constant. The second experiment in which 200 cattle were vaccinated dealt with a series of vaccines in which the amount of virus was constant and the aluminium hydroxide was varied.

The results of these experiments indicated that satisfactory foot-and-mouth disease vaccines can be produced, containing greater concentration of virus than had commonly been previously used. It was found that the dose of a monovalent vaccine could be reduced from 15 ml. to 2-4 ml. by maintaining the same amount of virus and reducing the excess aluminium hydroxide. Thus, in 1951 there was evidence that a concentrated vaccine was as effective as the ordinary vaccine and had practical advantages. However, there was little tendency to change from the old formula for vaccine production.

Until 1953, the common way of producing vaccine was the following: Virus material was extracted in water, centrifuged and filtered through a Seitz E.K. filter and then adsorbed to aluminium hydroxide. Filtration always caused a considerable loss of virus. However, in 1953, Pyl (137) and Pyl and Möhlmann (138) reported on some experiments in which chloroform instead of water was used for the extraction of the virus from the virus material. It was shown that virus can be extracted in chloroform without any loss of virulence and than no filtration is needed. In 1954, Pyl and Röhrer (139) gave further information on the new concentrated vaccine. Attention was drawn to the above-mentioned Danish-American experiments in which it had been shown that the effect of the vaccine depends on the amount of the antigen and that the

amount of aluminium hydroxide had little influence. Some large-scale experiments have since been carried out in Germany in which comparisons were made of the classic and the concentrated vaccines (140). It was found that this new vaccine was as satisfactory as the classical one.

The concentrated trivalent vaccine is used in a dose of 5 ml. as compared with a dose of 30 ml. for the classical vaccine: this is of considerable advantage. Furthermore, the concentrated vaccine is cheaper, for the virus extract is not filtered and so, contains more virus per gram. This concentrated vaccine is now in common use in the Federal Republic of Germany and in East Germany.

Modification of Foot-and-Mouth Disease Virus by adaptation to the Embryonated Egg

In 1949 Traub (141) reported that he had succeeded in adapting virus of foot-and-mouth disease to embryonated egg. Since then, much work has been carried out on the problem in the hope of producing a live virus-vaccine by modification in the egg. In 1958 Kemron and Goldsmit (142) reported on the successful modification of foot-and-mouth disease virus of types O, A, C and Asia I.

The modified live virus of Asia I type was used on a large scale in Israel for vaccination of cattle during the epizootic of 1959-60 caused by virus of Asia I type. At the Seventh Session of the European Commission Kemron gave some information on the results and at the Eighth Session, Sturman completed this information.

When Israel was invaded in October 1959 by virus of the Asia I type the country had no means at its disposal to control this epizootic caused by an exotic type of virus. However, some experience had been gained in experiments in Israel of the value of the egg-modified Asia I type of foot-and-mouth disease virus as an immunising agent and it was decided to carry out a field trial. Vaccination was started at the beginning of November, 1959 and was first carried out in already-infected settlements within the infected area (a settlement comprises 2 to 200 herds, with an average of 15 cattle). When one or more herds in a settlement became infected the rest of the herds in it were vaccinated. As the first experiment showed satisfactory results the trial was extended and modified virus was used also in non-infected settlements. As from late December 1959, an additional kind of vaccine was used in the field: kidney tissue culture virus-vaccine prepared in the classical way by adsorption of the virus to aluminium hydroxide and then inactivated with formalin. Some 93,000 cattle were vaccinated with the live vaccine and some 77,000 with the inactivated vaccine. By the middle of February vaccination of all the graded herds had been completed. Ungraded herds remained unvaccinated and the disease continued to spread in them. The results of the vaccination with modified virus were the following: in vaccinated herds the spread of foot-and-mouth disease stopped in six to eight days following vaccination. Young vaccinated animals showed no reaction of any kind following vaccination. Up to 0.5 percent of the adult animals, however, reacted in three to seven days, showing some slight lesions in the mouth and on the udder. In herds vaccinated with inactivated vaccine two weeks or more elapsed before the disease was brought under control.

Modification of Foot-and-Mouth Disease Virus in Rabbits

Numerous authors have worked on this subject: Lickhachjev and Gribanov (143), Cunha and Eichorn (144), Verge, Paraf, Dhennin, and Asso (145). In 1954, Gribanov reported that several experimental vaccines had been prepared using lapinized virus, and that such vaccines had been found effective in both laboratory and field experiments.

In 1959, Böiko (146) reported successful results of experiments with lapinized virus. From 1959, the classical vaccine was no longer used in Russia, but aluminium hydroxide vaccine containing lapinized foot-and-mouth disease virus is produced. It is thought that this method is the most efficacious and is more practical for the preparation of the vaccine. In 1958, thanks to the use of this vaccine, foot-and-mouth disease was eradicated from a whole territory in Siberia. Mass vaccination of all bovines is carried out over very large territories where there may be danger of infection.

The above Review was prepared in accordance with the request made at the Commission's Session in 1961. In order to complete the Section on "Control of Foot-and-Mouth Disease in Europe", it was felt that mention should also be made of the action taken by the European Commission for the Control of Foot-and-Mouth Disease since its establishment in 1954. A special note has been prepared and is appended to this Review as Appendix II.

Summary of the Pattern of Foot-and-Mouth Disease in Europe during the Period 1937-1961

During the period 1937-1961 there was a large number of epizootics of very different severity and epizootiological importance in Europe.

The epizootic which started in France in 1937 had its origin in North Africa, and was caused by a virus of type O of exceptionally high virulence and infectivity. It spread to practically all European countries. This first wave of infection was followed by more localized epizootics caused by virus of type A. In some countries they were as extensive as the former but, in most, they were limited. During the epizootic some sporadic outbreaks caused by virus of type C also took place. The total number of outbreaks in a group of countries which includes France, Belgium, Luxemburg, the Netherlands, Germany and Denmark during 1937-39 was about 1,500,000.

During the war foot-and-mouth disease was enzootic in most of the countries.

At the end of 1945 an epizootic, caused by virus of type C of extreme virulence, started in Italy and spread mainly over the Po Valley. It lasted for about three years. This was the first time that virus of type C had been known to spread throughout an area causing an epizootic.

In 1951 another regional epizootic took place in Greece, Yugoslavia and Turkey; Syria and Irak were probably included. In Greece virus of types A_5 and C were demonstrated, in Yugoslavia, A_5 and in Turkey, types O, A_4, A_5 and C.

During 1951-52 there was another extensive European epizootic, which seems to have had its origin in the Federal Republic of Germany. During the early part of 1951 there were some outbreaks caused by virus of types O and A_4 in that country, but on the whole the foot-and-mouth disease position there appeared to be fairly steady. In May/June outbreaks caused by virus of type A_5 occurred in northern Germany. At the same time virus of type C was demonstrated. The type A_5 virus was extremely contagious and spread in all directions from its origin, with the involvement of practically all European countries. The virus of type C also showed a tendency to spread, but more slowly than A_5 virus, and appeared in many countries, 2-4 months after the appearance of the A_5 virus. Thus, there were two waves of infection spreading from the Federal Republic of Germany throughout Europe: the second wave of infection did not cause nearly as many outbreaks as did the first one. This was the second occasion on which virus of type C has assumed an epizootic character and had spread over a wide area. The total number of outbreaks during the 1951-52 epizootic in the same group of countries mentioned above: France, Belgium, Luxemburg, the Netherlands, the Federal Republic of Germany and Denmark, was some 700,000. Countries such as Switzerland and Sweden almost avoided this epizootic because of measures taken. From the Continent the epizootic also spread to Great Britain.

It has been suggested that there was a connection between the epizootic in Greece in 1951 and the European epizootic in 1951-52. The virus of type A_5 had appeared in Greece in 1950 and in Germany in 1951, and the strain from Greece and that from Germany were shown to be identical from both a serological and a clinical point of view. There is, therefore, reason to believe that, in some way or another, the infection from Greece had reached Germany.

After the epizootic of 1951-52 was over, the foot-and-mouth disease situation in Europe remained quiet for some years. In 1956-58, however, there was a flare-up in France and the Federal Republic of Germany: the numbers of outbreaks in France were - 1956 - 6,800; 1957 - 99,424; and 1958 - 14,127, respectively: and in the Federal Republic of Germany - 1956 - 1,401; 1957 - 6,383; and 1958 - 1,265, respectively. In both countries the three classical types of the virus O, A and C were present during the epizootic. There was some spread from these two countries into neighbouring countries and also to some more distant countries, but in most, the infection was slight.

It was only in Spain and Portugal that epizootics developed, probably as a result of invasion from France.

Independently of the flare-up in western Europe, a severe epizootic caused by virus of type O and with a high mortality rate occurred in Turkey in 1957. It began in May in the eastern part of the country, probably as a result of invasion from Iraq where there was also a flare-up at the same time. The disease spread westwards in Turkey and soon reached European Turkey. It lasted from May to December and affected some 8,000 villages. Such an extensive epizootic had not been experienced in Turkey where the normal picture is 300 - 800 outbreaks annually with small periodic flare-ups. From European Turkey the disease spread also into the neighbouring countries, Greece and Bulgaria, where further spread was arrested.

The occurrence of foot-and-mouth disease in Russia in former times was of much importance to the rest of Europe because of the repeated invasions. From 1910 until 1958-59 , however, no such invasion is known to have taken place. In 1958-59, there was undoubtedly spread of the disease westwards from Russia although probably on a limited scale, resulting in the infection appearing in Rumania, Bulgaria, Yugoslavia, Hungary, Poland and Finland. At the same time, there were outbreaks in Czechoslovakia and Austria, but their relationship to the presence of the disease in Russia is not known. In all these countries the disease was brought under control.

In 1960-61, in Greece there was an epizootic caused partly by invasion from Turkey and partly by infection introduced in imported frozen meat. All three types of the virus, O, A and C were demonstrated. The epizootic was brought under control.

In 1959-60 an epizootic occurred in Israel caused by virus of the Asia I type. This epizootic was of much importance to Europe because this was the first occasion on which virus of the Asia I type had shown an epizootiological character and also because of the proximity of the disease to Europe.

The epizootiology of foot-and-mouth disease in the United Kingdom has some special characteristics. From time to time the disease is introduced into the country either from the Continent or in imported frozen meat from South America. Each of these infections has a clear pattern. When the disease is introduced from the Continent the primary outbreaks in the United Kingdom occur in certain coastal regions: whereas primary outbreaks whose source is considered to be imported meat occur in any part of the country where such meat is distributed. All three types of the virus, O, A and C have been identified over the years.

In the Netherlands the foot-and-mouth disease situation has been extremely satisfactory since systematic vaccination combined with slaughter was introduced.

During 1960-61 there have been some flare-ups of foot-and-mouth disease in different countries.

In Belgium, in November 1960 the disease caused by virus of type C spread from some important markets. Compulsory vaccination brought the disease under control.

In the Federal Republic of Germany and in East Germany during 1960 and 1961, there was a flare-up of the disease, caused mainly by virus of type C and largely confined to pigs.

The situation in Switzerland always reflects the position in neighbouring countries. This was the case also in 1960-61.

In Italy, since the epizootic of 1951-52 until the autumn of 1960, foot-and-mouth disease was enzootic with numbers of annual outbreaks varying from some 7,000 to some 13,000. All three types of virus have been present in Italy over the years but their proportion has varied considerably. In 1960-61, there was a new flare up caused mainly by virus of type C which showed a marked affinity for pigs.

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With the severe epizootic of 1937-39 the foot-and-mouth disease situation in Europe became more and more serious, for the number of infected herds steadily rose and the disease spread in a severe form to more and more countries. This position is probably related to the steady up-grading of cattle in Europe, the growing traffic in livestock and, perhaps, increase of the virulence of the virus. Recent examples of this increased virulence are the epizootic in Turkey in 1957 caused by virus type O, the epizootic in Israel in 1959-60 caused by the Asia I type and the change the virus of type C has undergone in Italy, and later on, in other European countries.

There are probably five main sources of infection for Europe:

(1) the existing centres of infection within Europe, which may flare up and cause spread of the disease to many countries;

(2) Russia, which in former times, was a source of infection and from which, again in 1959, infection was introduced;

(3) the Near East through European Turkey; the existence of virus of the Asian type in this region is of special importance;

(4) Africa, from where the European epizootic of 1937-39 started; from Africa there is also the threat of the introduction of the three South African types of the virus;

(5) imported meat from South American countries, which is a source of infection for importing countries.

It must not be forgotten that infection in Europe is also a source of the disease for other regions in the world.

Summary of Modes of Transmission of Foot-and-Mouth Disease

In the review the following modes of transmission are cited: transmission by human beings, by milk, by meat and offal, by wind, by birds, by fodder and vegetables, and by spread from foot-and-mouth disease laboratories. A study is also made of the epizootiological importance of virus excreters.

The human being is regarded as the most important of the intermediate carriers of foot-and-mouth disease. He comes into close contact with cloven-footed animals and enjoys much freedom of movement. Observations made in Denmark during several minor epizootics emphasize this point. Ten outbreaks are mentioned in Norway where the virus seems to have been carried by boots from an infected railway line into the herds. Two examples of long distance contamination by man are mentioned: from France to Yugoslavia in 1937 and from Germany to Canada in 1952.

Infected milk and skim milk can be most dangerous sources of infection if they are not sufficiently heated. In 1926, in Norway for instance, infected milk from one farm resulted in spread of the disease to more than 100 farms. The disease can also be spread by infected milk cans, milk waggons, etc. In Denmark, during the epizootic in 1920 the following example is given: a dairy had three milk routes and on two 3/4 to 4/5 of the herds became infected, while all herds belonging to the third remained completely free. Also, during the epizootic in the United Kingdom in 1951-52, infected milk played a considerable role in the spread of the disease.

Meat and offal infected with the virus of foot-and-mouth disease are sources of infection for susceptible animals. In many laboratory experiments it has been shown that virus can survive for long periods in infected carcases and offal, at temperatures ordinarily used in the meat trade. In one case virus was demonstrated in imported frozen meat. The epizootiological importance of infection from meat has clearly been shown in the United Kingdom and Greece. In the United Kingdom it is considered that there are two sources of infection: from the continent of Europe and from imported infected meat and meat products. The pattern of the infection of these sources is clear. Invasions from the Continent have been found in eastern, south-eastern and southern coastal areas of Great Britain, while primary outbreaks, the source of which is considered to be imported meat, occur in any part of the country in which such meat is distributed. In Greece, outbreaks have occurred several times in piggeries where the pigs were fed on waste material from imported frozen meat.

Veterinary authorities in the Scandinavian countries are strongly of the opinion that airborne transmission of foot-and-mouth disease virus is possible and accounts for the occurrence of some primary outbreaks. When northern Germany is infected, primary outbreaks appear on the Danish islands opposite Germany. When eastern parts of Denmark are infected outbreaks occur in the southern part of Sweden, and when the most northern part of Denmark is affected, outbreaks occur in south-eastern Norway. Air-borne transmission was also investigated in two laboratory experiments, one of which was negative and the other showed that transmission of virus by air was possible.

It is considered highly probable that foot-and-mouth disease can be spread by birds. This subject has been studied mainly in the United Kingdom. In connection with the epizootic in Great Britain in 1937-38 some laboratory experiments were carried out: they did not show much evidence in favour of the hypothesis but did not exclude it. The subject was again examined in connection with the epizootic in 1951-52 and it was concluded that migrating birds in both autumn and summer were responsible for introducing infection.

In several instances virus has been demonstrated in imported fodder and vegetables. This method of transmission has shown to be of much epizootiological importance.

In recent years, it has been reported officially that virus of foot-and-mouth disease has escaped from foot-and-mouth disease institutes: Yugoslavia in 1959, Netherlands in 1960 and the United Kingdom in 1960. It is highly probable that such escapes have taken place also from other institutes in the past but have not been detected because of the presence of the disease in the respective countries.

In many outbreaks in the field it is believed that infection is caused by recovered animals, either by simple transmission of the virus or by its excretion. Recovered animals may, however, be regarded as virus carriers only if they are introduced into susceptible herds in clean stables or pastures, and only on the presumption that there is no other possible source of infection. Some examples from Sweden and the United Kingdom are given from which it seems very likely that recovered animals have introduced infection.

The problem of virus carriers in the field has been studied mainly in Switzerland. According to experience accumulated over a number of years it was estimated that about 3 percent of recovered animals remained virus carriers and that the largest incidence of reinfections is at 5-6 months after the original infection. Among the numerous observations in the field, 16 are quoted but in only five of them were recovered animals introduced into clean herds; in the remaining 11, infection could already have been present.

In some laboratory experiments, 20 cattle from Switzerland thought to be virus carriers were investigated. In no case did they transmit foot-and-mouth disease to susceptible animals. In experiments with some 20 animals recovered from experimental foot-and-mouth disease, material was taken from the foot lesions. Virus was demonstrated in one case.

In Denmark, suspected virus carriers from the field were investigated in connection with the epizootic of 1951-52. In no case was virus demonstrated.

In some experiments in 1928 material from the hoofs of 103 recovered cattle and 9 pigs was investigated. In one case virus was found but it was considered that there was some possibility of accidental infection.

The fact that cattle recovered from foot-and-mouth disease can excrete virus over a period of several months, has been proved experimentally. In the first experiment it was found that blood and urine from recovered cattle contained virus. The following comments were made about the experiments: The

cattle had previously been used for production of hyper-immune serum; it was necessary to concentrate the virus up to a thousand times before its presence could be demonstrated. In another experiment it was found that a large proportion of cattle which had recovered from foot-and-mouth disease excreted virus in the saliva over several months. The virus could be demonstrated by the inoculation of saliva into unweaned mice or into the tongues of cattle. Susceptible cattle were not infected, however, by such virus carriers through contact or even when their mouths were swabbed with the infected saliva.

Some experiments, including a very large number of recovered animals, have been carried out and observations made in the field in different countries.

In the USA, in the early part of November 1914, 747 cattle contracted foot-and-mouth disease. On 25 March 1915, 50 young cattle were placed in contact with 740 of them after they had recovered and on 8 April, 50 pigs were added to extend the test. Until 30 May, when the observations were discontinued, no cases of foot-and-mouth disease had developed.

In Sweden, in connection with an epizootic in 1924-27 in the southern part of the country the following observations were made: when the epizootic was over . on 1 July 1927, some 158,000 cattle in a southern district had had foot-and-mouth disease (65.5 percent of the total number of cattle in the district). About a month after the disease was over, some 18,000 cattle in the recovered herds were gradually replaced, partly by breeding and partly by purchase of susceptible cattle. From 1 July 1927 until 4 December 1929 there were three outbreaks in the district. Furthermore, 20 days after foot-and-mouth disease was over in the district in question normal trade was again opened and about 100 cattle were then sold monthly to other parts mainly in central Sweden, and placed among susceptible animals. Thus, during $2\frac{1}{2}$ years some 2,500 cattle of which some 1,600 had recovered from foot-and-mouth disease, were sold out of the district. Not a single outbreak of foot-and-mouth disease appeared in herds which had received the recovered animals. It could, therefore, be said that chronic virus carriers did not play any part in the spread of foot-and-mouth disease in Sweden during the period mentioned.

In Argentina, the following observations have been made: in 1926 all of a group of 600 cattle had had foot-and-mouth disease and 20 days after their recovery they were mixed with 50 susceptible cattle. The two groups remained together on the same pastures for several months and no outbreaks of foot-and-mouth disease occurred. Similar experiments were repeated over some 20 years with cattle as well as with pigs. The experiments were carried out with groups varying from 100 - 800 cattle and from 10,000 - 18,000 pigs. Foot-and-mouth disease was never observed. In 1959, the statement was made from Argentina that there is no evidence of the existence of virus carriers in Argentina.

During the severe epizootic in 1938-39 in Denmark, some 100,000 herds (50 percent of all the herds in Denmark) or some 1,500,000 cattle contracted foot-and-mouth disease. The epizootic started in July 1938 and had its peak in November, with some 40,000 outbreaks and from February 1939 the number of outbreaks decreased rapidly until the epizootic was practically over by 1 July 1939. Among the 1,500,000 cattle recovered from foot-and-mouth

disease there should have existed thousands of permanent virus excretors. From a study of the course of the epizootic and of the outbreaks appearing during the last six months of 1939 there is no evidence that virus excretors played any role in the spread of foot-and-mouth disease.

Summary of Control of Foot-and-Mouth Disease

During the period with which this review deals, the following main methods of control have been applied in Europe under different circumstances: the stamping-out policy, isolation of infected herds, treatment with hyperimmune or convalescent serum, mass vaccination and vaccination combined with slaughter of infected herds.

By the stamping-out policy in the control of foot-and-mouth disease is meant slaughter of infected herds, combined with the application of strict veterinary measures without serum protection or vaccination. Only some few European countries with especially favourable geographical conditions have successfully applied this method over a number of years: the United Kingdom, Ireland and Norway. For the successful application of this policy of control many important questions related to it must be taken into consideration. It is necessary, for example, to have an efficient organization experienced in taking immediate action; sufficient funds must be available so that the policy can be continued to the end; the full co-operation of the farmers is necessary.

A comparative study was carried out on the value of isolation and of slaughter of infected herds. It was concluded that isolation was of doubtful value, while the stamping-out policy gave brillant results.

Before vaccination was introduced, hyperimmune and convalescent sera were b. being used on a large scale in several countries, with very satisfactory results. However, the passive immunity lasted only a short time and serum is expensive to produce, so this method could never find general application in the control of foot-and-mouth disease.

During the epizootic o 1937-39, several Continental countries (Switzerland, Poland, Denmark, and Sweden) carried out slaughter of infected herds on a large scale. Although this proved to be of some importance it could not prevent the disease from spreading in the countries, and causing a typical epizootic.

During this epizootic the Vallée-Schmidt-Waldmann vaccine appeared, and was used in Germany in the spring of 1938 and in Denmark in the autumn of the same year, in both countries at times when the threat of infection of vaccinated herds was very great. The results of the vaccination were highly satisfactory and the opinion was expressed that it would be possible to obtain complete protection by total vaccination. In 1948, it was stated that vaccination against foot-and-mouth disease is most effective when combined with slaughter of infected herds.

During the European epizootic of 1951-52 facilities for the production of vaccine were not nearly adequate to meet the situation, although vaccination where practised, certainly limited the number of outbreaks. This is clearly seen from a comparison between the number of outbreaks in 1937-39 and in 1951-52. In East Germany the number of outbreaks was negligible because systematic i vaccination of the cattle population had been applied before this part of Germany was invaded. In Switzerland and Sweden a combination of slaughter of infected herds, vaccination and the application of strict veterinary measures brought the invasion of the disease completely under control.

During the flare-up of foot-and-mouth disease in France and in Germany in 1956-58 vaccine was used on a large scale in both countries, with satisfactory results. During this flare-up the disease spread to neighbouring countries. In Denmark, Switzerland and Austria the invasions were met by slaughter of infected herds combined with vaccination and the application of strict veterinary

measures, and the disease was brought under complete control. In Belgium, mass vaccination of large numbers of the cattle was carried out and it is accepted that, because of this measure, Belgium avoided a widespread epizootic in 1956-57. In Luxembourg, there were some outbreaks in December 1956 and slaughter of infected herds was applied in the early cases. However, the disease spread rapidly and it was decided to vaccinate all the ruminants in the country. This vaccination completely eradicated the disease in Luxembourg. In the Netherlands, slaughter of infected herds was introduced in 1952, and systematic vaccination of the cattle population in 1953. This policy has brought foot-and-mouth disease in the cattle completely under control in the Netherlands.

Since the epizootic in 1951, Greece has had a number of outbreaks. However, a combination of mass vaccination and the application of strict veterinary measures has repeatedly eradicated foot-and-mouth disease from the country.

The Swiss system of controlling foot-and-mouth disease: a combination of slaughter, vaccination and the application of strict veterinary measures, has been applied in Austria, Denmark, Switzerland and Yugoslavia for some years and has succeeded in keeping foot-and-mouth disease under control in these countries. N

No exact information is available on the control measures in use in eastern European countries. It is understood, however, that vaccination is applied, combined with strict veterinary measures. The foot-and-mouth disease situation has been satisfactory in most of these countries for a number of years, for no large epizootics have developed.

In Russia, also, the foot -and-mouth disease situation is highly satisfactory. It is understood that vaccination plays a considerable role in keeping the disease so well under control. The vaccine in Russia is produced from virus cultivated in young rabbits and adsorbed to aluminium hydroxide.

The overall plan for the control of foot-and-mouth disease in Europe, put forward by the Commission's Standing Technical Committee, was adopted by the Commission at its 4th Session in 1957. It was recommended that in a country where there is a heavy weight of infection the policy should be systematic vaccination, varying in accordance with the circumstances in the particular country. When the number of outbreaks is sufficiently reduced, slaughter of infected herds may be introduced, and later, the stamping-out policy may be used as the main method of control.

A study of the results of vaccination in France in 1956 and 1957 was carried out. In general, the results were highly satisfactory, for protection was produced in 99 - 99.75 percent of vaccinated herds.

At an international meeting in 1958 where practically all foot-and-mouth disease workers in Europe were present, the subject was again discussed. It was appreciated that vaccination is of high value in the control of foot-and-mouth disease and that without vaccination, control of foot-and-mouth disease in Europe would be impossible.

While the immunizing value of the Vallée-Schmidt-Waldmann vaccine in cattle is generally recognised, little official information is available on the value of the vaccine in sheep and goats. However, the vaccine has been applied in sheep and goats in Italy, Greece and Cyprus for several years and it is claimed that the results are very satisfactory.

In pigs, the effect of vaccination is far from satisfactory as has been shown in many laboratory experiments. However, field observations indicat indicate that the vaccine may have considerable protective value. Intradermal vaccination seems to be more effective than the subcutaneous route.

When the vaccine first appeared in 1938 the source of virus was natural virus material produced in cattle tongues. This was very expensive and other sources of virus have therefore been sought.

In 1947 cultivation of foot-and-mouth disease virus in explanted cattle tongue epithelium was introduced, and in 1950 this method had been developed into large-scale production of virus. This source of virus in the vaccine has now been used in the Netherlands for more than ten years and has been introduced into several other countries. It has been of much importance in the control of foot-and-mouth disease in some parts of the world.

In recent years, cultivation of virus in kidney monolayer tissue cultures has been introduced. This culture virus has been shown to possess a satisfactory antigenicity, and vaccine prepared with it has already been used in field vaccination in Israel, Greece and Italy. This new method is now in full development in many countries.

The vaccine-foot-and-mouth disease virus complex produced in the skin of cattle is also a source of virus for the Vallée-Schmidt-Waldmann vaccine. This vaccine has found a considerable application in France.

When the vaccine first appeared, the dose of the monovalent vaccine was 60 ml., which was very large for field use. Many experiments have been carried out with the object of concentrating the vaccine. A concentrated trivalent vaccine in which the dose is 5 ml. is now in general use in the Federal Republic of Germany and in East Germany.

Foot-and-mouth disease virus was adapted to the embryonated egg in 1949, and in 1958, the successful modification of virus of types O, A and C and Asia I was reported from Israel. This modified virus of Asia I type was used on a large scale in Israel during the epizootic of 1959-60 with very satisfactory results.

Foot-and-mouth disease virus can also be adapted to rabbits. In 1959, it was reported that such lapinized virus was used in Russia in an aluminium hydroxide vaccine. It is claimed that very good results follow its use.

APPENDIX I

In order to appreciate to some extent the survival of the virus of foot-and-mouth disease in meat and offal, some information on the changes which take place in a carcase after slaughter is desirable.

The soluble proteins in meat coagulate and lactic acid is formed from the breakdown of glycogen, there being a change in the meat from a slight alkaline to an acid reaction. The occurrence of rigor mortis indicates that these changes are taking place, although the production of rigor mortis is not dependent upon this altered reaction and may develop in the absence of any such change. The muscle fibres relax as rigor mortis subsides. Lactic acid changes the collagen of the connective tissue to gelatin. Fats, unless at a temperature above that of the refrigerator do not undergo change: at warmer temperatures, hydrolysis causes the production of glycerol and fatty acids from them. In areas exposed to oxygen, a further breakdown takes place and aldehydes and lower fatty acids are formed. The pigment in exposed muscle surfaces is oxydised to produce a darker surface colour.

The rate at which the chemical changes take place is affected by storage temperature.

Changes in pH depend upon two factors - the glycogen content of the muscle at the moment of death and the buffering capacity of the muscle. At slaughter, beef has a pH of about 7.2 which may fall to 6.5 - 6.8 during the next hour. When a muscle is in full rigor the pH may drop to 5.4 - 6.0. After storage at slightly above freezing point, for 48 hours, the pH is usually 5.6 - 5.8 but after 96 hours, it rises again to 6.4. In normal healthy animals, meat after hanging for ripening has not been found to have a pH less than 5.3.

Some disease conditions tend to prevent the formation of lactic acid with the result that pH readings may be high. The pH of pork and mutton seldom falls below 5.7, because they contain less glycogen.

Inactivation of Virus in Muscle

Inactivation of the virus in the muscles of a carcase is brought about by the chemical changes, the primary factor being considered to be the formation of lactic acid. Prolonged survival of the virus occurs in meat when the pH does not fall below 6.2. The practical occurrence of this phenomenon is the prevention of acid formation in quick freezing.

The investigations by Henderson and Brooksby were carried out with bovine material under abattoir conditions. They showed that, in infected meat stored at 4°C, virus was demonstrated in muscle tissue for 24 hours but was not recovered on the third day, when the pH was 5.3. In frozen meat, however, the virus was found to survive for many months. These workers failed to recover virus from pork of infected pigs after it was kept at the usual "holding" temperature as well as in similar pork held at freezing temperature for 12 days; virus was, however, recovered from the bone marrow of these carcases at these times.

It was shown by Wittman that pork from infected pigs, frozen at -15°C contained live virus for at least 55 days and that the frozen pork, thawed and kept at room temperature contained virus for at least five days.

It was shown, some years ago, from work carried out in Great Britain that virus survived for at least four days in infected blood splashed on to the surface of a pig carcase kept at -15°C. In this connection, Zhytenko found that virus could be recovered for long periods from the surface of freshly-killed carcases contaminated with blood, after storage as well as from other parts of the carcase and equipment used in meat handling.

Virus in Bone Marrow

Bone marrow does not develop sufficient acidity to inactivate the virus. The workers in Great Britain recovered virus from bone marrow in beef held at room temperature for 76 days, in chilled pork for 42 days and in frozen pork for 76 days. Those workers also showed that in the bone marrow of beef carcases, held at -1°C for up to 80 days, virus was still present and that alternate freezing and thawing had but little effect on the survival of the virus in bone marrow.

Virus in Lymph Nodes and Blood

The same degree of acidity is not developed in lymph nodes and blood clots as in muscle tissue although they may be in close proximity to it. The British workers found virus in the lymph nodes of beef, stored at -10° to -20°C for nearly six months. It is pointed out that the pH of the infected nodes and blood was 6.5 while that of the muscle was about 5.6 They also failed to recover virus from beef lymph nodes in carcases stored at 4°C for five to six months.

They found virus in defibrinated blood samples, stored at 4°C for six weeks. Wittman also examined lymph nodes and blood: he recovered virus in blood clots stored for 70 days at 4°C and demonstrated its presence in fresh and frozen lymph nodes.

Virus in Internal Organs

The British workers reported that the non-papillated pillars of the rumen of cattle are frequently the site of small vesicles that may escape notice and they found virus in the rumen tissue, stored at -20°C for nearly six months. They also demonstrated virus in the liver and kidney, stored at -20° C for six months and seven weeks, respectively. Niggli showed that virus in liver and spleen kept at 4°C survived for more than 24 hours but was not recovered by the 48th hour. Wittman found virus in the liver, lung, spleen, kidney, brain, stomach and intestine of infected pigs and that it persisted in these organs for long periods when they were kept in a frozen condition. He found virus in some of these organs up to the fourth or sixth day, when they were kept at room temperature (21°C), but in the kidney and blood, up to the 10th day. Virus in the spleen appeared to become inactivated readily whereas the kidney seemed to favour its survival. Virus was also recovered from the heart blood of a pig 34 days after slaughter. Lother Girndt found that virus survived in the heart muscle of cattle for 32-40 hours when kept at 10° to 12°C, but failed to survive 48 hours.

Virus in Mixtures used for Curing

Tests carried out in guineapigs showed that solutions and mixtures containing varying proportions and combinations of sodium chloride, salpetre, sodium bicarbonate, sugar and boric acid had little effect on the virus. In four tests the virus persisted for as long as 7 - 11 days but not until the 18th day; in other tests it survived for up to 49 days. A pickling solution containing vinegar destroyed the virus rapidly because of the low pH. It was reported by Pyl and Klenk that the virus survived for more than two years in a pickling solution containing 24 percent sodium chloride. Rumiatev found virus surviving at least 26 days in sodium chloride solution and Dronin demonstrated the virus in salted tongues 14 days after infected animals were slaughtered.

Work has been carried out more recently, at Plum Island, U.S.A. The results have been published in the following article:- The Survival of Foot-and-Mouth Disease Virus in Cured and Uncured Meat, by G.E. Cottral, B.F. Cox and D. E. Baldwin, Vet. Res. (1960), XXI, 288.

The results may be summarised as follows:

A total of 72 cattle were used. The animals were infected with virus type A and were slaughtered 33 - 35 hours later, when viraemia was established and secondary lesions were beginning. Meat samples were tested fresh, after storage at 4°C for 72 hours and after storage in wooden barrels at 1°C for 16, 30 and 50 days. In the barrels were either cured meat, i.e. meat ripened and salted or unripened, unsalted meat. Samples of muscle, blood and lymph nodes were also tested. Infective virus was found in all the fresh samples, in ripened blood, in ripened lymph nodes and in cured lymph nodes at 30 and 50 days.

Virus was also found in rib bone marrow in carcases stored at 4°C for 14, 60 and 73 days and in lymph nodes, blood and muscle so stored for 60 days. Muscle stored for 73 days gave negative results. (Virus becomes inactivated in muscle tissue during the ripening process but virus in lymph nodes, large blood clots or bone marrow does not appear to be much affected.) In transverse sections of muscle tissue taken from rapidly chilled carcases, the pH readings show a general increase in acidity from the superficial towards the deep areas. Conditions are more favourable for survival of the virus in the superficial portions for nearly 48 hours.

The conclusion made was that meat derived from animals infected with foot-and-mouth disease was not rendered free of the virus by the usual commercial procedures of ripening, boning, salting and storage: virus can survive in certain tissues customarily included in such meat.

It is also stated in the article that from a practical standpoint, it would be nearly impossible for any abattoir to provide cured meat free from tissues which are conducive to virus survival. It would also be impossible to guarantee in an enzootic area that infected animals would never be used for meat. Therefore, the virus may survive and be demonstrable in commercially boned, cured or uncured meat, if the meat were obtained from an area where foot-and-mouth disease is present.

In 1961, an account of some further investigations carried out at Plum Island, U.S.A. was published in an article entitled "Further Studies on the Survival of Foot-and-Mouth Disease Virus in Meat" by B.F. Cox, G.E. Cottral and D.E. Baldwin.

Cattle were inoculated with virus type A contained in pooled tongue epithelium of artificially infected cattle and tissues were examined for the presence of virus through exposure of susceptible cattle.

The results were:-

1) Virus was present in a prescapular gland, removed surgically 20 hours after the steer was inoculated and four hours before any rise in temperature or any other clinical symptoms appeared.

2) Virus was present in pooled lymph nodes collected nine days after slaughter of an infected animal and when there were no longer any clinical symptoms: virus was not demonstrated in samples of muscle or rib bone marrow at this time.

3) Haemal nodes in the carcase of an infected steer, which showed clinical symptoms, contained virus when examined in the fresh state and after hanging at 4°C for 72 hours.

4) Virus was demonstrated in rib bone marrow in a carcase hung at 4°C for 194 days.

5) Virus was not demonstrated in lymph nodes from the carcase of an infected animal after the nodes were stored in a barrel of cured meat for 194 days.

6) The titre of virus in the supernatant fluid of rib bone marrow of an infected carcase had a titre of 10 - 4.5 bovine i.d. 50 per ml. Pigs fed with this marrow together with fragments of bone became infected, but when the fragments of bone were omitted, no infection occurred and the fed pigs resisted challenge at a later date.

From such results, it is stated that "meat from animals in the stages just preceding and shortly after the regression of signs of foot-and-mouth disease would be hazardous to export from countries where foot-and-mouth disease is present".

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APPENDIX II

N O T E

on the Work of

the European Commission for the Control of Foot-and-Mouth Disease

The European Commission for the Control of Foot-and-Mouth Disease was established within the framework of the Food and Agriculture Organization of the United Nations on 12 June 1954 to "promote national and international action with respect to control measures against foot-and-mouth disease in Europe". Its first Session was held on 27 July 1954 and Sessions have been held, annually, since that year. The Commission has its own budget, financed by the annual contributions of its 15 Member Countries and its own Secretariat. The history of the events which led to the final establishment of the Commission is given in some detail in the section on "Report of the Work of the Commission during the Last Five Years" in the Report of the Commission's Sixth Session (Meeting Report No. AN 1959/1 of FAO).

The disease in Europe

While the Commission has been active in many directions since its establishment, two of its most important accomplishments have been the acquiring of an intimate knowledge of the epizootiology of foot-and-mouth disease in Europe and the planning of control measures, applicable to different countries, with the object of, eventually, introducing an overall stamping-out (or slaughter) policy of control throughout Europe.

As discussed in the "Review", the work of the Commission has resulted in a clear appreciation of the sources of the viruses, causing outbreaks and epizootics in Europe, and their spread throughout Europe. This study has been made possible from discussions and information received at the many visits by members of the Secretariat to both member and non-member countries in Europe, from information given by representatives of both member and non-member countries at the meeting of the Commission's Executive Committee in different

countries and at the Sessions of the Commission, by a careful study of available literature, and by the important and regular information provided by the Director of the Office International des Epizooties, Paris. Soon after the establishment of the Commission an agreement was reached whereby the reporting of outbreaks and the position of the disease in countries in Europe would remain in the hands of the O.I.E., who would keep the Commission informed. This arrangement has been highly satisfactory, especially during more recent years.

A study of and discussions on methods of control operated in different countries, together with the knowledge of the effective results of vaccination against the disease according to the several systems in practice, led to the evolving of the Commission's "Overall Plan for the Control of Foot-and-Mouth Disease in Europe" - a plan recommended for the implementation in stages to meet the conditions in the various countries. (The plan is fully described in the Report of the Fourth Session of the Commission - Meeting Report No. 1957/5). It is of interest to note that by the adoption of this plan, a position has been reached in some countries whereby, together with vaccination, slaughter of infected herds is carried out.

Collaboration

The Commission has always realized and appreciated the importance of maintaining close collaboration with all organizations, especially international organizations, concerned with or interested in foot-and-mouth disease in any part of the world. No opportunities have been neglected to strengthen such collaboration.

With its Secretariat stationed at FAO Headquarters in Rome, the Commission has many opportunities of acquiring information on the foot-and-mouth disease position in many parts of the world. Reports from FAO veterinarians from many countries and regions are always available and first-hand information is received from those veterinarians when they visit Rome.

Collaboration with the O.I.E. has been increasingly established over the years. There are now regular consultative meetings between the Secretariats of the European Commission and the Foot-and-Mouth Disease Commission of the O.I.E. (Already there have been joint meetings on measures to be adopted should exotic strains of the virus cause outbreaks in Europe; on measures to prevent the introduction of exotic and classical strains of the virus into Europe in imported meat and meat products; and for the study of the position and control of foot-and-mouth disease in the south-eastern countries of Europe). Again, a satisfactory agreement was reached and is practised whereby the Chairman and Secretary of the Commission of the O.I.E. attend the annual meetings of the Laboratory Group of the European Commission's Standing Technical Committee. Members of the European Commission's Secretariat always attend the annual sessions of the O.I.E. and the meetings of its foot-and-mouth disease commission, and the O.I.E. is always invited to send representatives to the Sessions of the Commission.

Contact and collaboration was established with the former O.E.E.C. which resulted in the mounting of a symposium by that organization in Amsterdam in 1955 on typing and cultivating foot-and-mouth disease virus, on behalf of the European Commission. Further joint projects, unfortunately did not materialize due partly to the reorganization of O.E.E.C.

Collaboration with the Council of Europe resulted in a member of the Commission's Secretariat visiting Dublin in 1957 and addressing a meeting of the Council's Committee on Agriculture. The outcome was a recommendation by the Committee, accepted by the Committee of Ministers as follows:-
"The Assembly recommends to the Committee of Ministers that they again invite member Governments which have not yet joined the European Commission for the Control of Foot-and-Mouth Disease to become members or at least to find ways and means of giving effective support".

From the beginning there was contact with the Pan American Foot-and-Mouth Disease Center at Rio de Janeiro: the contact was considerably strengthened by the visit to the Center of the Commission's Chairman (Sir John N. Ritchie) in 1958.

There is much mutual interest in the European Commission and the recently established Plum Island Animal Disease Laboratory (U.S.A.) where research on foot-and-mouth disease is carried out. The Secretary of the Commission attended the official opening of the Laboratory in 1956 and in 1960 he spent three months there, at the invitation of the U.S. Government to assist in the planning of future research work.

The disease outside Europe

While the European Commission is essentially a regional organization concerned with the control of foot-and-mouth disease in Europe, a considerable amount of attention has been given to the position in other parts of the world, especially those from which there is a risk of virus, classical or exotic, being introduced into Europe. Over the years, there has been an increasing amount of circumstantial evidence that outbreaks of foot-and-mouth disease have been caused in Europe, particularly United Kingdom and Greece, by virus whose source was frozen meat and/or offal imported from certain infected South American countries. The proximity of the exotic African and Asian strains of virus to Europe has also been of some concern to the Commission.

The Commission felt so strongly concerning meat importations from infected South American countries that a request was made to the Director-General FAO to appoint a consultant to visit the various countries concerned and report on the position. This resulted in the visit made by Sir John Ritchie (chairman of the Commission) and Dr. K.V.L. Kestevon of FAO, whose report and recommendations were transmitted to the Commission (see Report of the Commission's Sixth Session - Meeting Report AN 1959/1).

Following the recognition of the Asia I type of the virus as the cause of outbreaks of foot-and-mouth disease in Israel, two visits were made: one in 1959 by the Secretary and one in 1961 by the Chairman and the Secretary. In addition to a study of the epizootiology of the invasions, much valuable information was received on the production and the results of the use of the egg-adapted attenuated virus-vaccine, which was evolved in Israel.

The Commission has also directed attention to the increasing development of livestock production in parts of the world, especially Africa, in which exotic strains of the virus have been found in outbreaks and the potentiality of markets in Europe for meat and animal products from such regions. A joint Commission - O.I.E. meeting made recommendations for the minimising of the risk of introducing infection through such marketing and also made resolutions inviting the Director-General of FAO and the Director of the O.I.E. to make prescribed recommendations on the subject to the European Governments (Report of the same Session) the Commission supported Resolution No. 22/59 on Livestock Disease Control, adopted at the 1959 FAO Conference, stressing the importance of establishing FAO veterinary posts on group-country or regional bases.

Other activities

At its Third Session, the Commission established its Standing Technical Committee composed of veterinarians from member countries, some with much experience in the policies and practices in controlling foot-and-mouth disease and others with much laboratory experience. At its periodical meetings this Committee discusses and advises on problems referred to it by the Commission and its members are available to travel to countries in which "on-the-spot" advice is requested.

The Commission fully appreciates the impetus which has been given to Research on foot-and-mouth disease and the need to be kept informed of developments and results. To this end, the Secretariat keeps in close touch with

research institutes, not only in Europe but in all parts of the world. Many visits have been made to the institutes in Europe and some institutes outside Europe. In addition, the laboratory members of the Commission's Standing Technical Committee meet each year at the laboratory in a member country when informal discussions are held on current work and problems. Representatives of the O.I.E. Foot-and-Mouth Disease Commission participate in these meetings to which other research workers on the disease may be invited to make contributions on some special subject. Reports of these meetings are presented at the Sessions of the Commission.

The Commission lays much stress on the regular typing of virus causing outbreaks and epizootics. While in most of the European countries there are adequate facilities for such work or satisfactory arrangements have been made to have typing carried out, the Commission participated with FAO in appointing the Research Institute (Animal Viruses) Pirbright as the World Foot-and-Mouth Disease Reference Laboratory, by making an annual financial contribution. It is only in exceptional cases that the Pirbright Institute carries out routine typing of virus for European countries, but it is always prepared to assist any member country in which typing difficulties arise.

Because of the facilities at the Pirbright Institute, an agreement was arranged jointly by the Commission and the O.I.E. that the Institute makes available samples of antisera of exotic strains of the virus to typing laboratories in countries in Europe: and further, the Institute will prepare and store small amounts of inactivated vaccine of exotic types for emergency use in the event of outbreaks caused by such viruses in any country in Europe.

The finances of the Commission do not permit of expenditure to any great extent for supplies of vaccine for member countries in which vaccine is not produced, or in which supplementary amounts are needed in emergencies or to operate part of a control program. The Commission, however, has taken some

action: following enquiries in vaccine-producing countries, a list has been compiled showing the institutes from which vaccines may be made available to member countries in need of supplies, at a price which is usually only a small amount above the cost of production.

There is no doubt on the importance of vaccination as part of control policies for foot-and-mouth disease in most European countries and that vaccination will continue to be used in them for some considerable time. For this reason, countries which formerly did not produce vaccine are now establishing or have recently established foot-and-mouth disease institutes. On the recommendation of the Commission, financial assistance has been provided by or through FAO for the purchase of equipment for some of these institutes. The Secretary of the Commission has also spent some time in them, advising on their operation.

The above notes describe briefly some of the past and present activities of the Commission. No reference has been made to the day-to-day work of the Secretariat at Headquarters where individual problems are handled involving interviews, discussions and much correspondence.

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3. Production annuelle normale : 800 000 - 1 200 000 doses de vaccin monovalent.
Capacité hebdomadaire maximum : environ 480 000 doses de vaccin monovalent ou 240 000 doses de vaccin bivalent ou 160 000 doses de vaccin trivalent.

France

1. Institut français de la fièvre aphteuse (I.F.F.A.), Lyon;
Laboratoire Roger BELLON, Neuilly s/Seine;
Institut bactériologique de Tours (I.B.T.);
Laboratoire d'opochimiothérapie, Toulouse (ce laboratoire vient d'entreprendre la production de vaccin qui est pour l'instant peu importante);

2. Les quatre laboratoires produisent tous le vaccin Vallée-Schmidt-Waldmann. Le vaccin produit par l'I.F.F.A. est en outre saponiné.

Sources de virus :

- I.F.F.A. et laboratoire d'opochimiothérapie de Toulouse : virus de culture (méthode de Frenkel).

- Laboratoire Roger Bellon : soit virus naturel récolté sur des bovins inoculés expérimentalement, soit une association de virus naturel et de virus de culture (méthode de Frenkel).

- I.B.T. virus aphteux cultivé in-vivo sur la peau de génisse en symbiose avec du virus vaccinal.

3. La production totale a atteint 15 200 000 doses de vaccin trivalent en 1962.

République fédérale d'Allemagne

1. Behringwerke AG., Marburg-Lahn;

Farbenfabriken Bayer AG., Maul- und Klauenseuche Station, Köln-Nippes, Ossendorferstrasse 1a;

2. Vaccin Vallée-Schmidt-Waldmann sous la forme concentrée (méthode de Pyl);

Sources de virus : virus naturel provenant de langues de bovins.

3. Vaccins monovalents, bivalents et trivalents.
Capacité annuelle : environ 20 000 000 de doses de vaccin trivalent.

Grèce

1. Laboratoire pour la fièvre aphteuse, Aghia Paraskevi Attikis, Athènes;

2. Vaccin Vallée-Schmidt-Waldmann;
Sources de virus : virus cultivé sur cellules rénales de veau

3. Capacité annuelle : environ 233 000 doses de vaccin monovalent pour bovins ou environ 700 000 doses de vaccin monovalent pour ovins, caprins et porcins.

Italie

1. Instituts fabriquant des vaccins en Italie :

a) Istituto Zooprofilattico Sperimentale del Piemonte e della Liguria, Via Bologna 148, Turin

b) Istituto Zooprofilattico Sperimentale delle Provincie Lombarde, Via Cremona 282, Brescia

c) Istituto Zooprofilattico Sperimentale delle Tre Venezie, Padoue

d) Istituto Zooprofilattico Sperimentale dell'Umbria e delle Marche, Via S. Costanze, Pérouse

e) Istituto Zooprofilattico Sperimentale del Lazio et della Toscana, Via Appia Nuova 1411, Rome

f) Istituto Sperimentale Zooprofilattico della Sicilia, Piazza Generale Turba, Palerme

2. Sources de virus :

a) Turin - Vaccin Vallée-Schmidt-Waldmann et culture de tissus;

b) Brescia - Vaccin Vallée-Schmidt-Waldmann, Frenkel et culture de tissus;

c) Padoue - Vaccin Vallée-Schmidt-Waldmann, Frenkel et culture de tissus;

d) Pérouse - virus de culture sur cellules rénales de veau in vitro;

e) Rome - Vaccin Vallée-Schmidt-Waldmann et culture de tissus;

f) Palerme - Vaccin Vallée-Schmidt-Waldmann, culture de tissus et prochainement le virus sera aussi produit par la méthode de Frenkel.

3. Les vaccins produits sont monovalents, bivalents et trivalents. production annuelle de l'ordre de 3 000 000 de doses. Capacité annuelle de production de l'ordre de 10 000 000 de doses de vaccin trivalent.

Pays-Bas

1. Centraal Diergeneeskundig Instituut, Cr. Wattenburgerstraat 7, Amsterdam-C.

2. Vaccin Vallée-Schmidt-Waldmann.
Source de virus : virus de culture (méthode de Frenkel).

3. Capacité annuelle de l'ordre de 3 300 000 doses de vaccin trivalent.
Des mesures sont prises pour accroître la production de 50 pour cent environ, résultat qui ne sera probablement atteint que vers la fin de 1962.

Espagne

1. Los Laboratorios BECA, S.L. de Lugo;
Los Laboratorios ZELTIA, de Porrino, (Pontevedra).

2. Vaccin Vallée-Schmidt-Waldmann;
Source de virus : BECA : virus naturel provenant de langues de bovins
ZELTIA : virus de culture (méthode de Frenkel).

3. Production annuelle :

BECA : 500 000 doses de vaccin bivalent pour bovins et 50 000 doses de vaccin trivalent pour bovins. Cette production peut être facilement doublée.

ZELTIA : 500 000 doses de vaccin bivalent pour bovins et 50 000 doses de vaccin trivalent pour bovins. Cette production peut être quadruplée.

Suisse

1. Institut vaccinal fédéral, Hagenaustrasse 76, Bâle.

2. Vaccin Vallée-Schmidt-Waldmann.

Source de virus : virus naturel provenant de langues de bovins.

3. Production annuelle normale : 500 000 doses de vaccin bivalent. L'institut prépare des vaccins bivalents OA et OC. Il fabrique pour l'exportation de petites quantités de vaccin O, A et C qui servent à la préparation de vaccin trivalent par mélange.

Turquie

1. Laboratoire anti-aphteux, Etlik, Ankara.

2. Vaccin Vallée-Schmidt-Waldmann;

Source de virus : virus naturel provenant de langues de bovins;

3. Quelque 250 000 doses de vaccin monovalent ont été fabriquées en 1961 et on espère produire à l'avenir plus de 500 000 doses de vaccin monovalent.

Royaume-Uni

1. Virus Research Institute (Animal Virus Diseases) Pirbright, Surrey;

2. Vaccin Vallée-Schmidt-Waldmann;

Source de virus : virus de culture (méthode de Frenkel);

3. Capacité annuelle : environ 6 000 000 de doses de vaccin monovalent.

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