THE PROPHYLACTIC VALUE OF INOCULATION IN

GENERAL COMMUNITIES DURING EPIDEMIC PREVALENCE

OF TYPHOID FEVER.

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MA., MB., Ch.B. (Edin):

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"The severest trial of typhoid vaccination will for many years be among the general population, and failures will continue to occur among the vaccinated, and only in decreasing frequency with the increasing percentage of a community that is vaccinated. If the people would hasten the ultimate obliteration of the disease, they might do so by being vaccinated, not when threatened with an unusual exposure to typhoid fever, but under the ordinary conditions of existence in which one is relatively protected in civilised communities". (Gay).

Prophylactic Inoculation has been practised in practically all the armies engaged in the Great War but has not been carried out to any extent in mixed civil communities, even when conditions of unusual exposure to infection from typhoid fever have made their appearance.

The results achived by inoculation in the armies are so striking as to admit of no denial of its immense utility as a prophylactic measure, and one has little hesitation in asserting that if inoculation were adopted and repeated in civil communities it would render typhoid fever a disease of rare occurrence in these communities. The latest statistics regarding the cases of typhoid fever in the British armies in France from the commencement of operations to December 19th 1918 are:

Typhoid - Brit			Cases.	Deaths. Case Mortality		
lnoculated with	n T.A.V.	or T.A.E	3. vaccine	1715	76	4.43%
Uninoculated	8	85	19	696	128	18.33%
	73455		Total	2413	204	8.45%

These figures relate to a Force of over 2,000,000 men, of whom about 80% were inoculated, this standard being kept up by yearly reinoculation.

The opportunities afforded for arriving at a reliable estimate of the value of prophylactic treatment by the vaccination of the members of a general community of considerable dimensions during the actual prevalence in its midst to an exceptional degree of typhoid fever have not been many. Most of the observations recorded have been made under circumstances in which the treatment has been given long before the individuals have been exposed to infection, and these lead to a certain amount of confliction of opinion as to the advisability of resorting to inoculation on an extensive scale when typhoid fever makes its appearance in epidemic form.

The fears of what might happen during the "negative phase" after inoculation to an individual who is incubating typhoid fever, have led many to follow Wright in advocating against the use of antityphoid vaccine in the course of an epidemic of the disease. Others are not at all certain of the existence of a "negative phase" of immunity after vaccination. It is well known that even repeated inoculation is not an absolute safeguard against infection from the disease even after a period when the individual might be considered to be at the height of his immunity.

What is required to enable one to judge whether general inoculation ought to be practised in the presence of a typhoid epidemic is accumulated evidence that where it has been put into force its influence in limiting or artually stopping the spread of the disease has more than compensated the community for any serious effects that have ensued in individual instances.

Spooner reports the occurrence in a Vermont village of a water borne epidemic, where after 17 cases had developed, 29 of the remaining 48 inhabitants who had been exposed to the disease were inoculated, 19 remaining uninoculated. 5 Cases subsequently appeared among the latter; while among the former one mild case was met with, the symptoms coming on immediately after the first injection of vaccine. He remarks that "Inoculation in the time of epidemics must be performed with care since it is inevitable that many must be inoculated during the incubation period. The result of this accident is not serious, however. My experience would indicate that the onset of symptoms was hastened by this step but that the infection was shorter and of a less severe character --". he notes also in another instance, the small morbidity among a number of nurses and others who were intimately exposed to the disease before & during inoculation. with which, he says, is in perfect accord with the observations of Pfeiffer Leishman and Russell that the period following injection is one of increased resistance.

Elmer records a food infection epidemic in St.Louis City Hospital where 43 cases occurred among 250 persons exposed to the infection. 261 persons in the hospital were inoculated, practically all the vaccine being given during the time when all of the cases of typhoid developed. "The fact that only 20 of the 261 who received the vaccine developed typhoid ----

speaks against any marked increase of susceptibility, and the fact that 20 did develop typhoid is against any marked increase of resistance following recently given vaccine.

Basten reports the results of inoculating 245 members of a sanitatskompagnie in which 15 cases of typhoid fever had occurred, 3 of which died. Three doses of ½ce, 1 ce, & 1 ce of antityphoid vaccine were given at intervals of 8 days. After the first injection 13 cases of typhoid fever occurred, 2 being fatal; after the 2nd, 9 cases occurred, one being fatal; after the 3rd one case occurred.

In a Feldlazarett, 4 cases occurred after one injection; one after the second; while after the third 5 men had elevated temperatures for 5 days, one dying in the 3rd week after a relapse; and two other men mildly ill 4 weeks after inoculation but gave bac.typhosus in blood culture.

In a Telephone Section in which 4 cases had occurred, many men had temperatures for 2 or 3 days after inoculation. Basten remarks" --- we have to take it for granted that these cases (which developed the disease) were at the time of the vaccination in a state of incubation. This accounts for the fact that with the exception of one case in the Baggage Train, typhoid developed after vaccination only in the Units most exposed to the infection i.e. the Sanitary Company and the Hospital ---. Only in these two Units and the Telephone Section, in which also some cases of typhoid occurred before the vaccination, did we notice reactions with fever lasting several days. The course of the fever in these latter cases resembles that of an abortive typhoid."

And again " --- it may be stated that no further cases of typhoid (the first of which developed three months and the last one month ago) occurred after the vaccination had been completely carried out."

Furth, Pfugbeil and Oertel describe the compulsory inoculation of the civilian inhabitants of Ostend in Oct.-Dec. 1915, repeated July-August 1916 in an article entitled "The vaccination against Typhoid Fever in Ostend, an example of vaccination with favourable results in a large town". They note the deficient hygienic conditions in Ostend. the defective water supply, bad housing, and ignorance of health principles of the working classes. Typhoid fever was endemic, the number of cases in August 1915 Of a population of 32811 in 1915, rising to 38. 27472 received 3 doses of Vaccine, and out of 32728 in, 1916. 27008 were given a full prophylactic course. They report the results of the vaccination thus " Consequences injurious to health were observed in no case. Two facts in particular speak for the excellent effect of vaccination.

Before the inoculation, typhoid fever occurred sporadically in the whole district. It disappeared totally in the same proportion as the vaccination in the districts vaccinated one after the other, but did not show any change in the districts not yet vaccinated. With the completion of vaccination it ceased. 2 In the district in question were observed

Before the vaccination

Dec.'14 - Nov.'15

After the vaccination

Dec.'15 - Nov.'16

Typhoid fever cases

Deaths

213

18

0

Of the 6 persons down with typhoid fever, 4 were not vaccinated. Two persons affected in spite of vaccination live with a bacillus carrier".

This inoculation at Ostend was the first instance of compulsory inoculation applied to a large general community.

Circumstances of a similar nature arose when on the 20th December 1918 a British Army Corps Headquarters arrived at Euskirchen in Germany to take the place of another Corps which had been located there for the 10 Euskirchen is a county town some days previously. twenty miles west of Bonn having a civilian population at the time of British occupation of about 13,000. Some six days after his arrival the D.D.M.S. of the Corps received information that there were cases of typhoid fever in the civilian hospital, and immediately took steps to have a thorough investigation made by British Medical officers in conjunction with the Kreisartz and the Burgomeister into the extent and origin of the outbreak with a view to the limitation of the infection, and especially to the prevention of spread to the troops.

I was then Specialist Sanitary Officer, commanding a Sanitary Section attached to one of the Divisions in the Corps, and was instructed to undertake this investigation. The German civil authorities at Cologne appointed Dr.

Josef Basten, who had had special experience of epidemics of infectious disease in Galicia and other theatres of war, to assist the local Kreisartz.

As I was unfortunate enough to be unable to speak the language, a German with a knowledge of English was put at my disposal as interpreter. Throughout the whole period, I co-operated with Dr. Basten, communicating with him in French, and whatever information either of us

was able to acquire was freely put at the disposal of the other. Conferences were held at frequent intervals by the D.D.M.S. which the Kreisartz and the Burgomeister attended, where the factors involved in the epidemic were considered and instructions issued to the civilian authorities for the carrying out of certain measures of precaution.

To arrive at a conclusion regarding the source and means of spread, it was decided that Dr.Basten and myself should visit the patients and their relatives and collect information which might lead to the discovery of some common origin of infection. At the same time attention was paid to the water, milk and butter supplies, and certain precautionary measures adopted, including compulsory inoculation of the civilian inhabitants, without waiting for the cause of the outbreak to be made clear.

A serious drawback in the early stages of the investigation was the fact that all samples requiring bacteriological and chemical examination had to be sent to laboratories at Cologne and Boun, which involved considerable delay before results could be communicated to us. Ten days after the presence of the disease in the town was notified, a military bacteriologist began to assist in the examinations, and 4 days later a British mobile Bacteriological Laboratory was stationed at Euskirchen and materially facilitated the work.

On the 3rd January 1919 a case was reported in each of the villages of Weilerswist and Gross Vernick and the outbreak there also began to assume proportions of considerable magnitude. Still later in January it came to our notice that another epidemic was in progress in the villages of Sechtem, Merten, Trippelsdorf and Walberbey, all of which were within the area of Corps administration.

The investigation therefore had to be extended to embrace these two outbreaks as well as that at Euskirchen, and the same methods were pursued.

## History of the three outbreaks.

To obtain a true perspective of the effects of the inoculation it is advisable that these three outbreaks should be considered in some detail as to their origin, spread, and extent at the time of commencing the injections.

The Euskirchen Outbreak.

A reference to the attached map of the Kreis on which are marked the cases of typhoid fever notified during the years 1913-1918 (October) will give an indication of the extent to which the disease is endemic in that part of Rhineland. It is probable that, if the group of cases at Sechtem, there to can be considered to furnish a reliable criterion, many cases have occurred in recent years which have not been notified, no doubt partly owing to the number of medical practitioners being insufficient, and

partly to confusion of diagnosis with that of influenza which ravaged the district in 1918.

Suspicion was first of all directed against the water supply, the source of which is a gallery running at a depth of 16 feet into a hill side, the collecting pipe covered by layers of sand and gravel, and the "well" or collecting chamber being efficiently protected from contamination. The land around, though cultivated, was not manured with human excrete, and no dwellings were within half a mile. The pressure in the pipes was constant and very high, no supply is given off above the town, and in the streets of the latter the drains in the centre lie at a lower level than the water pipes which run at the sides.

Examinations were made of samples taken at various parts of the town and at the source by Prof.R.O.Newman of Boun and by Capts.McLead and Ritchie of No.8 Mobile Laboratory without any contamination being indicated.

The milk supply was carefully investigated. One farm was found when a case had occurred at Euenheim but none had been supplied to the town later than Oct.6th 1918.

Extensively conducted bacteriological examination of employees at farms, milk shops and milk sterilizing depots to detect possible carriers gave negative results.

All the butter consumedin the town passed through

the shop of a wholesale merchant and was distributed to retailers. It was collected from numerous farms in the county at 7 centres. At one of these, a farm, Russians and Poles had been working up till the beginning of November but had not been engaged in the butter manufacture. There also, the whole of the produce was supplied to Euskirchen which was not the case with that of the other centres. The whole family and employees gave negative excreta examinations and three who had been ill with influenza in November were also negative toWidal test.

The source of origin and spread of the infection could not be discovered in contaminated water, milk or butter supplies and no other article of food appeared to be common to the patients. Although, therefore, the very wide distribution of cases in the town, the presence of diarrhoea about the same time, and the large proportion of children affected made one incline to believe in the existence of a water or food infection, there was no evidence adduced to prove it. The families where cases had occurred in recent wears were then examined for carriers but none were broughtto light.

One of the first cases to occur was that of Frat Heines who nursed her brother Fritz Kupper, a case at Evenheim, and she undoubtedly infected three other cases in her street. It is highly probable that there were several sources in

previous cases in the town; in undetected cases; perhaps in carriers among German troops who passed through the town in the patter part of November, resting there a night or two on their way to cross the Rhine by a pontoon bridge at Wesseling; and perhaps in some contaminated article of food.

The avenues for contact infection were many. The inhabitants were badly hourished and in no fit state to resist disease. The schools were closed, the children played in the streets, consorted with German troops, visited one another's houses to an increased extent, and frequented the banks of the Erft stream and its branches, into which the untreated sewage of the town discharged. A lack of disinfectants at the hospital and the fact that several privies in the poorer quarters discharged directly into the various tributaries of the stream, no doubt also conduced to widen the distribution.

When on the 20th of March I handed over further investigation to my successor, 131 cases of typhoid fever had been notified. As very strict injunctions had been put on the civilian doctors and the Burgomeister to notify every case, diagnosed or suspected, and house to house visits had been paid by six female Kreisfurzorgerin or Health Visitors, it is unlikely that many, except perhaps abortive, cases escaped hospital treatment.

Appended is a table showing dates of onsets of all cases notified in Euskirchen from the beginning of November 1918.

### Outbreak at Weilerswist and Gross Vernich.

The combined population of these two villages which are contiguous is 2492.

A reference to the appended map which indicates the water distribution of the county will show that these villages obtain their supply from the same source at EICKS which feeds the town of ZULPICH. The quantity distributed to the villages was known to be deficient in December and the inhabitants were driven to use local wells and the contaminated ERFT stream for domestic supplies. It was anticipated, therefore, at the outset of the investigation that cases would in all probability arise there, and these fears found justification before many days passed. Before a case actually came to notice, however, a consultation between the LANDRATH, the various water officials, Dr. Basten and myself led to steps being taken to improve the supply, and by about the 10th of January an adequate piped supply was re-established in every house.

The earlier cases in both villages had made use of the Erft stream, and in every other case with only one exception, contact infection could be established. The villages were not large and much intervisiting was done while the children played together and used privy closets in common.

Up to the 20th March 26 cases were known to have occurred.

On the attached sheet are detailed the dates of onset of all cases notified.

# Outbreak at Sechtem, Merten, Trippelsdorf and Walberberg.

The combined population of these 4 villages which are closely grouped is 5010.

It was not until the last week of January that this outbreak was brought to our notice, although on probing its history, one was able to trace cases of illness in these villages which had undoubtedly been typhoid fever with onsets as far back as the beginning of December.

It appears probable that the infection was carried to Merten by a girl who had contracted the disease at a distance and came to live with her parents there after discharge from hospital; the earliest case in Merten was related to her and had an onset about 10th December. The first cases at Sechtem occurred 27th Dec. and no connection with previous cases could be traced.

The spread in the four villages seems to have been due chiefly to contact infection, 14 of the patients actually belonging to 5 inter-related families.

The water was not accountable for spread of the disease but in all probability the milk carried infection

in a small proportion of the cases, since the cow-tender at the principal farm in the neighbourhood was affected early in January, and again the husband of a woman who retailed milk in Sechtem was also a victim and was nursed by the latter before removal to hospital. In the vast majority of the cases, however, contact infection could be established.

Up to 20th March a total of 46 cases had been known to occurr, and the attached list shows the dates of onset.

It is to be noted that not a single case occurred in any inoculated soldier who was billeted in the area

#### Inoculation of civilian inhabitants.

instructions were issued by the British authorities for the compulsory inoculation of the civilians with British T.A.B.vaccine.

An attempt had been made previously by the Kreisartz to obtain a supply of German antityphoid vaccine from Berlin for voluntary inoculation but circumstances rendered its delivery impossible.

T.A.B. vaccine contains in 1 ce. 1000 millions bacilli typhosi ---

500 million bacilli paratyphosi B, and 500 million B.para A., the routine method in the British Army being to give two doses at intervals of 10 days.

It was decided that all persons between the ages of 6 and 45 years should be inoculated with the exception of those certified by a doctor to be suffering from an ailment which contra indicated such treatment, and women three months before and two months after childbirth.

The limit of 45 years was afterwards felt to have been inadvisable, and when inoculation of the inhabitants of the other districts was practised it was raised to 55.

The doses were graduated according to age; the first dose for persons between 6 & 10 years was  $\frac{1}{8}$  cc.

" " " " 
$$11 \& 17$$
 " "  $\frac{1}{4}$  " "  $\frac{1}{2}$  " "  $\frac{1}{2}$  "

Instructions to the above effect were issued to the Kreisartz and at a meeting of German doctors which he convened, a detailed scheme was planned on the lines of that followed in October 1915 when the Germans inoculated the people of Ostend.

On 7/1/19 an article was contributed to the local newspapers

newspapers by the Kreisartz detailing the precautions which it was essential for the inhabitants to take to prevent limit the spread of the infection, one paragraph reading: - "Experience during the War has shown that the best precautionary measure against typhoid fever is inoculation. The people are therefore urged to volunteer for inoculation as soon as the necessary arrangements can be made, about which further particulars will be published" (Euskirchener Zeitung 7/1/19).

A further notice in the public press appeared on 10/1/19 to the following effect. "The British Military Authorities have ordered the inoculation of the inhabitants of the town between the ages of 6 & 45 years. The inoculation will be done in two doses with an interval of 10 days between them. The following persons are exempt:- 1. All persons suffering from a fever.

2. All persons with serious lung disease.

These are required to furnish a medical certificate to the Police at 7 Bischofstrasse.

Also exempted are all women three months previous to and two months after childbirth. They will be required to show a medical or midwife's certificate.

The inoculation takes place on the following days
(list of centres follows at which dwellers in enumerated streets were to present themselves on particular days)

Everybody has to be inoculated on the day ordered.

The dates for the second inoculation will be published

later."

The inoculation was carried out by the German doctors at six public centres, and also in private. T.A.B.vaccine, hypodermic needles, and methylated spirit were supplied by the British medical Authorities. Besides the doctor at each centre, there were engaged: 1.A clerk who entered up the name, age and address of each person inoculated 2.A Female attendant who prepared the site of injection with tincture of iodine. 3. An attendant to sterilize the needles and 4. A policeman. Visits were paid to the centres daily by a member of the Administrative medical Staff of the British Corps or myself.

The civilian population of Euskirchen on 16th Jan.

1919 numbered 13,010, of whom 8385 were between the ages

of 6 and 45 years. Inoculation was commenced on the

11th Jan. and the daily numbers receiving a first dose

varied from 1000 to 1400 till the 17th., by which date

8339 persons had been dealt with.

The 2nd injections were commenced on the 21st, and by the 28th 8076 had received the second dose.

On 4/2/19, 112 persons who from various causes had failed to report previously were given a second dose, so that about (Since some of those appearing at the second session may not have been treated at the first) 8198 of the inhabitants were protected by two doses of the vaccine, representing approximately 62% of the population. A number of those were demobilised soldiers who had previously been the recipients of prophylactic injections

of German vaccine, antityphoid only.

Cases continued to occur after the vaccination was commenced and I have been kept informed up to date of their occurrence.

From the 11th Jan. to the 14th March, the number of cases reported with onsets during that period was 32. Of these 15 were uninoculated i.e. were under 6 years, over 45, or had been exempted on account of illness.

8 Developed the disease after one injection; 9 had been inoculated on two occasions.

I propose to discuss the effects of the vaccination in this epidemic along with those observed in the other two outbreaks at a subsequent stage of this thesis.

#### Inoculation at Weilerswist & Gross Vernich.

It had been hoped that the disease in these two villages would not be wide spread since the people themselves and the medical practitioner were aware of the probability of its occurring. Notwithstanding this and the fact that a good water supply was reestablished early in January, however, the infection continued to be propagated by contact, largely owing to delay on the patients' part in consulting the medical man. It was decided therefore, that the inhabitants should be protected by vaccination, all between 6 and 55 years being treated.

In this instance, the villages were informed by proclamation by the Burgomeister of the arrangements which were similar to those adopted at Euskirchen. The combined population was estimated at 2492.

Inoculation was commenced on the 1st and completed on the 23rd of February, 1763 persons receiving a first dose and 1788 presenting themselves on the dates advertised for the larger dose, so that it is obvious that some of the latter received only one injection of the vaccine. It is safe to reckon, however, that over 70% of the population of these villages were protected by two doses.

From the date of commencing the treatment, to the 2nd March, twelve cases had onsets, of which 11 had been inoculated, 9 having received a single dose only and 2

a second dose.

### Inoculation at Sechtem, Merten, Trippelsdorf & Walberberg.

As soon as it was made apparent at the end of January that the outbreak in these villages had already assumed unsuspected dimensions, authority was obtained for vaccination of the inhabitants between 6 and 55 years. The arrangements took rather longer to complete in this case as the doctors and their assistants were confronted with difficulties with regard to transport. The combined population of these villages was 5010. Inoculation was commenced on the 9th of February and was not finally completed till the 27th of that month. 3314 Persons presented themselves for a first dose and 3417 at the dates hotified for the second dose. Between 65% and 70% of the inhabitants received the full course.

Subsequent to 9th Feb., 9 cases of typhoid fever occurred in this district, of whom 8 had been inoculated, 4 having received one dose only and 4 two doses.

For various reasons, it was not possible to have the second doses injected at a 10 days interval after the first in these villages and at Weilerswist and Gross Vernich.

## Effects of inoculation as observed in the three outbreaks.

When compulsory inoculation was proposed, the point was raised by the German doctors as to the advisability of forcing the vaccination since it had been observed by one of them (Dr.J.Basten) that, when similar treatment had been adopted among infected troops, many who received the vaccine while in the incubation stage developed the disease in a severe form. This point had been considered on the British side also.

Wright has questioned the advisability of inoculating in such conditions, but, on the other hand, other opinions are recorded to a contrary effect, some observers holding that even after infection has been contracted, if inoculation is performed early, it reduced the virulence of the attack.

It is recorded also by the German observers during the inoculation at Ostend in which it is most probable that some of the inoculated were incubating the disease, that "consequences injurious to health were observed in no case".

Spooner also states, as is mentioned above, that in such cases "the infection was shorter and of a less severe character".

For the probable good of the majority, the objections were over-ruled.

On analysing the cases in which inoculation was

performed presumably during the incubation period, or in which the patients were infected immediately after inoculation, one finds the following results:
A.21 Cases occurred after 1 dose of the triple vaccine.

10 of these developed within 12 hours; 2 died, 6 were mild cases 1 moderate, 1 severe.

2	11	11	"		n	24	. #	1 mild, 1 severe.
4	11	n	11		n ·	48	tt	2 " 2 moderate
ī	11	11.	11	*	**	72	11	1 "
2	11	11	11	**	H :	96	11	l severe, l mild.
1	11	, tr	11	. 3	oh the	8th	day	mild.
		•		1.2				and the same of th

16 Cases occurred after 2 doses of the vaccine.

5 developed within 12 hours after the 2nd dose, 1 died, 4 mild cases.

2 " " 48 " " " " both mild cases.

1 " on the 8th day " " " died.

2 " " 9th " " " both mild.

1 " " 12th " " " mild.

l " " "l4th " " " " mild - had relapse serious.

3 " "22nd " " " l died. Other 2 sever

1 Case had onset on the 31st day, being infected apparently some days after the inoculation.

The total number of cases which were brought to my notice up to 4/4/19 was 203 with 37 deaths giving a case mortality rate of 18.22%. The number of cases among uninoculated persons during that period was 166, with 32 deaths, a rate of 19.28%.

The number of cases developing in inoculated persons was 37 with 5 deaths, 13,544 individuals were inoculated, a few of whom received only one dose. The case incidence among the inoculated was .27% with a case mortality of 13.5%.

of a mild type, though, apart from the 5 deaths, 5 cases were severe in character. If one might hazard an opinion with reference to the 3 severe cases (one of which died) in which the onset of symptoms was on the 22nd day after the 2nd inoculation, (and one case occurring on 14th day in which there was a serious relapse) it is that these cases

were infected during the period immediately following the inoculation when the negative phase of immunity was present.

Three of the five fatal cases had onsets within 12 hours after injection of a dose of vaccine, while 2 severe cases developed within 24 hours. It appears probable that 1. inoculation of individuals incubating the disease and 2. the infection of individuals during the time after inoculation corresponding to Wright's negative phase of immunity may be attended by more serious results than when inoculation is done a considerable time before infection is contracted. This does not point to the existence of a period of increased resistance following injection as shown by Pfeiffer, Leishman and Russell.

It is noticeable that a large proportion of the cases after inoculation developed in an abrupt manner, the usual symptoms being prominent from the start of the illness. Goldscheider & Kroner note that the fastignim in the inoculated is either very brief or does not occur at all.

only in one or two patients had the temperature returned to normal before the expiry of three weeks: in one case temperature was normal after the 10th day of disease. The aborting of the disease noted by several observers in cases occurring when artificial immunity has been established was not prominent in this series of cases. Four patients were admitted to hospital suspected to be suffering from typhoid fever in whom the cause of the illness - lassitude headache, rise of temperature to about

39.c persisting for 2-3 days appeared to be due to reaction from the inoculation.

It is possible that mild aborted cases did occur and were not brought to the notice of the medical attendants.

It was impossible to come to any definite conclusion as to the effect of the vaccine in accelerating the onset of the disease. It would appear, however, since 15 of the 38 cases developed within 12 hours after the injections, that the incubation period is shortened in no inconsiderable proportion of cases. This conclusion has been arrived at by observers in other outbreaks where inoculation has been performed.

In two instances relapses of a severe nature occurred and one of the patients died. No serious complications occurred in other cases.

There are two points with regard to the vaccine itself in these epidemics which demand consideration.

- employed in the British T.A.B. vaccine differed from that of the infecting organism in these outbreaks, and it is open to conjecture whether the results of the inoculation might not have been improved if, as Vincent and others suggest, it had been possible to employ a polyvalent vaccine or even one manufactured from bacteria from the locality of exposure. It may be that the less unfavourable results on those who must have been incubating typhoid at Ostend when inoculated with German vaccine were due to the strain employed being more closely akin to that causing the disease there.
- 2. The British vaccine is directed to protect against Paratyphoid A & B as well as typhoid and .

theoretically at least it is probable that a less high degree of immunity against typhoid fever is attained in the same time as would be the case if an uncomplicated vaccine were used. Although this point may not have much practical bearing on the question as to the comparative degree of insusceptibility to infection of individuals inoculated with a mixed vaccine or a single vaccine when exposed to infection after the lapse of, let us say, weeks, it is, in my opinion, of some importance when vaccination during the presence of an epidemic is under consideration.

Castellani remarks that"--- in individuals inoculated with mixed vaccine the amount of agglutinius developed for each germ was nearly the same as in the control individuals inoculated with typhoid vaccine only, paratyphoid "A" only, or paratyphoid "B" only". On the other hand Gay's conviction that "relatively high protection may exist in an individual with or without agglutinius or antibodies in the circulating blood, and, conversely the presence of antibodies in the circulating blood is no indication either of absolute protection, which probably never exists, or of the degree of protection against typhoid infection" tends to diminish the weight of Castellani's statement.

Tables showing dates of onset of symptoms in cases of the disease furnish fairly clear evidence of the value of the exhibition of the vaccine in modifying the spread. In all three outbreaks it is observed that while the other measures adopted such as compulsory removal to hospital, disinfection of houses etc. may have accomplished a considerable mitigation, nevertheless cases continued to develop up to the dates of the commencement of the inoculations. In each instance, there then occurred almost immediately a remarkable increase in the number of cases, a further increase being again noticeable when the second doses were administered.

If 23 days can be taken as the probable limit of the incubation period, and a reckoning be made from the last day on which the first dose of vaccine was injected in the three affected areas, it is found that subsequent to the dates arrived at until the 13th of April when my latest information was obtained, ll cases were reported. After a lapse of 23 days from the last date on which a second injection of vaccine was made, only 2 cases were notified.

In all the cases among the inoculated, with the exception of 2 direct contact infection could be traced.

Among the uninoculated cases during the same period, contact infection was ascertainable in all but 1.

## Conclusions.

- 1. Inoculation against typhoid fever of members of a general community of susceptible ages during a period of epidemic prevalence will very materially assist in checking the spread of the disease.
- 2. Inoculation of individuals in the incubation stage of typhoid fever may in some cases mitigate and in other cases intensify the severity of the disease.
- afterwards infected with typhoid fever may aggravate the severity of the disease. In a proportion of cases the period immediately following inoculation is not one of increased resistance to infection.
- 4. It is advisable, where possible, to inoculate a community before it is faced with exceptional exposure to infection.

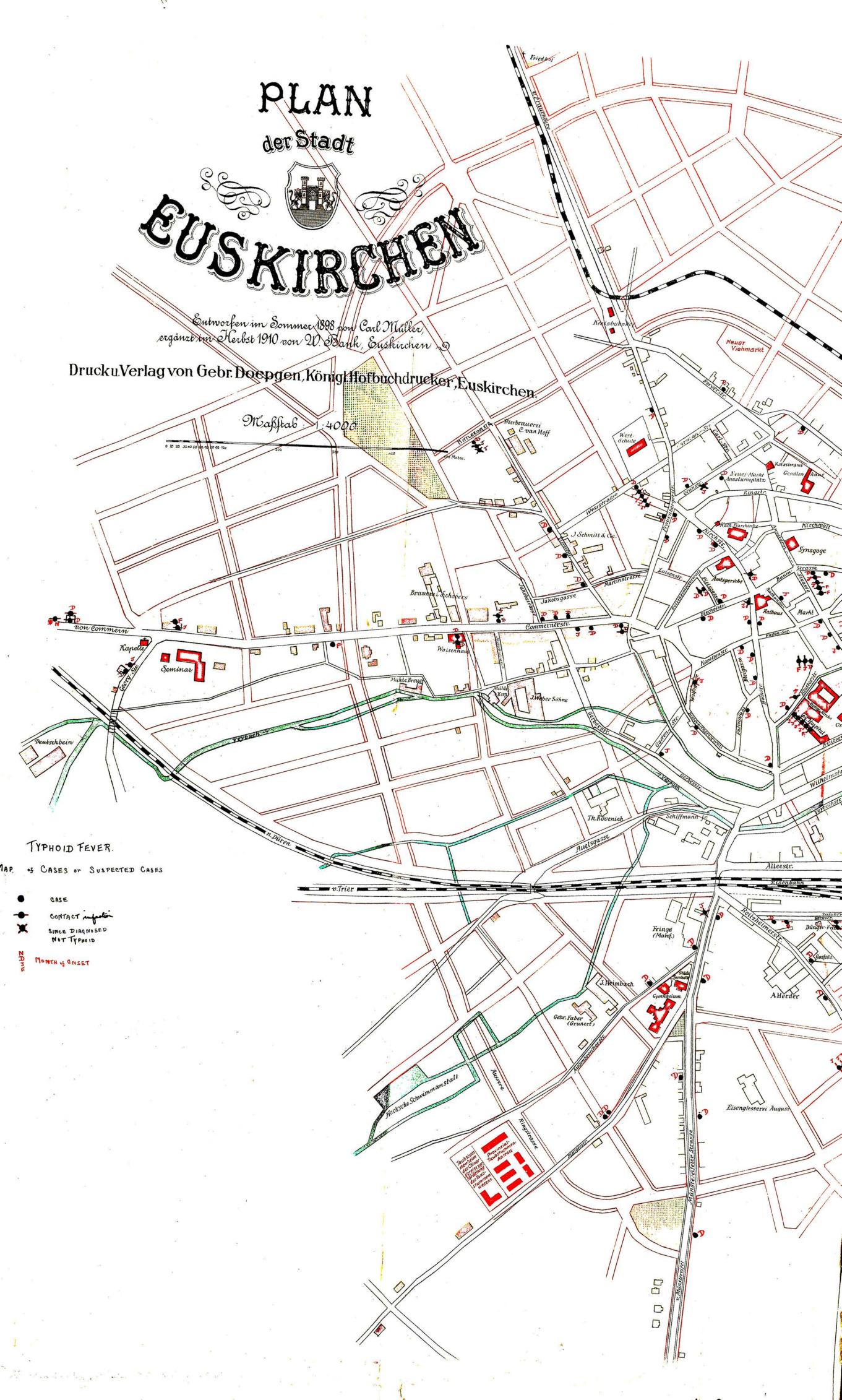
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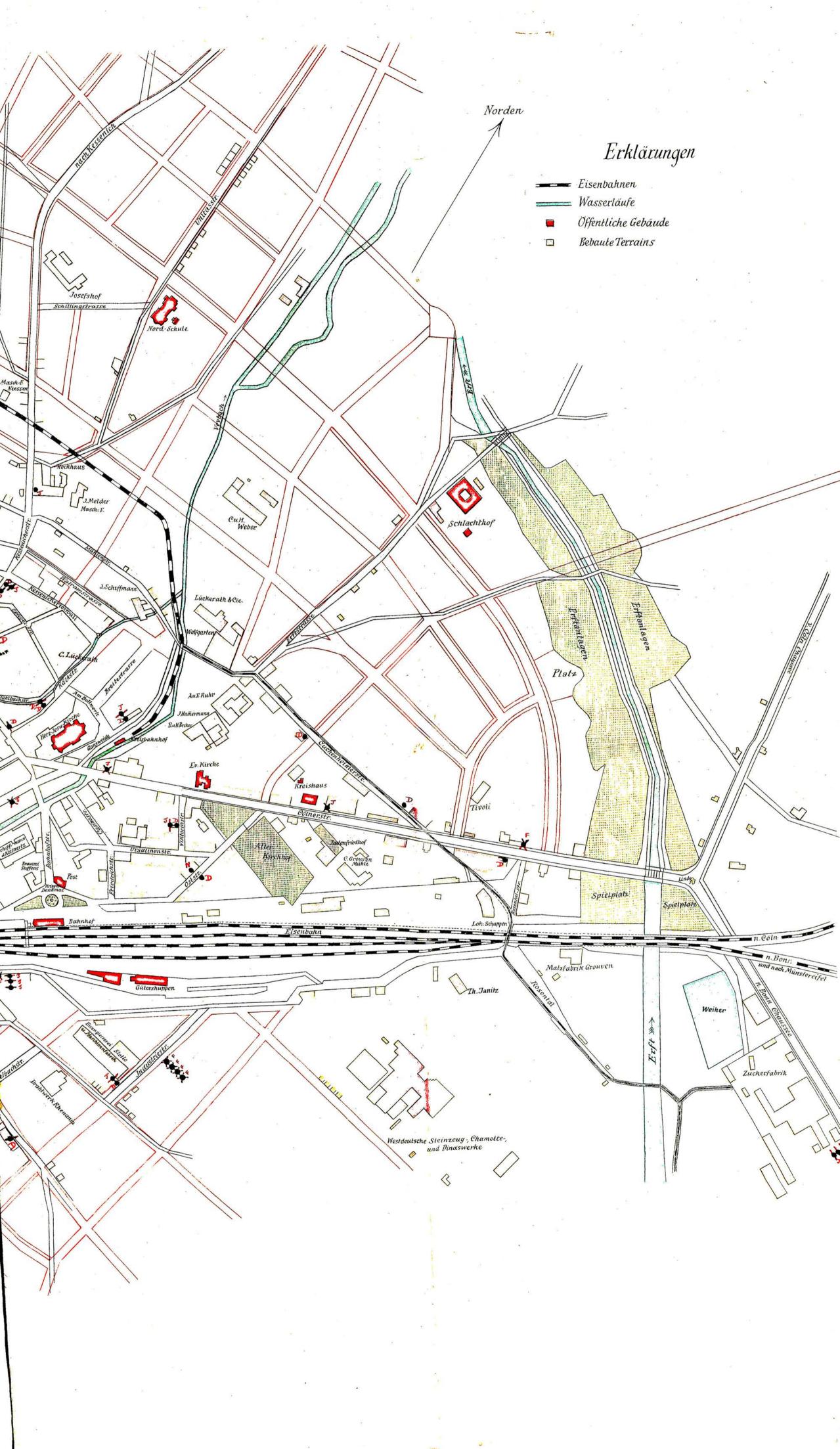
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39.

## Appended are 1. Tables showing

- a. Dates of Onset in 131 cases of typhoid fever in Euskirchen.
- b. " " " 46 " " " Sechtem etc.
- c. " " " 26 " " " " Weilerswist & Gross Vernich
- d. Synopsis of cases subsequent to inoculation at Euskirchen.
- e. " " " " Sechtem etc.
- f. " " " " " Weilerswist & G.V.
- a "Spot map" showing distribution of cases in Euskirchen outbreak
  - b. " " " " Weilerswist,
    Gross Wernich.
    & Sechtem outbreaks
  - c. " " " " " " in recent years in the County.
  - d. Map showing water supplied in the county.





Synopeis of cases having onsek subsequent to shoculation with TAB Vaccine

e	Ĩ	1 19 9	· 0-1-	1,443	0 ( - )	EUS	KIRCHEN.
NAME	AGE	Dose	DATE	2nd Justus Dose S	Date	Onset	Remarks.
ANNA DAHL	30	1/2cc	17-1-19			19-1-19.	BT+ in stool. T 38°C + tel 24.2. Symptoms wild
MARGARETA SCHMIT	Z 14.	1/4cc	15.1	1/2ce	25-1	<b>25.1</b> .19	Tup to 39.5°C lote 16.2.19. hild case.
MARGARETA GLEHN	8	1/8 cc	13.1	1/4 cc	23./	1:2:19	T up to 39°C+ tale 20.2.19. huld case.
CORNELIUS ZIMMER	12	1/4 ce	15.1			16.1	T up to 39°C tile 9.2.19. Serionaly ill, blood in slove.
GERTRUDE MANDT	22	1/2 ce	[4]			17.1.	7 " " 39°C la 3-3-19. Symptom moderatef severe.
ELIZA BARTH	18	lice	14:1			18.1	T 39°C la 2.2.19. Symptoms mild
GERTRUDE MARK	10	1/8 Cc	12:1.			12.1.	DIED 10/3/19.
AUGUST MULLER	11	1/4 Ce	16.1			24.1	Meld case. Three weeks fever.
Johann Glehn	39	lice	11-1			11-1	T 38-40° tile 15.2. Senously ill, blood in stool.
HELENA SCHMAUL	14	1/400	12:1	1/2 cc	22.1.	22.1	Mild Case.
SISTER AVIA.	28	1/2ce	13.1			13.1	BT+ stool 9.2. Tupto 39° late 25.2. Symptoms mile
MARGARETA GULDEN	22	Tree	13-1	Ice	28.1.	23.1	T 38-40°C bte 4:2 huld case.
JULIA GREMLITZA.	30	Izce	13:1	Ice	23.1	1.2.19	T 37-39 th 11.2. Mues case.
JACOB BESSELER	8	1/8 cc	11-1	1/4ce	21-1.	2 · 2 ·	T 38-39.5 tile 19.2: huld case.
FRAU BILLIC	32	1/2ce	12.1	Ice	22./	5.2.19	huld case but had serious relapse with blood motival 3.3.19.
ANNA MICHAELS	10	1/8 ce	14-1	1/4 ce	24.1	15.2	BT+ in store 24.3 maderate symptoms
MICHAEL MICHAELS	44	Lee	14-1	rce .	24.1	24.2	BT+ in stool 24.3. Symptoms moderate
PETER BILLIE	44	1/2 ce	174	1 00	33.1	14.3	Seurnacaser

		SECHT	EM. MERT	EN T	RIPPELSDORF WALBERBERG
NAME	AGE	14 INOCULATION Dose DATE	2. INOCULATION DOSE DATE.	ONSET	REMARKS.
FRAU ANNA DAHMEN.	39	1/2 cc. 14-2-19	ì	14-2-19	Temperature over 39.5°C tile 4-3-19. Uneld case.
FRAU ANNA CREMER	34	1/2 cc 11.2.19	7	11.2.19	T. between 38° , 39° tile 7-3-19. Dearrhoea on 24-2-19. Wild case.
PETER REY.	19	1/2 ce 9.2.19	7	102.19	T 38° - 39.5° tile 3/3/19. BT in Stool 22-2-19. Theed came
ELISE MIESEN	10	1/8 cc 12-2-K	1/4cc 28-2-19	2.3.19.	T to 39° totton 8.3.19 When last Sean. Dearrhoen on 4.3.19. Mild case.
Side PLACIDINE	30	1/2 cc 13.7:19		13. 2:19	Unild case
FRAU BRAUN	24	1/2 ce 9.2.19	lec 23.2.19	23.2.19	7 to 38.5 the 17.3. Wild case. Wild case
SYBILLA DAHMEN	13	1/4 ce 10.2.10	1/2 cc 23.2.19	16.3.19.	Had a relapse and died 4.4.19.
ANNA ZISTIG	26	1/2 ce 12.2.19	1 cc 28.2.4	2.3.19	hild case. T 40°C - 37°C lite 25/3

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TABLE showing dake of ONSET of cases at WEILERSWIST - GROSS VERNICH.

26 cases.

DEC 16 - - - - DEC 10

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JAN	2	3	4	5	6	7	ç	9	10	"	12	/3	14	15	16	17	18	19	20	2/	22	23	24	25	26	27	28	29	30	3,	
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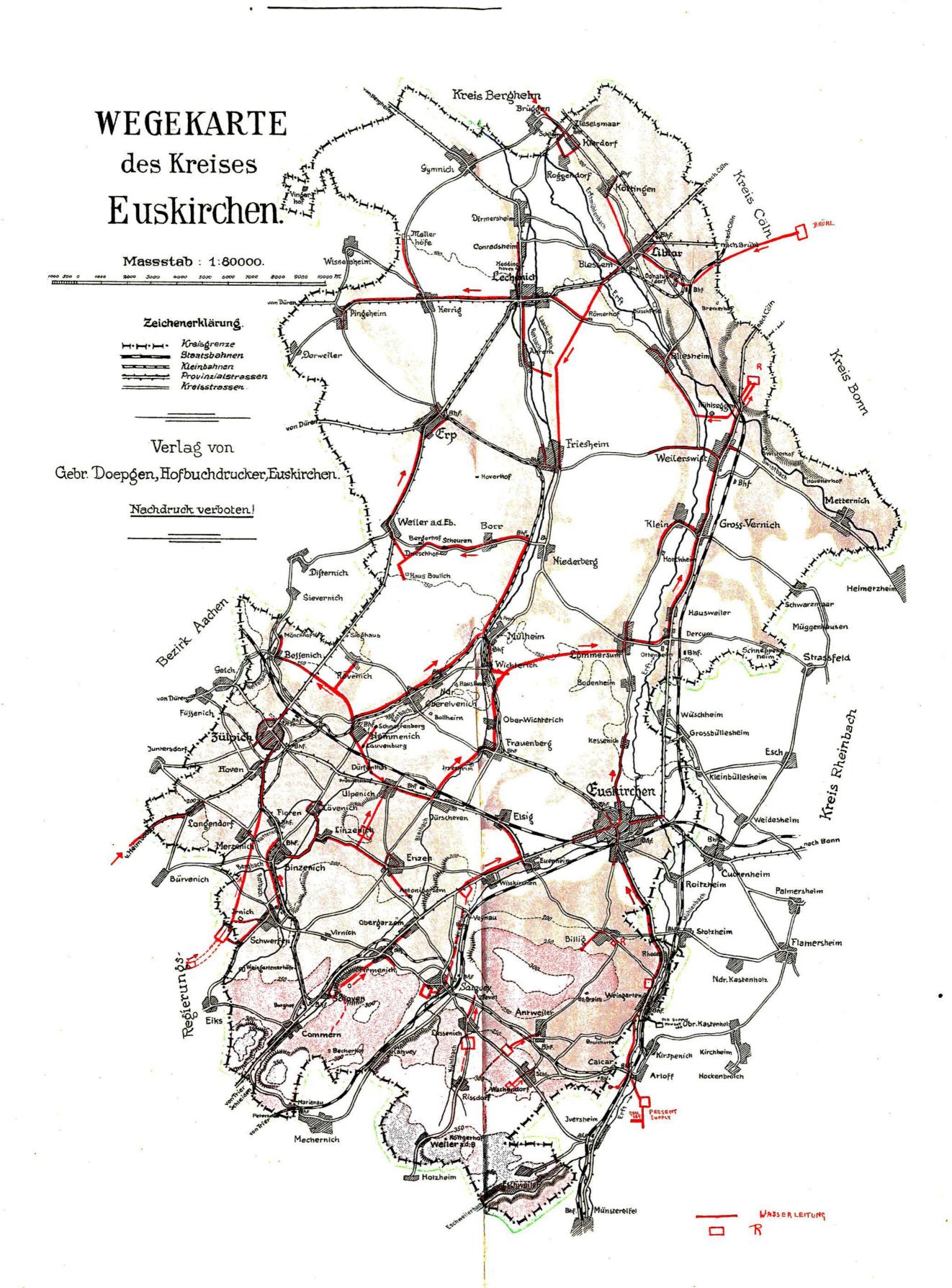
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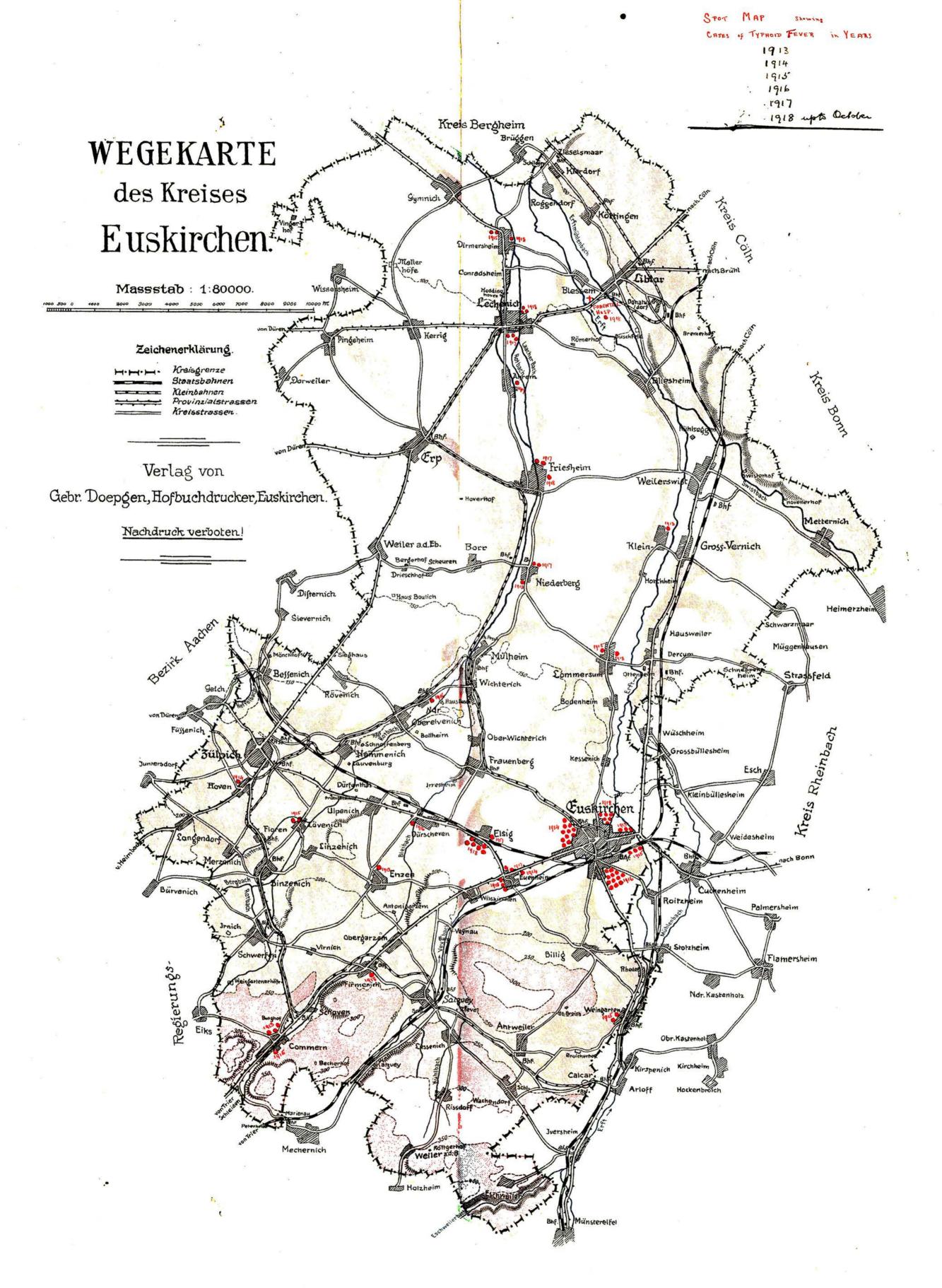
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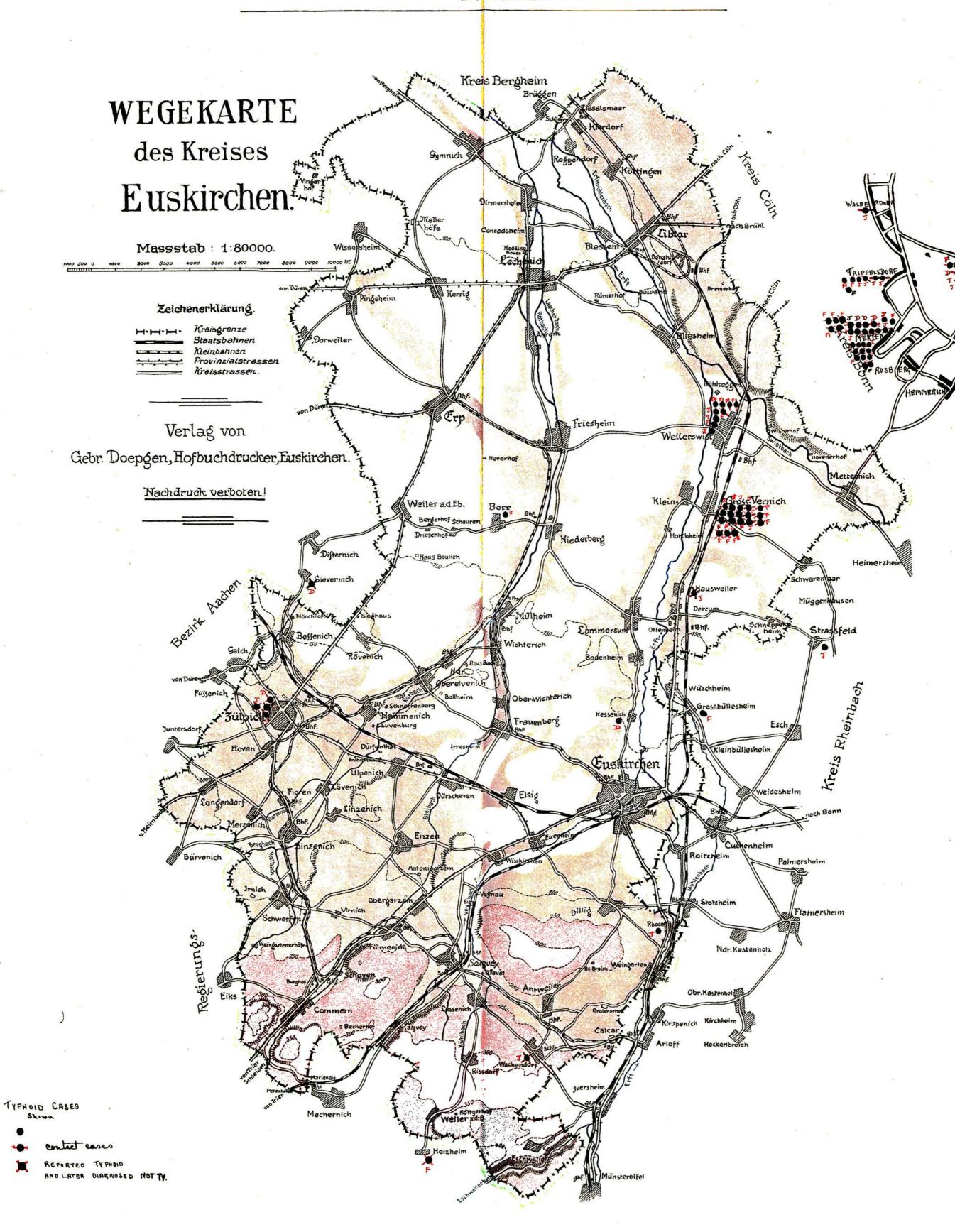
TABLE showing dake of ONSET in cases at SECHTEM, MERTEN, WALBERBERG, + TRIPPELSDORF.

46 cases

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Came 3	1	1	1	1	1	-	-	_	6	-	1	-	_	-	1	-	-	1	3	-	,	2	2	-	-	1	1	4	-	-	
FEBI	2	3	4	5	6	7	8	14	dose 10	vae.	ina 12	13	14	15	16	17	18	19	20	21	12	23	24	25		lose 17	28				
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Synopsis of cases having onsels subsequent to desculation with TAB Vaccine.

WEILERSWIST

GROSS VERNICH.

NAME	Ae	₿E.	DOSE		14 INOCULATION DOSE DATE	ONSET	REMARKS
TOHANN WEIN	EN 8	3	1/8 cc	1-2-19		1-2-19.	Mild case
ANTON HONIO	10	0	1/2 cc	1-2-19.		1. 2.19	med case .
KATERINE ROS	Line 16	6	1/4 ce	2.2-19	*	4.2.19	Tupto 39° let 6.3.19. Symptoms wild.
JOHANN KRAE	MER II	ı	1/4 ce	1.2.19		3.2.19.	7 37-39° tu 18.2. Mild case.
KARL VITT	35	2	½ ce	3.7.16		3.2.19	DIED 8.3.19. Had been tubereular Subject.
MARGARETA VI	т 28	3	½ ce	3-2-19	Ice 17-2-4	17:2:19	DIED 28.2.19.
JOSEF KADE	R 9		1/8 CE	2.2.19		4.2.19	T up to 39.5° la 22.2. Mild case
HELENA PETE	RS. 10	5	1/8 ce	2.7.19	*	2-2-17	BT in Stool 1.3.19. T & 38°C lite 4.3. Dearrhoea +. Symptoms moderatel severe.
FRAU BOLL	18 24	+	1/2 ce	3.2.19		7.2.19.	Servously ill: blood in stools.
MARGAKETA KRI	MER 16	0	1/4 cc	11.1.19 at Enskinels		20.1.19	Mild case
Heinrich esse	R 20	0 1	12ce	1-7-19	1cc 23·2·19	2-3-19	DIED 16.3.19. BT+ Stook whene Blood calture.