OBSERVATIONS ON AN EPIDEMIC OF INFECTIVE HEPATITIS IN GERMANY, JUNE - DECEMBER, 1945.

by

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C O N T E N T S

I. INTRODUCTION.

The epidemic discussed here took place in the latter half of 1945, when I was medical officer of a battalion on occupation duties in the Rhineland. The references to the literature were obtained during a post-graduate (ClassI) appointment held in Glasgow during February-July, 1946. At the time of the epidemic I was unable to leave the area for any length of time, and further investigation of cases and follow-up were difficult. Any detailed examination of cases, other than purely clinical, was therefore out of the question.

I am indebted to Capitaine-Commandant F. Julien of the Belgian Army for permission to investigate this epidemic among troops under his medical care.

II. Review of certain previous accounts of epidemics.

Epidemics of jaundice have long been recognized as a concomitant of war and as a disease, in particular, of armies in the field. Epidemiological studies are however rare until the last century. It is noteworthy that Pope Zacharias, writing between 741 and 752 A.D. (Migne (42)) to St. Boniface, suggested the importance of segregating cases of jaundice lest the contagion be passed to others. Pliny at an earlier period merely remarks on the curative effect of gazing at a golden oriole, which is immediate, but fatal for the bird. The earliest reference I can find in military history is an outbreak in Minorca in 1745. Woodward, who is quoted by Lucké(37) studied jaundice as a whole in the American Civil War, noted the epidemic character of the disease and gave a clinical description which included an incubation period of 1-6 weeks a pre-icteric phase and liver enlargement. It was not, however, until 1886 that Weil (64) made the first attempt to distinguish between the various forms of infectious jaundice after Virchew's description of catarrhal inflammation of the vile ducts in 1864. Cockayne (8) made the first attempt to distinguish between Weil's disease and 'catarrhal jaundice'.

During the 1914-18 war, epidemics were numerous and much literature was published, that relating to the Dardanelles campaign being of especial interest. It is discussed at length in the 'Medical History of the War'. Certain of the deductions which can now be drawn are made by Van Rooyen and Gordon (62). It is interesting to note that despite the prevalence of dysentery it was generally accepted that droplet infection was to blame though some

workers/

workers suggested the possibility of pathological changes due to infection by paratyphosus B organisms - a line still being followed as recently as 1940 by Senevet and others(57).

Since the war of 1914-18 the probability of a hepatitis and not catarrhal changes being the cause of jaundice in this epidemic form was stated by several workers, though this view did not at once find general acceptance. Between the wars a number of epidemics were described in various countries notably in the United Kingdom, U.S.A., and in Scandinavia. In this connection, Marshall (40) as recently as 1945, found competent French observers inclined to the view (untenable, as we know) that the disease was one of the Anglo-Saxon countries. (Against this he might have cited the dictum quoted by Ford (21): 'Il ya des mois où il pleut de la bile à Paris', a proverb regarding seasonal prevalence). It is proposed to review certain of the literature published during those years:

Blumer (6) in 1923 reviewed the recognized American epidemics. He could find no record of any in the U.S. War of Independence, but there were epidemics in 1812, and thereafter only eleven recorded outbreaks until 1886, mostly in the Southern States. (This does not include the52,477 cases mentioned by Woodward in the U.S. Civil War.) Reports thereafter became more frequent and in 1920-22, 200 outbreaks were recorded in New York State alone. He observed that epidemics tended to occur where troops were concentrated, and classed epidemics broadly under five headings:

1. family - small outbreaks in country or city, confined to families.

2. considerable outbreaks in schools and institutions.

3. City outbreaks which might be limited to certain wards or social strata, or distributed generally, sometimes involving satellite towns.

4. Country epidemics in sparsely populated districts, in which case spread often focussed on the village school. (The comments of Pickles (51) on the wider aspects of this point, discussing Sonne dysentery, are interesting and apposite.)

5. The state-wide epidemics of New York State in 1921-22.

Blumer considered that though the 'fall' was the main season for epidemics, they might occur at any time and that personal contact was essential for transmission; children and adolescents were most commonly affected. Transmission might, he thought, be due to droplets, possibly to insects, especially in country districts, but he found no evidence of alimentary tract infection and noted that two kitchen employees who were infected did not pass the disease by way of food. His estimation of the incubation period was 7-10 days, sometimes 28, rarely 2. He recognized the occurrence of subicteric cases, but does not seem to have recognized infection from pre-icteric cases, and has fallen into the pitfall of mistaking cases infected from a common source and occurring within a few days of each other, for source and infection themselves. He could find no difference between the cases he described and arsenical jaundice.

Pickles (51) discusses his epidemics in Wersleydale in 1929-30, and in 1935-36, in his work 'Epidemiology in Country Practice', during which he made a series of careful observations, charting cases as they occurred. He established an incubation period/

period of 26-35 days, and working in a fairly closed community, traced the majority of his cases to their source. Infection centred on schools is noted and a demonstration shows of one case affecting thirteen others. He observed the fallacy of assuming a short incubation period, which had misled other workers, and shows how early common infection can lead to this. He mentions the infectivity of serum, and cites an instance of laboratory infection of 41 days' incubation period.

Bashford (4) in 1934 described an outbreak at the London G.P.O. in which there were 48 cases, scattered over different rooms, in which there was no instance of a patient conveying the disease home. He suggested a high immunity level in adults, and tried to distinguish between cases preceded by gastroenteritis and those not, as cases of catarrhal jaundice and infective hepatitis respectively.

Barber (2) in 1937 reviewed the situation and continued this differentiation, considering Catarrhal Jaundice as a gastritis passing to the duodenum and then causing catarrhal obstruction, and infective hepatitis as an acute hepatitis occasioning a true toxic jaundice. He discussed the sporadic outbreaks occurring in Derbyshire in the four years preceding, especially an epidemic occurring in Derby Royal Infirmary described by Richards, of 'arsenical jaundice' in adults (120 cases) in which 'all except one had received an arsenobenzol compound but the epidemic was due to contact in the waiting room and died out when this was remedied' (This outbreak is interesting in the light of more recent work on syringe transmission; was anything else remedied at the time, or was the epidemic merely dying a 'natural death'?). Barber quoted other epidemic studies, including those of Pickles published at that date, and the account by Glover and Wilson (also mentioned

by/

by Pickles), of an epidemic in a country town of 200-300 cases. There were no cases in a girls' school while 95 occurred among boys, including 7 out of 9, and 5 out of 9 in dormitories. They pestulated nasopharyngeal spread. (Certain of their conclusions are critized by Pickles).

Sargeant (56) in 1937 described an epidemic in Gateshead, among school children, beginning in the month of January. There were 31 cases in one school, 13 scattered over 6 other schools, and one parent and two children below school age, affected. He observed that there were only two instances of more than one in a family being affected (in one of which, one child infected a father and young sister.) The public water supply was chlorinated and 'above suspicion'. The school milk was pasteurized and the same as that supplied to the schools. He refers to the 'explosive' character of one outbreak in which 19 children were affected at intervals of three or four days. (This is an extremely common finding). There was no conclusion reached about possible origin. All cases were slight.

In the same year, Lisney (35) described an epidemic in Leicestershire, affecting a village, 60% of the cases being children. He discussed the work of Weil and certain British epidemiological studies, and the probably aetiology of the epidemic under consideration. Milk and water supplies were various, a part of the water being derived from village pumps. He considered the possibility of both being at fault, but finding no conclusive evidence of this, presumed droplet infection, though most cases could give a history of personal contact. Infection appeared to be pre-icteric, and in cases in which content could be shown, the incubation period was about 4 weeks. The origin in this village

he ascribed to factory workers bringing it from the town.

In 1939 Norton(49) described an epidemic of considerable interest in U.S.A., affecting Silver Peak, a mining area, over the period May 15th - December 15th, 1938. This was an isolated camp five miles from a railway, where conditions were extremely bad, especially the sanitation. There were fly-infested privies, the water supply being derived from the lower slopes of the valley, from wells; complaints were made of the turbidity and odour of the water in the rainy season. Milk supplies were all 'raw', and derives from one dairy which was not clean. The average age of patients was 14 years, and clinically little difference was detected between them. Six cases of personal contact could be shown, and probably contact in other instances. The Incubation period averaged 31 days (26-45).

Cullinan (10) in 1939 reviewed the literature published at that date. He first considered the position of Weil's Disease, from Weil's definition of it in 1886, and the discovery of the Leptospira Icterohaemorrhagica in 1915 by Ino and Inada. He noted that recorded cases in this country numbered 200 (discussed by Alston and Brown in 1937). The possibility of missed cases was not overlooked, as according to Davidson, there have been mild cases, and the question of occupation may help with diagnosis. The incubation period is 7-13 days, and the duration 4 to 7 days' jaundice with sudden onset, fever and conjunctivitis, the mortality rate being 15%. Cullinan then discussed 'common infective jaundice', and listed the outbreaks from 1927 to 1939 - 1900 cases in all. He referred to the frequency and infective nature of the disease/

disease, and stated that it is 'widely scattered but wherever the syndrome is seen it has the same essential clinical and epidemiological features suggesting strongly that it is one disease process and probably has one specific cause.' Outbreaks were commonest between August and March, but might continue throughout the year. Less usually, there were summer outbreaks. The disease, he stated, was not essentially rural, despite a common belief to that effect, but it tended particularly to involve communities, and adults, especially young adults were by no means immune. In this connection he cited Bashford's experiences and the opinion of Pickles that all ages were liable to the disease, but that schoolchildren were especially exposed to the opportunity of infection; his own opinion was that, on the whole, adults enjoyed some degree of immunity and that sex distribution was equal. The clinical picture he gave followed that given by Pickles and others. He noted the absence of leucocytosis and the presence, often, of leucopenia. Convalescence was from 1-3 weeks in most cases. Recurrences occurred occasionally and Findlay Dunlop and Brown were quoted on this point. Liver complications were stated to be rare, and no reference was made to C.N.S. complications. On the method of spread, Cullinan's conclusions were that there was no spread by milk, food or water, and that 'it is quite clear that spread is from person to person,' and that usually close association could be traced (which he admitted was not true of Bashford's epidemic). The probability of droplet infection was indicated, he suggested by dormitory and family spread, and the degree of infectivity seemed to be highest 'when contact is close as in schools or similar institutions/

institutions, or families. On the question of the incubation period he agreed with Pickles, whose views he quoted. The length of the infective period seemed to be short, and he saw no objection to admitting jaundiced cases to the general wards of a hospital. The occurrence of gaps in epidemics was noted, and the probability of missed cases discussed. The negative results of investigation made in search of the causative agent, the absence of transmission to laboratory animals, and the probability of a virus being the cause were mentioned. Cullinan discussed the pathological findings at that date limited to post-mortem, and referred to the absence of evidence of bile-duct obstruction; he discounted the work of Hurst and Simpson in 1937 in favour of catarrhal changes. He also referred to the Gallipoli epidemics, and considered that the exact nature of the epidemics among troops 'saturated with paratyphosusB', was never settled. The relationship of infective jaundice to subacute necrosis he considered probably but not established; an earlier paper (9) of Cullinan's was quoted in support of this. He suggested that post-arsenical jaundice and infective jaundice were identical, and noted that in the former, the incubation period might be up to 119 days. The probability of post-measles inoculation and yellow fever jaundice being identical as well, was also discussed.

An epidemic reported by Bloch (5) in 1939 affected students in a camp, 23% of their number being involved. Bloch postulated personal contact or drinking water as possible causes, usually the former, and noted the incidence in late summer and the tendency of the/

the disease to affect young adults.

Cullinan's paper covered the position at the outbreak of the recent war. During the war the disease became widely prevalent again, and all the belligerents began to report cases. The epidemic reported by Senevet et al (57) in 1939 in Tunisia is interesting on being one of the few major epidemics reported by French observers. Marshall (40) quotes French hepatologists on this relative immunity, which contrasted sharply with the incidence among German troops, and later among the Allied armies.

German literature contains many references to epidemics. It appears that these occurred among German troops on all fronts, and also in Germany. Gutzeit (25) reports a minor epidemic in 1939 in Germany, and says that jaundice was general in the German Army everywhere by 1941. He surveyed the German cases to that date, and stressed the contagious nature of the disease and the necessity of early recognition and isolation. He notes the duration of the illness as being six weeks or more on occasion. Stuhlfauth (60) reported an epidemic in Norway, where the disease is stated to have been endemic in certain areas. In 1940, 300 cases appeared among school-children and young adults, and early in 1941, 200 cases among German troops stationed in the area. These derived from a focus in the nearby town, but he mentions the interesting case of 53 men in different camps who had been on a ski course of a fortnight's duration, three weeks before the onset of the disease. 80% of patients were under 25 years, and there were only two deaths (civilians) in all the cases he observed, (this is an incidence noted by other observers, as for instance Lisney (36), who estimates 3 to 5 deaths out of 1062 cases).

cases.) Stuhlfauth made a detailed study of 100 military cases and concluded that the incubation period was 24-40 days and transmission due to personal contact or possibly blankets. He suggested virus as the possible cause, with virulence heightened by the reflux of susceptable subjects. He pestulated the existence of a predisposing factor in the shape of a non-specific enteritis which was prevalent, and suggested that the immunity conferred by subclinical infection might account for the sparse nature of the epidemic.

Dietrich (13) gave an account of the disease among German troops in Belgium in 1940-41, noting the epidemic character of the disease and the apparent immunity conferred by infection. He associated outbreaks with respiratory and intestinal disease, and noted an early winter peak. Mild cases were numerous, and in addition there was a tendency for the older patient to have a disease of more gradual onset with greater liver damage than the usually recognized form in the young. The incidence of infective hepatitis in the peacetime German Army of 1919-29 paralleled that of arsenical jaundice.

There were numerous other German reports, e.g. Meythaler's (41) ~~in which~~ quoted by Marshall (40) which states that 2500 cases occurred in Crete, and that there was a tendency for symptoms to vary in the different geographical areas in which the German Army had been affected.

In 1940, Findlay (16) discussing the literature published at that date, considered the possibility of two forms of jaundice - infective hepatitis and 'catarrhal jaundice', He quoted Stokes in 1829 who first demonstrated liver damage, and subsequent workers, summing up with the opinion that there is not an epidemic form of catarrhal/

catarrhal jaundice. The evidence for filterable virus aetiology was discussed.

Klieger, Btesh, and Koch (34) reported fully an epidemic among immigrants into Palestine (mostly German) in 1938-40. They summarised the situation in Palestine as:

1. Endemic. The disease was rare in adults of 10 years or longer residence.

2. Affecting those aged 15-20 years, mostly immigrants; this showed a sharp rise in 1938, sparadically.

3. Actual epidemics among the recently arrived, in that age-group and milder outbreaks among children of 1-5 years born in Palestine. The increased incidence began in September 1938, with a peak in December 1938 or January 1939.

The first epidemic began on February 25th, 1940 Immigrants on arrival were confined to camp where (as usual with this disease) mass infection was favoured by the arrival of a susceptible population into an endemic area under restricted conditions. The source of the first case was not known. It seemed unlikely to be in the camp because there were six in a row (March 20, 21, 27, 29 (2), 31). There followed 14 cases in April, 19 in May and 41 in June, until in all 97 cases out of 1928 had occurred - a 5% incidence. There were no new arrivals in the camp after March. Most cases were 16-30 years, but the proportional age incidence is not known. Spread was investigated and it was found that all the camp had the same food etc., under the same conditions. Flies were not thought to be a likely cause because of there being few flies or sandflies until after mid-April. The incidence in huts was discussed and results tabulated,/

tabulated, showing that though there were 15-20 immigrants in a hut, there were not more than five cases in any one hut, and in most there were only one or two. In the daytime, all occupants of the camp mixed freely. The incubation period was 24-35 days; the epidemic ended with the release of all the immigrants in July.

The second epidemic in the same camp began in November,1940. There was no jaundice on the voyage, which lasted over a month. Boat M. docked on November 3rd, and the first cases appeared on November 28th, December 3rd (2), 4th (2), and December 13th and 16th. Boat P. docked on November 1st and the passengers of the two boats mixed on and after November 8th. The first cases among immigrants from Boat P appeared on December 7th. Both boats' passengers had had contacts with dock officials. Details of infection are vague because of the mixing of passengers, and the (apparently) unknown factor of the dock officials. The incubation period in this epidemic was the same as in the first. The case incidence the following year is shown in the paper, with a peak in January 1941. Children were twice as often affected as adults, the sex distribution was the same, and the majority of patients 30 years or younger, though cases did occur up to 60 years. It is not apparent whether the severity varied with age, from the paper. Transmission was not settled. Sanitation was good, food was the same throughout the camp, and there were virtually no outside contacts, visitors being rare, and the immigrants being confined to camp. Insects were rare at the times of epidemic peaks.

The account by Ford (21) of 300 cases in an outer London borough/

borough in a period of 9½ months is of interest because most of the cases were in families. He showed the incidence of cases by houses, and demonstrated the comparative rarity of multiple infection in one house and the improbability of droplet infection being a primary cause. Age and incubation periods followed the usual patterns. In summing up the evidence, he says 'It is probably..... by droplets, but this so far has not been proved and may well have been by faecal contamination spread by fingers.'

Cameron (7) summarised epidemic studies of the years preceding, including those of Sargeant, Lisney, Barber and Cullinan. He noted, in Palestine, a tendency to sporadic outbreaks rather than epidemics, and the susceptibility of young people newly arrived in an area, and suggested the possibility of subclinical infection of settled children giving them an immunity not enjoyed by immigrants. He tabulated 242 cases in 1940, and 126 in 1941. The clinical picture was as usually described, and the incubation period 32 days (apparently longer in a few cases, suggesting that at the time of infection the liver might be normal and liver damage follow lowered resistance - chill, alcohol, low diet or fatigue). No deaths occurred. He ascribed the heavy incidence accompanying active service to faecal infection, and the maximum infectivity he placed in the pre-icteric stage.

Edwards (15) described an epidemic of 'catarrhal jaundice' which he attempted to differentiate from infective hepatitis, in which he stated that there is an absence of pre-icteric symptoms (following presumably, the views of Hurst and Simpson). The epidemic consisted of 64 cases over 8 months, and affected school children and teachers in the Spring and Summer months. There was

no evidence of alliance with enteritis or influenza. It began in one school, to which it was confined for some months and involved others after the summer holidays. The epidemic, unlike many others, was not explosive. Milk was bacteriologically good, and water supplies chlorinated. Edwards hypothecated droplet infection (but in the light of other observations it is unfortunate that he did not discuss the school sanitary arrangements). Spread was studies in some detail, and the transmission in one case to the household of a teacher is discussed. Other features correspond to other epidemics, and the brevity of the probable infective period is stressed.

Kirk's (33) account of infective hepatitis among New Zealand troops at El Alamein in 1942 is a detailed discussion of the pros and cons of different modes of infection. The first group of cases took place 35-40 days after the arrival of the 2nd N.Z. Division at El Alamein, and ended 35-40 days after their withdrawal. There were 1059 cases out of 7500, compared to ~~and~~ 78 out of 3900 in another group nearer the rear than the first. Initially the disease was localized among the N.Z. troops at the southern end of the line, but British and Indian troops were later severely involved. The area concerned was five miles square, and one severely fought over. The whole line was under similar conditions as regarded food, water and living conditions, and N.Z. troops had not shown previous evidence of susceptibility. Reinforcements and resting troops were equally involved. Against the possibility of droplet infection, Kirk cited:

1. the absence of any special increase in catarrhal infection.

2. the men were in isolated groups with little or no intercommunication.

3./

3. These small groups showed no special tendency to infect each other.

4. There was a low incidence among the field ambulance personnel handling the cases.

5. Visitors were frequent but did not carry the infection elsewhere.

6. Although congestion was much greater further back, there were no epidemics.

This ~~persisted~~ pointed. to the site being the key to the problem. Flies were present 'in incredible numbers.' Diarrhoea and dysentery were rife and the ground heavily contaminated with enemy faeces and inadequately buried bodies. There was known to be epidemic jaundice among emeny front-line troops. It was never possible to achieve good sanitation and the units which occupied the area after the N.Z. Division withdrew had an epidemic at the end of the incubation period. Absence of spread at the time Kirk ascribed to the prevailing wind being northerly, and to the presence of Indian troops with a partial immunity between the New Zealand and British troops. His conclusion was that excreta were to blame, and spread was by flies.

In 1944 Havens (26) described infective hepatitis in the Middle East reviewing 200 cases in a military hospital. This was written before a clear-cut distinction between homologous serum hepatitis and infective hepatitis had been made. He divided the disease into pre-icteric and icteric phases, noted that the former was present in 167 out of his 200 cases. Patients' ages were 19-50 years, only three, however, being over 40, ~~and~~ He. gave a clear and detailed/

detailed description. He discussed laboratory methods, including blood data and hepatic function tests.

Dixon (14) in 1944, described infective hepatitis in Malta from 1938 to 1942. The seasonal incidence was August - February with a peak in November, and a parallelism with gastro-intestinal infection was noted, jaundice beginning 1 month later. The incidence among the Maltese was negligible, and as in other epidemics it was the newly-arrived troops who proved most susceptible. Women were uncommonly affected. The highest occupational incidence was among officers (e.g. 40 out of 1000 in 1940), and cooks. He refers to the probably short duration of the infective period, in the pre-icteric phase, and assumes transmission to be by droplets and contact. Flies he thinks are not incriminated, though the season coincided with the sandfly season (sandfly fever having to be considered as a differential diagnosis in febrile cases, which also simulated acute abdominal emergencies and led to some cross-infection in surgical wards.) One attack appeared to confer immunity. Clinical data are as in most other reports; he notes that afebrile cases were comparatively symptomless, that pre-icteric cases occurred, and that recurrence took place in less than 3% of cases. Mortality was less than 2 per 1000.

The most important recent paper is that of Neefe and Stokes (45) dealing with an epidemic in a summer camp in mountain country near Philadelphia. This consisted actually of two separate camps for boys and girls, independent for office, kitchen, dining and infirmary facilities, and each camp had its own staff, though there/

there was a good deal of intermingling. The campers were all Jewish, and mostly arrived in the camp on June 30th, 1944. Boys numbered 275 and girls 250; and their ages were 3-17. Visitors were numerous, but there was little change in the people actually in camp before the epidemic. The staff were aged 17-30 years; visitors were mostly under 40, and were 78 in number. Each hut contained 7-10 campers and 1-2 'counsellors'. All dishes were washed in 'germicide'. Water was drawn from two wells; the boys' well being often inadequate the supply being supplemented from the girls'. Sanitation was into cesspits, there being a number of these round the girls' well at varying distances.

The first case occurred 3 days after the opening of the camp. Gastrointestinal upsets took place in the third week in the girls' camp, affecting 25-30% of the girls. Diarrhoea was infrequent. Similar outbreaks occurred in the boys' camp in the 4th and 5th week.

In all, in thirteen weeks, 350 out of 570 persons developed hepatitis, 344 of them in seven weeks. This is apparently the highest recorded incidence in the U.S.A. over such a period. At least nine visitors developed hepatitis. 175 of the campers returned home when the epidemic appeared, and in all 175 of the cases developed hepatitis after leaving the camp, but there appeared to be only 5 secondary cases. No deaths occurred. Neefe draws attention to the high incidence of the disease, the high total incidence among the girls, who predominated among the early cases, while the boys predominated later. He notes the ease with which the disease was contracted, compared with the rarity of secondary cases away from the camp, and the occurrence of so many simultaneous cases not in personal contact.

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For these and other reasons, attention was focussed on the girls' water supply. It was noted that visitors who did not eat at the camp were affected in several cases, and that flies were unlikely to have carried the infective agent, first because of their not infecting anyone at a nearby boarding house, and secondly because of negative results with transmission experiments. Nor could mosquitoes, which were prevalent, be incriminated. A large number of transmission experiments were carried out. Summarized, they showed:

1. Failure to transmit the disease to volunteers by nasopharyngeal droplets and secretion.

2. Faeces were infective and probably the main source.

3. Flies did not appear to be infective, using an extract of crushed fly.

4. The agent was Seitz filter-passing.

5. A decrease in the amount of infective agent given (faecal extract) lengthened the incubation period.

6. Water from the girls' well at the time of the epidemic was still capable of causing mild hepatic disease, after the epidemic, given to volunteers.

7. Faeces from experimentally infected patients were infective (i.e. second human passage). There was evidence of immunity after recovery.

8. Serum was infective after an incubation period similar to the normal period if given orally. Parenteral serum produced no disease after 132 days.

The causative agent was therefore considered not to be carried by fomites, insects, food, milk or direct spread from patients.

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The girls' well was the only source satisfactorily demonstrated. One cesspool was 150 feet from it, and was receiving excreta from the hut where the first case was detected, and the infirmary, and was in effect being continually refreshed with new supplies of infective material.

III. Clinical Features.

The degree of severity of the disease is discussed by most writers. A review was made by Hoagland and Shank (29) of 200 cases seen in hospital, to define the degree of liver damage, the extent of repair and the time needed for this, as well as to assess the effect of therapeutic measures, and the features described may be summarised:

1. Malaise, exceptionally to the point of toxaemia as in acute yellow atrophy.

2. A prodromal period of 1-9 days (occasionally 10-15, and rarely 20-25), with well defined symptomatology, lassitude, nausea, anorexia, fatigue.

3. 10% of patients complained of jaundice as their initial symptom, and 5% had no subjective manifestations at all.

4. Usually the end of initial symptoms coincided with the onset of jaundice.

5. The degree of icterus varied from scleral, just perceptible, to an extreme degree. Pruritis was present in 46%, in all degrees of severity.

6. Abdominal discomfort was common, but pain exceptional. Pain was epigastric if present, right upper quadrant pain being rare.

7. Enlargement of the liver was pronounced in 51%, and marked tenderness in 38%, but most patients showed some degree of both.

8. Splenic enlargement was detected in 10%.

9. It was noticed by patients that bile appeared in the urine 1-3 days before jaundice of the sclera, and less often, before change in the colour of stool.

Recrudescence was the cause of admission to hospital in

6 cases. A previous history was given by 5 cases, one of whom is stated to have had 3 attacks in 10 years. Differential diagnosis was not difficult, but upper respiratory infection and atypical pneumonia as well as Weil's disease had to be considered. (In this connection Pickles notes that occasionally adult cases may resemble acute abdominal emergencies, a point which I can personally confirm.) Liver function tests were carried out and the results tabulated. The blood picture was coincident with that given by the workers. The B.S.R. was normal in the disease and recovery, but raised in convalescence. (It is stated, however, by Davis (11) that the sedimentation rate is of little value in liver disease in general, owing to the widely varying changes in the constitution of the plasma that occurs.) No demonstrable value in treatment with amino acids, choline or crude liver extract was shown. It is considered by Hoagland and Shank that prompt hospitalization and freedom from activity are most important in speeding recovery.

Hughes (30) in a small series of cases, with one group confined to bed and dieted, and another at liberty and allowed to eat food of their own choice, found an appreciable difference in the time required for recovery in favour of the first group.

Recrudescence, according to Hoagland and Shank, occurred in some degree in 18.5% of their cases, clinically, or confirmed by liver function tests. This occurred on resumption of duty or normal activity following a period of sick leave (this was my personal experience, which I was unable to confirm in the cases in the epidemic) All the cases recovered completely and gave normal liver function tests after a further 20 days in hospital.

Rennie (53) considering the question of prognosis notes the incidence/

incidence of fatal cases in previous accounts of epidemics and discusses the clinical manifestations in 39 cases of infective hepatitis investigated by him. Anorexia, jaundice, and bile in the urine were present in all cases. 23 had abdominal pain and discomfort, 9 had headache, 8 had joint pains and 3 pains in the back (it would be interesting to compare large series in epidemics in respect of frequency of different symptoms if only to see whether there is anything in Meythaler's (41) theory of geographical variations). 23 had enlargement and 18 tenderness of the liver. In 21 cases, the pulse rate was less than 60. Pyrexia was present in 13. 9 cases had pruritus (this contrasts with Hoagland and Shank's 46%), and 2 had palpable spleens. The blood picture in the disease has been discussed by various workers. Rennie found in 25 patients, a leukocyte count of 2600 to 11,000 per c. mm. 9 patients had counts of less than 5000 per c.mm, and absolute lymphocytosis was found in 5 out of 10 counts. Pickles, in a personal communication, says that he finds a typical differential count to be:

Polymorphs	36%
Lymphocytes	56.5%
Eosinophils	1%
Basophils	5%
Monocytes	6% (occasionally increased to 15%)

It is not proposed to discuss the pathology of the disease here as being outside the intended scope of this paper, It has been covered by the liver biopsy studies of Dible, McMichael and Sherlock (12), and the autopsy studies in Lucké's (37) detailed paper; in the case of the latter it is not clear whether cases were infective hepatitis or H.S.H.

IV. The Infective Agent and Transmission of the Disease.

It has been shown that the infective agent is filterable through Seitz filters and can stand heating up to 56-60°C for 30-60 minutes. It survives freezing and drying and exposure to a weak solution of Phenol (Neefe (48), Havens (27,28))

Neefe (46) has shown that treatment of contaminated water with sufficient chlorine to give 1 part per 1,000,000 after 30 minutes did not inactivate or attenuate the agent. Super-chlorination, to 15 parts per 1,000,000 after 30 minutes did produce definite attenuation. Coagulation absorption methods did not completely remove or inactivate it, but may have had some effect on virulence.

Siede and Luz (59) claimed to have grown it in a series of 8 sub-cultures on fowl embryos, using duodenal fluid, but this work has not been substantiated, and amongst others, Findlay, Martin and Mitchell, (18) state their inability to confirm these results.

Clinically the agent would appear to be identical with that of homologous serum jaundice. The question of comparison between the two has been discussed by Neefe et al (48). It is not proposed to discuss homologous serum jaundice here, and Findlay et al, have considered it at great length (18), but the views of Neefe and his co-workers, a more recent paper, may be mentioned briefly. In resistance to heat and filter passing properties the agents are apparently the same. Clinically and pathologically the established diseases are identical. Both agents are present in the blood at some stage of the disease. It is pointed out that infective hepatitis/

hepatitis has usually more pyrexia than homologous serum jaundice ('H.S.H.'). The incubation periods are usually less than 40 days and over 60 days respectively. (This point had been considered by Findlay and others (18), who pointed out the length of incubation period needed for infective hepatitis if acquired by injection, which was 1-6 months. Sheehan (58) considered it to be 10-12 weeks. More will be said of this below.) In transmission experiments, H.S.H. has rarely been transmitted by other means than by blood or serum, (though Findlay and Martin (17) claimed to have transmitted it by nasal washings), while infective hepatitis has been transmitted by various routes, including, most successfully, by faeces extracted and given orally; Neefe et al. failed to transmit H.S.H. by this route. However, these points not being sufficient in themselves, an elaborate series of transmission experiments were carried out by Neefe et al, who conclude that there is evidence against the establishment of cross-immunity. Findlay, Martin and Mitchell (18), however, at the time of their paper were inclined to believe in the identity or close relationship of the two agents, but that it was not possible to go further than this. As regards immunity, they suggest that there is evidence enough to suggest that previous infective hepatitis <u>may</u> confer <u>some</u> immunity against subsequent H.S.H.

<u>Transmission</u>.

Transmission to animals has not succeeded. Anderson (1) claimed to have infected pigs, but this has not been confirmed, and Findlay and his co-workers (18) tried to infect a very large number of animals (baboons, six species of monkey, horses, hedgehogs, rats and many others.) German workers' claims to have infected canaries and

White/

white mice have not been borne out subsequently. Findlay claims that a species of monkey (injected with icterogenic serum and a course of six injections of N.A.B.) may have been infected, as extensive liver necrosis took place, while a control showed no changes. Some of the necrosed liver was injected into another monkey, which had received N.A.B. injections as well, and in this case there was an illness with a raised icteric index 28 days later with a degree of liver necrosis. At the time of publishing these experiments were continuing. Van Rooyen and Gordon (62) and Cameron and others (7) could infect no animal.

Transmission, accidental or experimental, to man has been shown repeatedly by different routes and with different vehicles. The principal demonstrations are listed.

1. Blood or serum. In this connection it is well to note the opinion of Findlay (18) that there is a possibility that the virus of infective hepatitis may appear occasionally in the blood of an immune subject; small amounts of virus being liberated and new quantities of antibody being formed. This might, he suggests, explain the finding that very small amounts of serum or plasma are as liable as, or more liable than, large amounts to cause jaundice, (it being known that a mixture of virus and immune serum may be harmless injected in large amounts but virulent in small).

a) Lainer (quoted by Findlay et al. (18)), in 1940 tried to infect himself and 3 others by direct transfusion of 300 cc. of blood of typical 'catarrhal' jaundice cases. Results were negative. We may note here not only the use of a large amount of blood, but also that fully developed cases of jaundice, no pre-icteric, were used.

b) Van Rooyen and Gordon (62) inadvertently transfused a patient with/

with blood from a pre-icteric case with negative results. It is doubtful here, as elsewhere in early series, whether sufficiently prolonged observation was carried out.

c) Murphy (43) noted two cases of jaundice following unintentional transfusion of pre-icteric blood in 24 and 47 days.

d) Voegt (63) used serum from pre-icteric cases, and had one positive result.

e) Cameron and others (7) using 1-2 ml. of serum from infective hepatitis cases intramuscularly obtained six positive results out of seven subjects (the other one being lost trace of). His incubation periods were 30 days to six months. A further five cases were also all infected within the same incubation period. As this was done under service conditions and in an area in which the disease was prevalent these cases are not absolutely satisfactory. Indeed, it would seem that the element of chance infection can only be really eliminated by locking the subjects up during the period of observation; a point which Havens (27,28) was able to achieve by experimenting on criminals in jail!

f) Oliphant (50) using serum subcutaneously, had 4 positive cases out of 21, in 85-106 days.

g) McCallum and Bradley (39) had 3 positive out of 6 cases, with subcutaneous serum.

h) Havens (27,28), using serum intracutaneously and orally, in three experiments, had 6 positives out of 11, the incubation period varying from 30 days (an oral case) to 84 days. He also tried serum from a case infected experimentally with faeces, and had 4 out of 8 positive results by intranasal subcutaneous and intracutaneous routes in 23-34 days.

i)/

i) Neefe (45,48) demonstrated oral transmission with serum in 4 out of 6 cases, in 26-33 days, and a subicteric case in 84 days.

j) Infection of 29 cases by Gardner, Stewart and McCallum (22). Initially they used sera from infective hepatitis cases, but as the object was to study the therapeutic effects of jaundice on rheumatoid arthritis, they abandoned these sources, and used an icterogenic serum instead. As full details are not given in the paper, it cannot be assessed what proportion of their infective hepatitis transmission succeeded.

k) Rennie and Brazer (54) inoculated 10 patients with rheumatoid arthritis with .5 or 1 ml of serum from two infective hepatitis cases. (One case was subicteric throughout and the serum was obtained from the other on the first day of jaundice). 2 positive results, both from the serum of the first case were obtained, in 55 and 60 days, (appearance of first symptoms.)

Transmission of H.S.H. has been carried out in other experiments which it is not intended to discuss here (e.g. Findlay and others (18), and other workers.

l) Finally it is necessary to note the group of laboratory workers accidentally infected by handling serum, described by Sheehan (58), and the case referred to by Pickles (51). Numerous cases of this kind can probably be traced.

2. Duodenal Fluid. a) Used by Lainer ~~until~~ with negative results.

b) Used by Voegt (63) who had 1 positive case out of 4 tried by the oral route. Voegt's results (quoted by Havens, and Findlay, Martin and Mitchell), and not seen in the original, appear to be rather vague.

3) Nasal Washings./

3. Nasal Washings. a) Neefe and Stokes failed to produce any cases by this means.

b) Tried intranasally by McCallum and Bradley (39) when 2 non-icteric cases were claimed out of 16 subjects, in 24 and 48 days.

c) Transmission (of H.S.H.) claimed by Findlay and Martin (17), who used nasal washings from pre-icteric or very early icteric patients. This is mentioned, though not infective hepatitis, because it is claimed by these workers that it is evidence probably in favour of this mode of infection in infective hepatitis as well.

4. Faeces. Transmission with faecal filtrates and extracts have been carried out by the following:

a) McCallum and Bradley (39), who had 3 positives out of 26 cases who had intranasal inoculation, in 27-31 days.

b) Findlay and Willcox (19) had 7 positive results out of 18 with faecal extracts (6, 2 of whom were positive, being given a Seitz filtrate.)

The same workers (20) carried out an extensive investigation on 99 cases (in a semi-closed community in a district with a very low incidence of infective hepatitis). Early icteric cases were used as the source of faecal material, 9 spontaneous (4 of whom did not give any positive results in subjects for infection) and 5 experimentally induced, cases were used. A certain number of cases were given neoarsphenamine at the same time in an attempt to establish whether this drug increased the susceptibility of the liver to infection, as it may have done in the monkey experiment of Findlay and others (18). Summarized, their tabulated results are as follows:

Source/

Source	Exposed to Infection	Total positive	Neoarsphen-:amine given.	Positive with neo-arsphena-:mine	Average Incuba-:tion period.
Faeces from spontaneous cases of Infective Hepatitis	47	11	4	2	29 days
Faeces from experimentally infected case.	26	6	4	3	31.4 days

c) Havens (27,28) using dried, and frozen, faeces and urine, had 2 positives out of 6 cases in 20 and 22 days. (This series, including his serum transmission experiments, also gave rise to a case of contact infection from a patient with øar 31 days incubation period.)

d) Neefe (45) using material from the camp epidemic did a large series of experiments, with various preparations of strained or filtered faeces, administered orally to a total of 74 cases, with positive results in 32, and incubation period of 18-37 days.

5) Urine. a) Tried by Voegt (63) with 1 positive result, orally.

b) McCallum and Bradley (39) had no positive results.

c) Havens' experiments just mentioned.

d) Findlay and Wilcox (20) in the experiment mentioned above, also infected 5 cases out of 17 with urine from infective hepatitis cases. (Of this series, 4, none of whom gave positive results, were having arsenicals). They infected 2 cases out of 9 with urine from experimentally infected subjects (of this series, 3 had arsenicals and one developed the infection). The incubation periods averaged 18.2 and 19.5 days respectively in these two groups.

V. The Epidemic.

This epidemic was confined, with certain exceptions, to Belgian troops of a Fusilier Battalion. The unit was formed at the end of 1944 and consisted almost entirely of young men, many of them students, of eighteen to twenty years of age, who had just been called up. It was trained in Belgium and moved into Germany in March, 1945. The map (see Appendix) indicates the areas involved. The first area the unit occupied (A) was heavily fought over during the U.S. Army's advance to the Rhine, and as a result sanitation was largely improvised and water supplies grossly contaminated or at best suspect. The unit was not very highly trained, and their sanitary standards were not those insisted on in an equivalent British unit. Further, the unit was dispersed in small detachments over a wide area which made strict supervision impossible. Gastroenteritis was fairly prevalent during the first two months. The two companies subsequently most affected were then at Baal and Düren.

There had been cases of infective hepatitis among the civilian population in these areas. There was no means of finding out what this incidence had been, owing to the disorganization consequent on defeat and administrative chaos. Some cases occurred in the area while the unit was there, but whether these represented an endemicity or whether cases had occurred before this among the German troops in the area could not be established. Also the previous Medizinalrat (M.O.H.) of the area concerned was no longer in office, and his successor had no records to hand.

During the months of March and Spril, the usual inoculations (T,A,B,, Tetanus Toxoid, and Typhus Vaccine) were carried out. There was/

were three cases of Infective Hepatitis in April, which were not investigated at the time. The unit Medical Officer, later on, looked up these men's records and found that they had all been inoculated four weeks before the disease appeared, but he decided that this line was unprofitable and was merely a coincidence with so many routine inoculations.

In the month of June the unit moved to Monschau, and it was in this area that the epidemic manifested itself. The township, or large village, of Monschau had somehow escaped all real damage though the German Ardennes offensive had been, in part, fought very nearby. Battalion H.Q. was in Monschau. No. 1 Coy was near Aachen, No. 2 was at Rotgen, No. 3 was at Vogelsang, No 4 at Marmagen, and No. 5 at Kalterherberg. The areas occupied were fairly good, and little damaged, but the water supplies had been greatly interfered with and in some places cut off completely, so that wells were being used. Companies were fairly scattered, as frontier posts were manned in part by this unit and in part by my own battalion. There was not a great deal of mixing, as companies were independent of central arrangements for cooking and most other purposes, though rations, mail and supplies were drawn from their unit H.Q. in Monschau. Recreational facilities in Monschau were to some extent shared with the unit to which I was attached at the time, which was responsible for rationing and general supervision of the Belgian battalion.

Each company had one or two medical orderlies, several of whom were medical students. This turned out to be of considerable value from the point of view of early recognition of jaundice, and to some extent countered a general aversion to 'going sick', which I think was connected with their views on the military hospital in

Liège./

Liege. There was a small 'isolation ward' at the unit H.Q. to which a small number of minor cases could be admitted for observation, as during most of the period covered the nearest medical unit was in Zulpich or Aachen, over twenty miles away and the British general hospital sixty. The unit's medical officer visited companies on most days, and was therefore not in Monschau a great deal. It was for this reason that I heard of the epidemic and of necessity saw a fair proportion of the total cases. It is proposed to deal with the epidemic by companies, as a convenient way of following its course, as it developed.

No. 4 Coy. This Company had twelve cases of infective hepatitis in the month of June, all of which it is presumed had been acquired in the previous area. The 'explosive' quality of the epidemic is noticeable here as elsewhere.

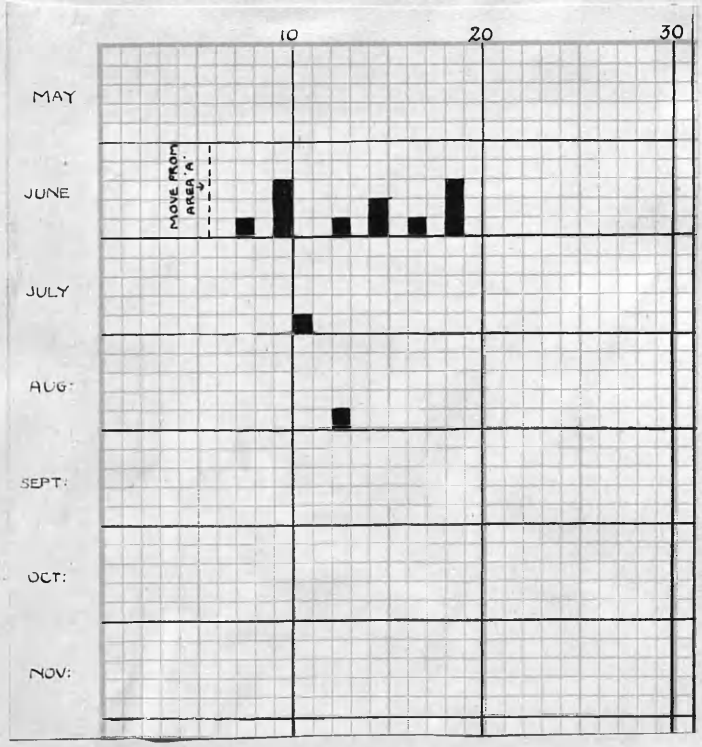

FIG. I. Incidence of Jaundice in No. 4 Company. Percentage incidence 8.3%.

At Marmagen this Company were in a good area, very little damaged, with a good water supply and sanitation and very little overcrowding. They had two cases after the June outbreak, one of whom was a contact of several cases at that time, and the other being the medical orderly of the company.

No. 5 Coy. This Company had about fifty cases of gastroenteritis, some with a severe degree of diarrhoea, in June and July. On investigation later, it seemed that three cases among these were mild or subicteric cases of jaundice, as typical histories of anorexia and malaise were given, but as this was based on subsequent enquiries among men who had felt ill

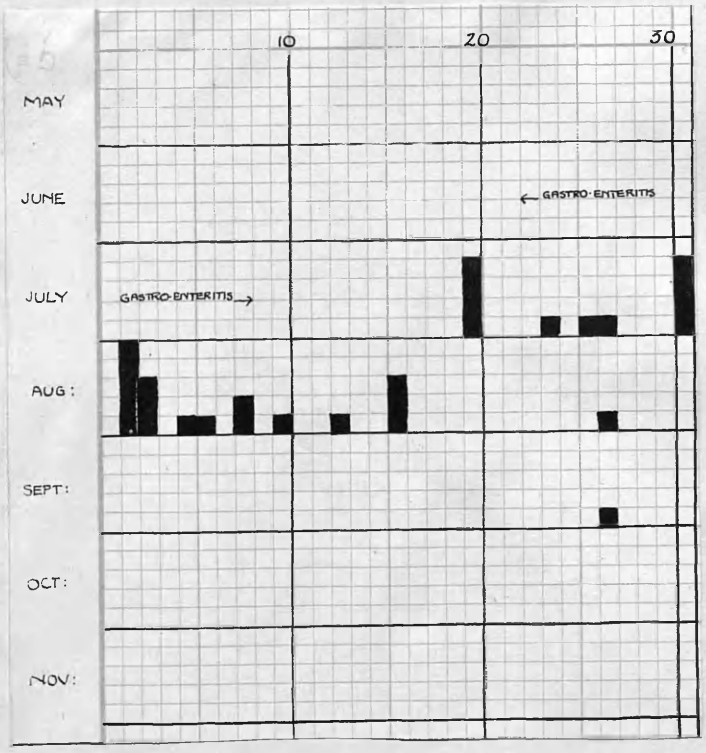

FIG. 2. Incidence of Jaundice in No. 5 Company. Percentage incidence 25%.

during that time but who had refrained from reporting sick, it has not seemed/

seemed to me to be justifiable to include them in the survey. The water supply was derived from wells, some of them very defective, in some of which contamination was practically certain by reason of fouling of ground and drainage into wells. Bacteriological examination was unfortunately not carried out.

The first cases appeared on July 20th, and the epidemic is seen to have begun 'explosively' in this company as in the preceding. My unit had arrived from another part of Germany at the end of June, and it was at this point that I was informed about the epidemic and we began to make investigations.

Having read in recent A.M.D. Bulletins and in Kirk's (33) paper, of gastroenteritis preceding the epidemic form of this disease, I enquired how many of the actual patients had had gastroenteritis, but it seemed that over half the company - i.e. some seventy men - had been affected, and this was plainly a pointless line of enquiry. The literature available at the time, including the views of Pickles (51) and Bashford (4) referring to droplet spread, and as flies, suggested as vectors by Kirk, were fairly plentiful, I suggested certain preventive measures. These included spacing out of beds ('heading and tailing'), and requisitioning of further quarters to reduce overcrowding. In addition, wells we suspected were placed out of bounds and chlorination of water-supplies and sterilization of cookhouse utensils (by boiling or immersion in a strong solution of water sterilizing powder) was ordered. Flyproofing as far as possible was also done. We were at this time ignorant of the resistance of the infective agent to chlorination (Neefe (46)), and I found out later that water from condemned wells was being chlorinated but not super-chl rinated,/

chlorinated, and also, much later, when the Company had moved elsewhere, that use was still being made of at least one well by men in a billet which had several cases of jaundice before and after the order. It was not possible to pin cases to definite water-sources, as the men used the nearest one at any given time of the day, but what was quite definite was the scattered nature of the epidemic among billets. Men in adjacent beds were seldom affected, though there was a fair degree of overcrowding.

This confirmed what appears to have been a general view in the Western Desert (Findlay, Martin & Mitchell (18)) that men who formed part of a tank or lorry crew in the desert seldom seemed to infect each other. This was true in an armoured force, in my experience, in Western Europe, ~~but~~ and as Findlay and his colleagues point out, there is a good deal of ventilation in a tank and men sleep in the open in rest periods or at night. This last point, on the other hand, I can disagree with, as in Normandy and later, until the Dutch mud made it impossible, our crews often slept in a trench under the vehicle, and in the closest possible contact.

Despite the precautions taken, some cases occurred, with a diminished frequency, but it will be noted that the end of the epidemic peak coincided with the end of the run of gastroenteritis one month before, which is probably significant. At the end of August, No. 1 Company and No. 5 changed places, and No. 5 had only one further case, in which there had been contact with the case of the 27th of August.

HQ. Company. This company remained in Monschau. The water here was a main supply from a small reservoir. This had been investigated bacteriologically/

bacteriologically in July and was safe for drinking, though as the woods contained unburied dead in places (the area was heavily mined), I had insisted in my own unit that chlorinated water only should be used. As the men were all in requisitioned hotels or houses, it is certain that a good deal of evasion of this order went on. Faecal contamination of the water did not occur here, however, as all buildings had water closet drainage which led into the River Roer. Rats abounded. No Weil's disease was seen, nor had the German Doctors any knowledge of any locally.

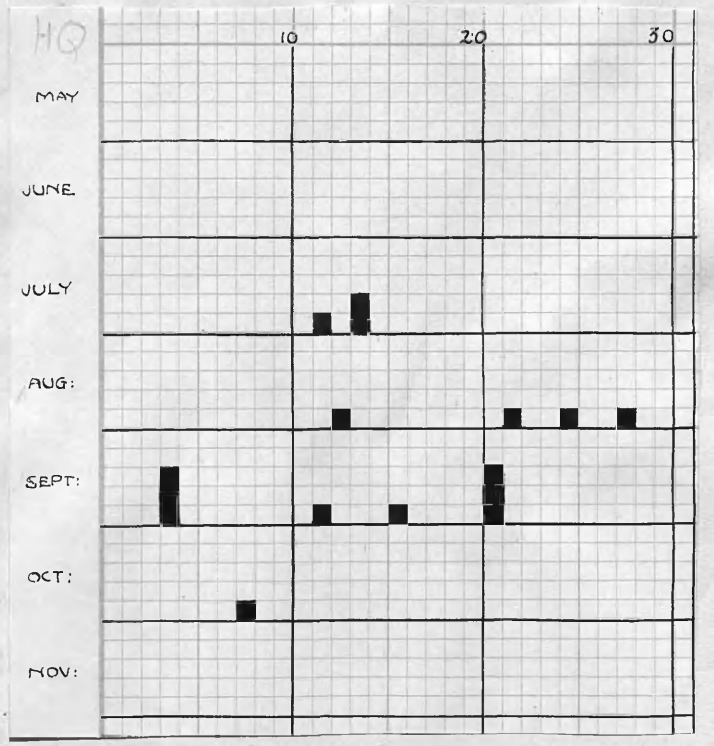

FIG. 3. Incidence of Jaundice in H.Q. Company. Percentage incidence 16%

This company showed a steady trickle of cases from July to October. The cases in July, three in number, had been for some days in/

in No. 4 Company's area, for the period 33 to 29 days before the onset of the disease. The case on 12th August who was the Medical Officer's driver had been a contact of these men's and also of the case in No. 4 Company on 11th July. The cases on September 4th had no established contents, but there was a great deal of mixing in this company and I do not put forward any suggestions as to contacts with much confidence in this instance. The cases of the 22nd, 25th and 28th of August are also not accounted for, though one of the cases of the 21st of September shared a room with two of these, and another messed with two of them. The case on 8th October, who shared quarters with, and often the utensils of, the case of the 12th September, and was one of some personal interest. He reported sick to me on the 6th of October, with malaise, pyrexia (100° F), headache and mild confusional signs. As no physical signs were detected, and he settled down in half an hour, he was kept in bed in our medical quarters for observation, and the following day felt much better, though he complained of loss of appetite, for which he blamed the British breakfast. He was examined fully but still nothing was found, his temperature was normal, and as he desired to return to duty it was intended to discharge him the following day. His urine was examined, as a precaution and found to give a positive Iodine Test. The following day he had slight conjunctival icterus and was sent to hospital. This case is mentioned at length because on the 8th of November I myself felt loss of appetite and malaise and was frankly jaundiced on the 12th. It seems that there is little dubiety about this contact as a source of infection.

No. 1 Coy: There were no cases in this Company until September. The first two cases on the 4th and 6th of that month had been in Monschau/

Monschau at various times, but nothing significant could be learnt about their movements. There were no more cases until the Company had been in the Kalterherberg area for seven weeks (having exchanged areas with No. 5 Company at the end of August.) Between the 15th of October and the 7th of November it will be seen that six cases occurred.

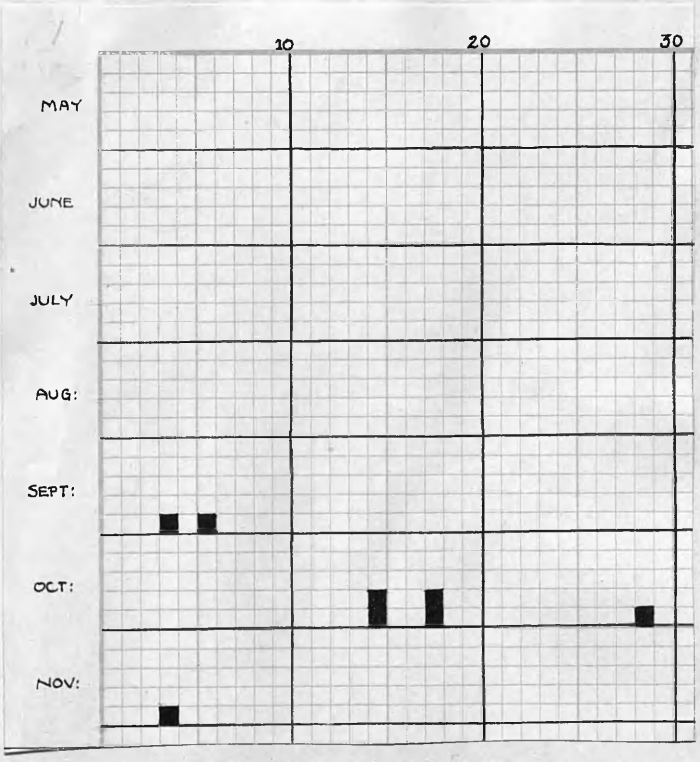

Fig. 4. Incidence of Jaundice in No. 1 Company. Percentage Incidence 6.6%

All these cases seemed to be sporadic. There was no indication of messroom contact or of contact with outside sources, and at the time I was inclined to blame use of wells, a habit which was beginning again. At the end, however, of October, parties from the unit began to move to another area, and closer observation became out of the question.

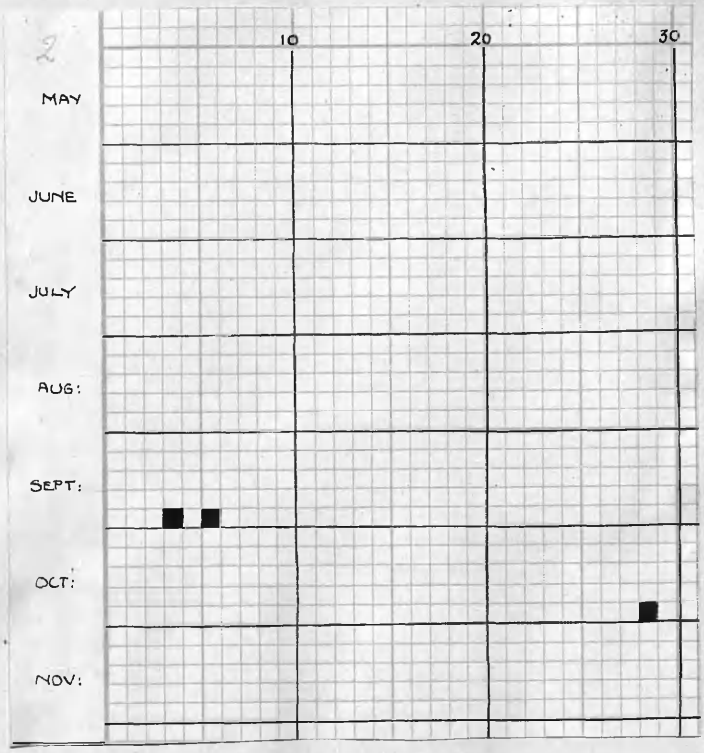

Fig. 5. Incidence of Jaundice in No. 2 Company. Percentage Incidence 2.5%.

No. 2 Coy. This company, in an isolated area with its own reliable water supply, had only three cases. The first two men had four weeks previously visited Monschau and had visited the sick quarters at a time when cases from No. 5 Company had attended, but I was not able to confirm that they had actually mixed with them. The coincidence, if it is one, is interesting. This company succeeded in getting their sick off the premises very promptly, and did in fact catch all their three jaundice cases in the pre-icteric phase, which may have favourably affected their incidence.

No. 3 Coy. This Company had only two cases. No contact or source could be suggested for the first, on 12th September. The second case had, however, visited Monschau and was a contact of one of the cases of the 21st of September some days before that date.

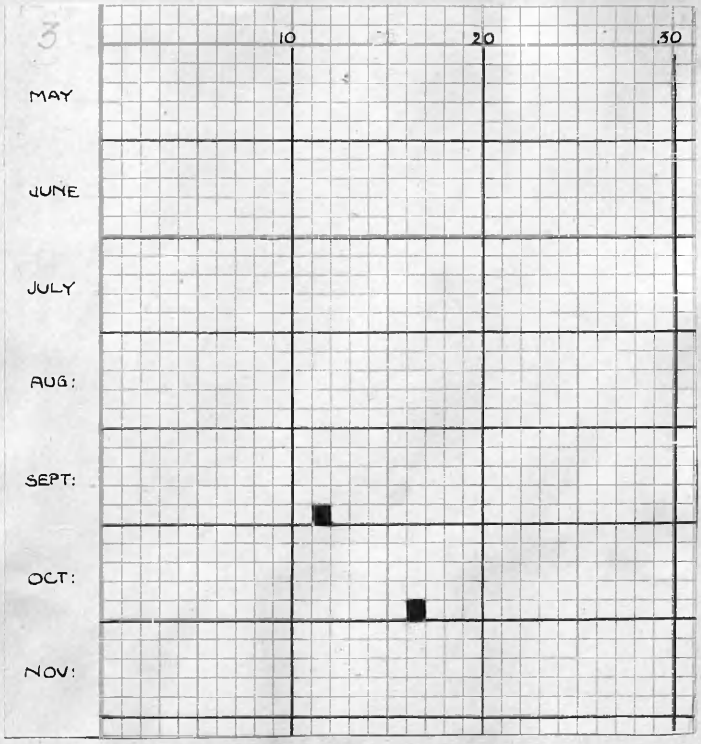

Fig. 6. Incidence in No. 3 Coy. Percentage Incidence 1.6%

British Troops.

During the period under review, odd cases of infective hepatitis occurred at intervals in the unit to which I was attached. There was a general, if low, incidence of the disease among many units at the time, and not all the cases can, I think, be ascribed to the Belgian epidemic. The case on the 20th of September was out of the area for a fortnight during the period covering the normal incubation period (th 15th-29th of August.)

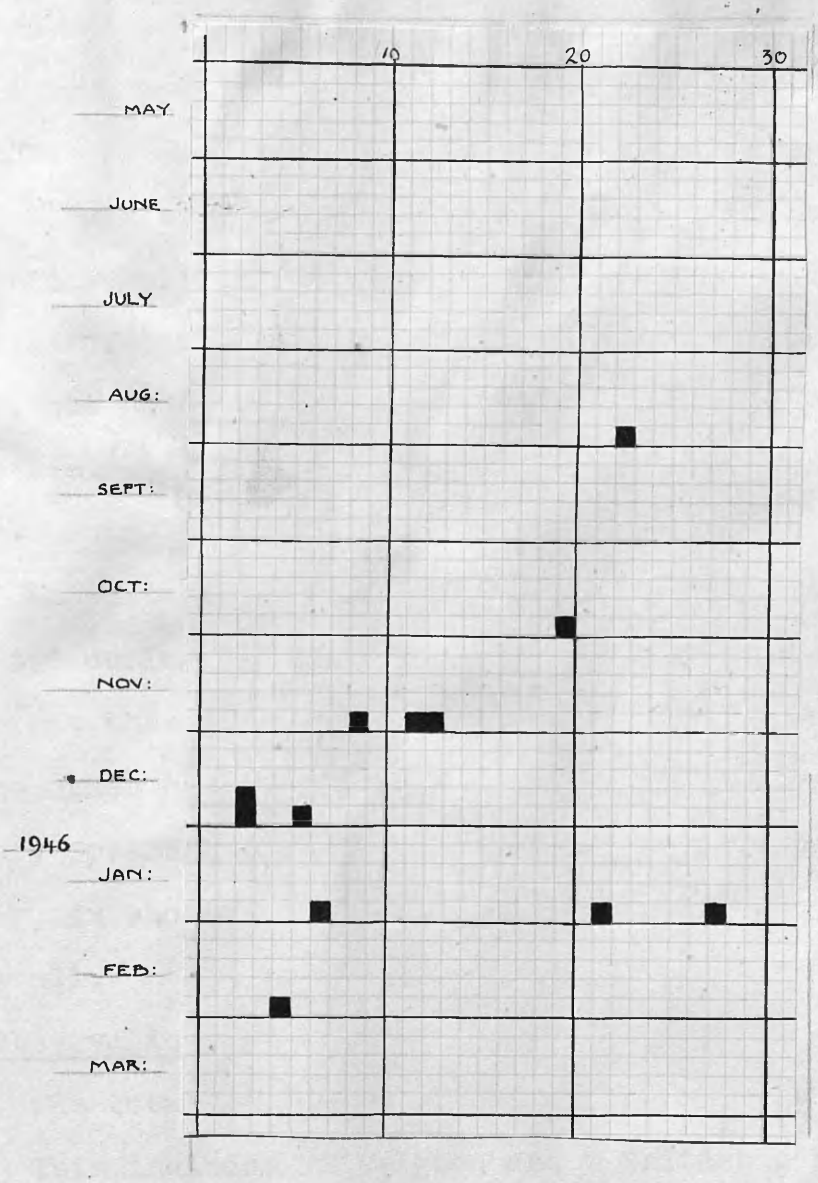

Fig. 7. Incidence in the —th Battalion. Percentage Incidence 1.3%.

Of the three cases in November, the first was myself, the second the post N.C.O. who worked with the Belgian postal orderly as a part of his normal duties. The Belgian developed jaundice on October 8th. The third case was an N.C.O. who had been lent to the Belgians at a time covering his incubation period, though I did not establish any definite contact, because the Belgians had gone, and I was/

was in hospital. Two of the cases in December were contacts of these two, and a room mate of one of these in his turn was diagnosed on 7th January.

I returned to the unit for two days only on 17th December and left for demobilization, and was therefore unable to investigate these cases further. Subsequent data supplied to me by post are indicated, but no definite epidemiological significance appears to be applicable.

Civilians.

Known cases among the local civilians in the Monschau area numbered two during the whole period. The local Medizinalrat was emphatic that there was no local endemicity in his area, and that he knew of no other cases. One of these was an interpreter employed by Military Government, and the other a farm labourer resident some miles away, in whose case nothing connected with any source could be traced at all.

General Observations.

The total number of cases involved to the end of December was 79. This includes 72 Belgian and 7 British cases, (not including one case which was probably infected elsewhere.) The total incidence week by week is shown in Fig. 8, over a period of thirty-one weeks. The Belgian unit moved from the Monschau area into Belgium about the 7th of November, and it was hoped to carry out a follow-up of cases in order to see whether any relapses occurred, but this could not be done on account of my being in hospital, and the unit's being disbanded in December. None of the infected men were receiving arsenicals at the time of infection. No cases admitted to previous history of jaundice at any time.

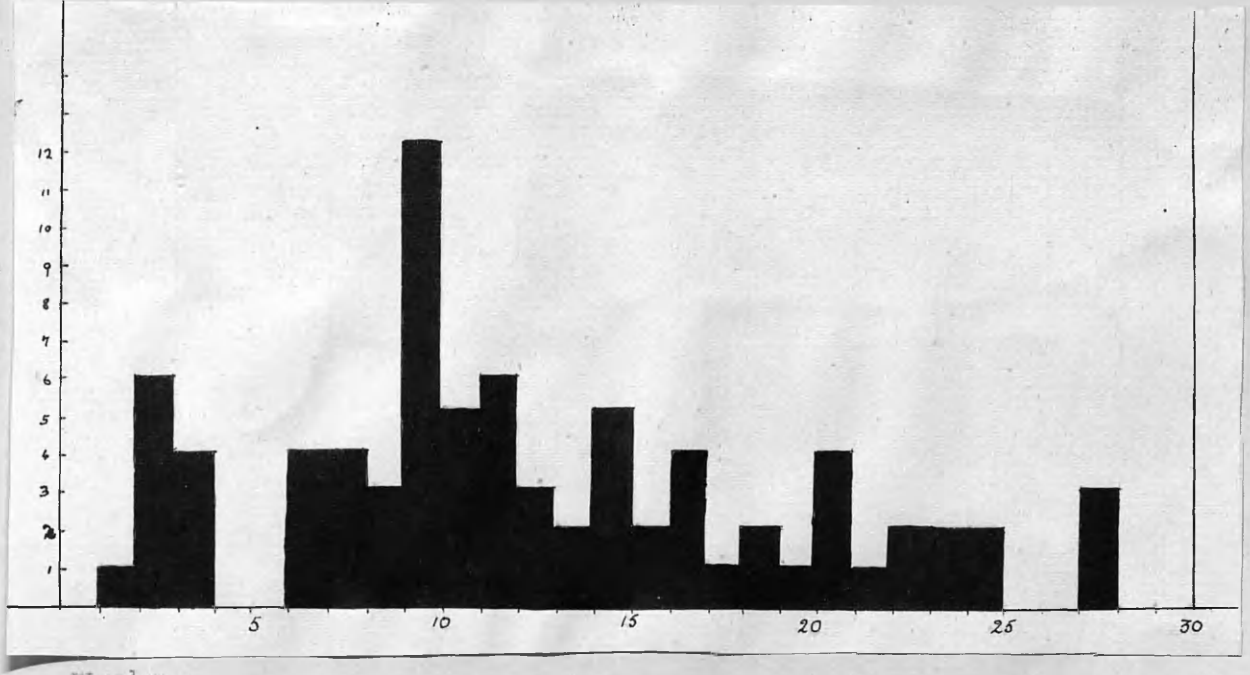

Fig. 8. Total incidence recorded by weeks 2nd June - 29th December, 1945.

Clinical Features:

1. Jaundice: Present in all cases except six. These were diagnosed on clinical grounds and bile pigment found in their urine. Jaundice was very pronounced in 25% of cases, and was rarely only conjunctival. Reference has already been made to probable missed subicteric cases.

2. Anorexia and Malaise: Present in all cases in the pre-icteric phase. In four cases, these symptoms, while present, were of such slight degree as to have been ignored, and jaundice was the presenting complaint, The pre-icteric phase lasted four to seven days, and exceptionally ten days. It was generally observed that the patients felt well after onset of jaundice, though some degree of anorexia presisted for a few days in certain cases.

3. Nausea: Present in 80%. Vomiting was much less common and only about 40% admitted to this.

4./

4. Abdominal pain or discomfort: Practically all cases had some degree of epigastric discomfort. Right upper quadrant pain was seen in five cases. Pain was severe in one case, and would, in the absence of a typical history of pre-icteric symptoms, have suggested an acute abdomen.

Enlargement of the Liver: Some degree of enlargement was present in most cases, as was tenderness of the liver. Enlargement was above one finger's breadth in 5% and tenderness very pronounced in 4%.

Pyrexia: Temperature elevation for the latter part, (usually two to three days), of the pre-icteric period was common, and is estimated at 50% of all cases, though not demonstrated in all because the men were not all under observation the whole of the time. Typical charts are shown in Fig. 9.

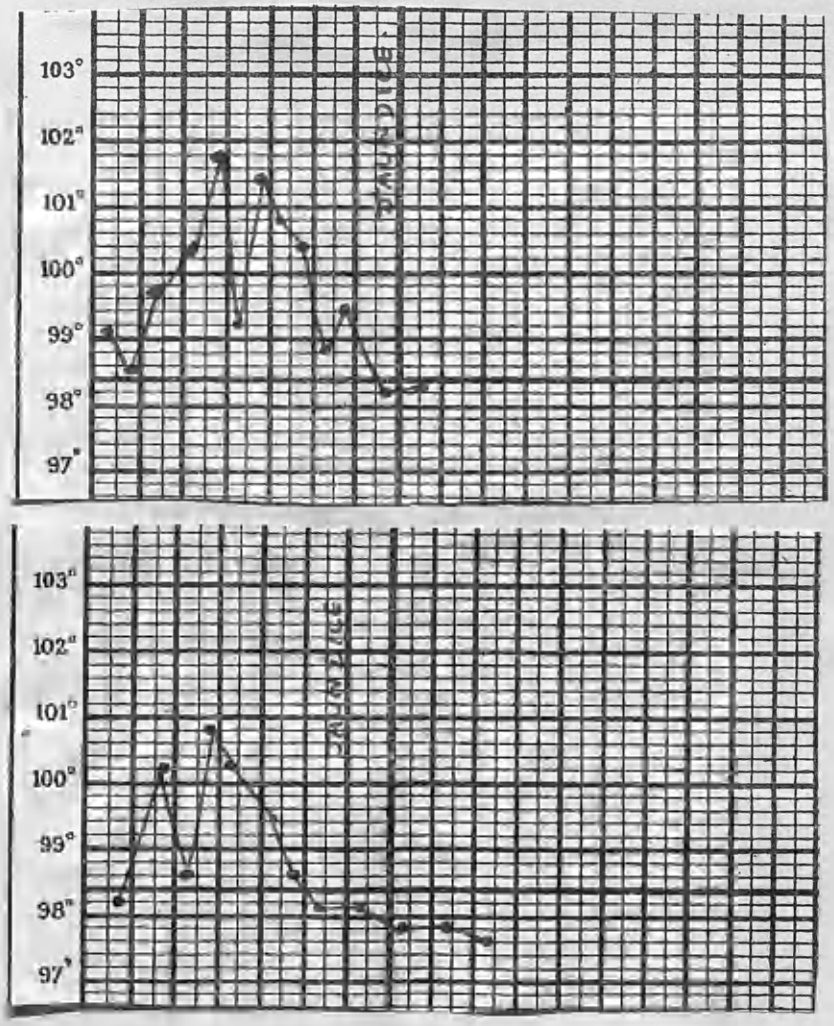

Fig. 9.

Fig. 9. Typical temperature charts. It will be noted that the onset of Jaundice accompanied the return to normal temperatures.

Bile in the urine: most patients noticed this before jaundice appeared. It was described as resembling 'bière brune' by one of them. The presence of bile was established in the case of all patients diagnosed.

Pruritus: This was present in 10% of cases. I did not see any skin rashes. Pruritus was not severe in more than three cases and was not prolonged over the whole period of icterus.

Backache: was complained of by 5% of cases. My impression was that this, usually lumbar in distribution, was an early symptom and that patients were inclined to diagnose their complaint as rheumatism. It may therefore have been commoner than appeared.

Headache: occurred in 15% of cases. It was not severe, except in the case of October 8th (H.Q. Coy.) who was at first very restless, and complained a great deal of his head. This subsided with rest and did not last over an hour.

Splenic Enlargement: I did not establish this not uncommon sign (cp. Hoagland and Shank, Rennie, and Findlay, Martin and Mitchell on this subject), in over about 5% of cases.

Other signs: Oedema and albuminuria were not seen.

Blood examinations: could not, unfortunately, be carried out.

Incidence: Percentage incidences in companies have been given with the appropriate chart. I was unable to find any evidence of epidemics among Belgian civilians, and the views of the Belgian doctors I met were these of the French - that the disease in wartime was in their country primarily one of the German troops. Marshall (40) refers to the difference in incidence of arsenical jaundice among French and British/

British troops attending the same hospital for treatment, and suggested (in a personal communication) that attention might be paid to the incidence of jaundice among Anglo-Saxon and Latin types in this epidemic as a matter of interest. The unit was predominantly Walloon (French-speaking), but I found the incidence among Flemings and Walloons equal in proportion to numbers.

Recovery: Most cases were free of jaundice and feeling well in 21 days, though some required 28 days and exceptionally 35. The tendency (noted by Hoagland and Shank (29)) for a degree of relapse to occur on return to duty was not observed. My own experience was that, after diagnosis on 10/11/45, admission to hospital 12/11/45, and discharge on 17/12/45, I developed pyrexia (99.6°F) with epigastric discomfort and anorexia on 27/1/46, with bile in the urine and clay-coloured stools on 28/1/46. This subsided and I felt quite well again on 31/1/46. This followed a period of activity packing up for a journey, while on release leave. By this time the Belgian unit had been disbanded, and I wrote to their former medical officer for details of any relapses of this kind, but he was unable to tell me of any.

Complications: There were no fatal cases, and no complications observed, but as has been explained, follow-up was not completed.

Other Observations: This epidemic in contrast to some others, avoided officers, with one exception, completely. It has been pointed out that in our own Army, officers were much more affected than the men (e.g. Dixon (14), Findlay, Martin and Mitchell (18)). The commonly accepted explanation to-day is that even in the field there is often some kind of officers' mess, and that infection derives from there. Certain observations by Truelove (61) indicate that this may not be the/

the whole story. He states that in a A.A. Brigade in the Middle East the officers and sergeants both lived in messes under similar conditions, but the sergeants' rate was the same as the O.R.'s - a quarter that of the officers. I am inclined to think that a detailed scrutiny of conditions might even in this case have revealed certain essential differences such as the sergeants keeping their own knives and forks, but it is likely that this point was enquired into. On Salisbury Plain I came across a small epidemic confined to officers in 1943, and it was a possible deduction that 'good' social origins might predispose. Pickles (51), it should be noted, stresses the apparent immunity of the local 'big' houses in his district from the disease. Among the troops affected in the Belgian epidemic there were wide differences in social origin among some of the patients, and no apparent immunity seemed to attack to any. Alcohol seemed to play no predisposing part at all; this seems to be generally agreed.

VI. Conclusions.

1. General observations. It has been established (Findlay and Willcox (19,20) McCallum and Bradley (39), Havens (27,28) Neefe (45,47,48) that faeces and urine ingested orally are capable of acting as vehicles for the infective agent in this disease, it being possible (Rennie and Frazer (54)) that a large dose is required. Although flies have not been incriminated as yet, it is conceivable that flies may, as suggested by Kirk (33) and others carry the infection. It is clear from the many epidemiological studies that have been made that an influx of young people, children or adult into an area where the disease exists is frequently followed by epidemic outbreaks (Kliegler, Btesh and Koch (34) Stuhlfauth (60), and others). It would appear that personal contact must sometimes play a part in transmission of the disease, and this is the conclusion of many workers. Kliegler, Btesh and Koch consider that the port officials, who were the only external contacts of the immigrants under review, may have been the source of infection, and saw no occasion to blame the camps' water-supply and sanitation. In this as in other epidemics, such as those discussed by Norton (49) and Lisney (35), work on the lines followed by Neefe (45) might have produced evidence of indirect faecal spread in water supplies, but it is suggested that in hot climates contamination of water may be comparatively unimportant compared with dust spread of dessicated faeces, which may have been important in the Western Desert. It would appear that the principal vehicle may vary with epidemics in different parts of the world and under different climatic conditions.

In the epidemic under consideration, there was a history of exposure to infective sources on arrival in the unit's first area in Germany/

Germany, of bad sanitation, and of the use of dubious water supplies. The course of the epidemic has been described, and it is suggested that the inferance is that initially the spread was through water supplies at a time when gastroenteritis was rife and infective material was spread about with a freedom which was the greater because unit sanitary standards were low at the time. The mode of infection of odd cases must remain to some extent in doubt, but it seems to be becoming more probable that dried faeces are responsible for 'contact' spread, though droplet infection has not been wholly abandoned as a possibility in certain cases by some workers (e.g. Findlay and Martin (17) who claimed positive results, subicteric in cases inoculated intra-nasally with nasal washings from H.S.H. cases).

It is now accepted that infectivity is maximal in the pre-icteric period, and few will disagree with the view that jaundiced cases can be nursed in general wards. The question of origin of epidemics is largely bound up with gastroenteritis, the spread of infective faecal material while jaundice is not apparent, and infection of individuals and groups through unsatisfactory sanitation so that an epidemic may be, in its early stages established before anyone is aware of its existence.

2. Suggestions regarding prevention in units.

In the light of work not carried out or not available at the time of the epidemic it seems that certain lessons can be drawn on prevention of this disease under the conditions in which it was encountered.

1. Hygiene measures. Normally under field conditions, water should be chlorinated; the process of super-chlorination has been that in use in the army during the recent war. It is clear that if all danger/

danger of infective hepatitis from water supplies is to be avoided, the fullest possible exposure to the action of chlorine is necessary, and the minimal period before dechlorination with sodium thiosulphate may need to be lengthened. In view of Neefe's and Stokes's (46) work on this subject, it seems that super-chlorination as practised does produce a definite effect on the infective agent. Kirk's (33) suggestion that flies may spread the disease has never been proved experimentally. I do not see that Neefe's (45) experiments do more than exculpate flies in that particular epidemic and surely in a camp of the kind described a fair attempt at fly proofing was in existence? The conditions cannot have been comparable in what appears to have been a well organized hutted holiday camp, with those at El Alamein. I am not aware that any investigator has exposed flies to infected faeces and then tried making an extract of the fly for experimental transmission, as where faeces are in the open in quantity it seems reasonable to suppose that this disease might like others, be flyborne.

Biting insects have not been incriminated by any worker. Cameron and his colleagues (7) tried bed bugs without success, but in view of the tiny amount of serum needed for accidental syringe transmission, this too is possible.

Faecal infection of food is a possibility, not demonstrated by anyone, and it is interesting to note that Dixon (14) states that the highest occupational incidence was among officers and cooks, though it seems that no actual epidemics of cookhouse origin were traced. Blumer (6) noticed that infected kitchen employees did not cause any further spread. Cooking would, of course, help to lessen infection from food, and it is just possible that Truelove's (61) tentative suggestion that tinned meat might be connected with disease outbreaks/

outbreaks may have been on occasion borne out where tins have been opened, and the meat served without heating, from a unit cookhouse.

'Contact' infection, cited by Pickles (51) in the village fête incidence, Lisney (35) and Sergeant (56) is probably due to finely divided dried faeces, though infection from nasal washings having been demonstrated (with H.S.H.) by McCallum and Bradley (39) it is just conceivable that droplets may play some part. Findlay and Willcox (20) still believe that this may be so. Infection of blankets and utensils is a strong possibility and every care should be taken to avoid mixing these. There does not appear to be any evidence of transmission in epidemics or experimentally by these means, but where men are unavoidably dirty it would seem more likely. I was unable to follow up this line in the epidemic because there appeared to have been a great deal of mixing of these articles in the unit generally. Overcrowding, apart, then, from droplet infection, probably contributes in some measure to the incidence of cases.

In respect, then of faecal transmission, prophylaxis seems to be limited to the standards of hygiene usually expected, and possibly further precautions as regards the method of superchlorination of water.

2. Diet. Dietary factors have been discussed a great deal, but there appears to be little indication that protein deficiency predisposes to infective hepatitis. This aspect of the liability of officers to infection does not seem important. It will be agreed that they do not, as a rule, eat less, but it is possible that officers, who when they have an organized mess, often take a full evening meal not available for the other ranks, do not actually have a much dissimilar day's intake from the rest of the unit; this point I roughly confirmed/

confirmed by observation on a few day's food consumption by the sergeants and by a squadron cookhouse. Alcohol can be dismissed in the ordinary case as a predisposing factor. This view was not challenged at the conference at which Truelove delivered his paper. I found no relationship to alcohol consumption in the Belgian unit at a time when strong schnapps of dubious origin was available in certain quantities for those who wanted it. There was no relationship at all in the cases referred to above on Salisbury Plain in 1943. Finally, we have Marshall's (40) views on the relative immunity of the protein-deficient French as compared with the well fed German troops.

Blood Spread.

This, apart from the wider issue of homologous serum jaundice, can be important. The incidence of infective hepatitis in V.D. clinics is well known, and the methods used by Salaman and his colleagues (55) have received wide attention. They cut the incidence of the disease to vanishing point by the use of syringes sterilized by dry heat (150-160°C) kept in sterile tubes until used, and re-sterilized after one injection. Sheehan (58) discussed this aspect of the epidemiology of infective hepatitis, considering instances of infection at V.D. clinics where syringes were sterilized between injections and where they were not, and where syringes were sterilized individually for a trial group. He drew attention to the occurrence of an incidence of abnormally high level among laboratory assistants handling sera, and finally to the occurrence of 85 cases in a sanatorium where the only reasonable source of infection appeared to have been the withdrawal of blood for B.S.R. estimation. Incubation periods were about 10-12 weeks.

That/

That infection could be caused by withdrawal of blood into the syringe, followed by further withdrawals from other patients, thus contaminating it, was satisfactorily demonstrated by Mendelssohn and Witts(38), in an experiment to show that the area of releasing the tourniquet usually applied to the patient's arm is followed by reflux of a tiny fraction of syringe contents; they pointed out that an infective dose of virus might be little larger than a large protein molecule. Subcutaneous injections of serum has been repeatedly shown to be a means of experimental infection, and Hughes (31) has recently shown that intramuscular injection can also be a source of syringe contamination (because of back pressure, spread of blood up the needle, or suction when the needle is removed from the syringe). It has not as far as I know, been demonstrated that routine inoculation may be a route of infection, but this now seems to be a distinct possibility. It appears that when an epidemic is present, or sporadic cases have occurred, every precaution should be taken to avoid such transmission both in giving injections and in removing specimens of blood for any purpose. Adequate sterilization has been carried out according to Sheehan with 'strong antiseptic', but further details are not available. This or thorough boiling is indicated on a far larger scale than is as yet generally accepted, and where exact quantities of blood are not needed, the use of needles alone, for withdrawal of specimens is not merely convenient but advisable.

Early recognition of cases.

As cases are most infective in the pre-icteric period the earlier such cases are detected, the less chance there is of their spreading the disease to their fellows. Apart from the obvious course of examining and isolating all cases of anorexia, malaise and other symptoms as early as possible, it is suggested that examination of the urine of possible contacts and groups of potential cases would be of value. Pollock's (52) paper, and others, discuss the existence of detectable degrees of liver damage before jaundice though the serum bilirubin is normal 2-3 days before jaundice and the use of Hunter's (32) test to demonstrate bile pigments in the urine, which is estimated at twenty times the sensitivity of the Iodine test. Testing for urobilin was of limited value. As Hunter's test is rather elaborate, it seems that the methylene blue chloride test, described by Barker, Capps and Allen (3), and more recently by Gellis and Stokes (23) is the obvious method of choice and could readily be done by orderlies in a unit at the time of an epidemic. Gellis and Stokes used a .2% aqueous solution of methylene blue chloride. This is added drop by drop to 5 c.c. of urine (the dropper recommended by Barker and others gives 19-21 drops/cc.) A positive test is given if the number of drops needed to change the colour from green to blue exceeds 4. 1000 normal patients gave negative results. As the 33 cases which gave positive results did so 1-6 days before jaundice, and 12 were positive while the serum index was still normal, it is clear that use of this case on all contacts or suspected early cases could at times materially reduce the spread of the disease by enabling very early isolation to be carried out.

5./

5. Once an epidemic has appeared, apart from general measures on hygiene which have been indicated, there are certain other possibilities. One which has received attention is the use of gamma-globulin tried by Stokes and Neefe (44). It was given intramuscularly to 53 out of 331 persons exposed to infection. The results, which it is claimed are statistically satisfactory,, indicated prevention or attenuation of the disease, as 20.8% of those inoculated were infected, as against 67% of the control series. For maximum effect, it should be given early in the incubation period, but it may have some value in the pre-icteric stage. This called for trial on a larger scale and with further tests of efficiency from the point of view of liver function.

A further investigation was done by Gellis, Stokes and others(24). A unit of the American Army Air Force was chosen which was exposed to epidemic infective hepatitis. It consisted of H.Q. (100 men) and 4 squadrons (500 men each). A and C squadrons were given 10 c.c. per man, intramuscularly, of gamma globulin from pooled human plasma. There was no reactions to this except an occasional mild burning at the site of inoculation. [The previous incidence was:

HQ: 4 cases, A; 56 cases, B; 81 cases, C: 19 cases, D: 35 cases].

Non-icteric cases were not included, to make the test more exacting. No inoculated men developed hepatitis in A or C during the next eight weeks, while 25 cases occurred in the other two squadrons.

This led to a larger series of cases being tried in the U.S. ground forces in Italy, in which the average incidence among controls was over 3% against under 1% in the inoculated.

It would therefore seem that the use of ~~immigration~~ immunization by

gamma/

gamma globulin may be considerable in prophylaxis, but the further trials are required to confirm this. It is possible that further developments in technique (repeated ~~incubation~~ inoculation or alteration in dosage) may be indicated.

Summary.

1. An account is given of certain important descriptions of epidemics before and during the recent war, and of observations made with regard to them.
2. Recent work on the nature of the infective agent and of transmission experiments is described.
3. An epidemic among troops on occupation duties in Germany is described and its features discussed.
4. Some suggestions are made regarding prevention of infective hepatitis in units, based on aspects of recent work. This includes the superchlorination of water supplies, and general hygiene measures, the avoidance of blood spread, the early recognition of pre-icteric cases by urine examinations, and immunization with gamma globulin.

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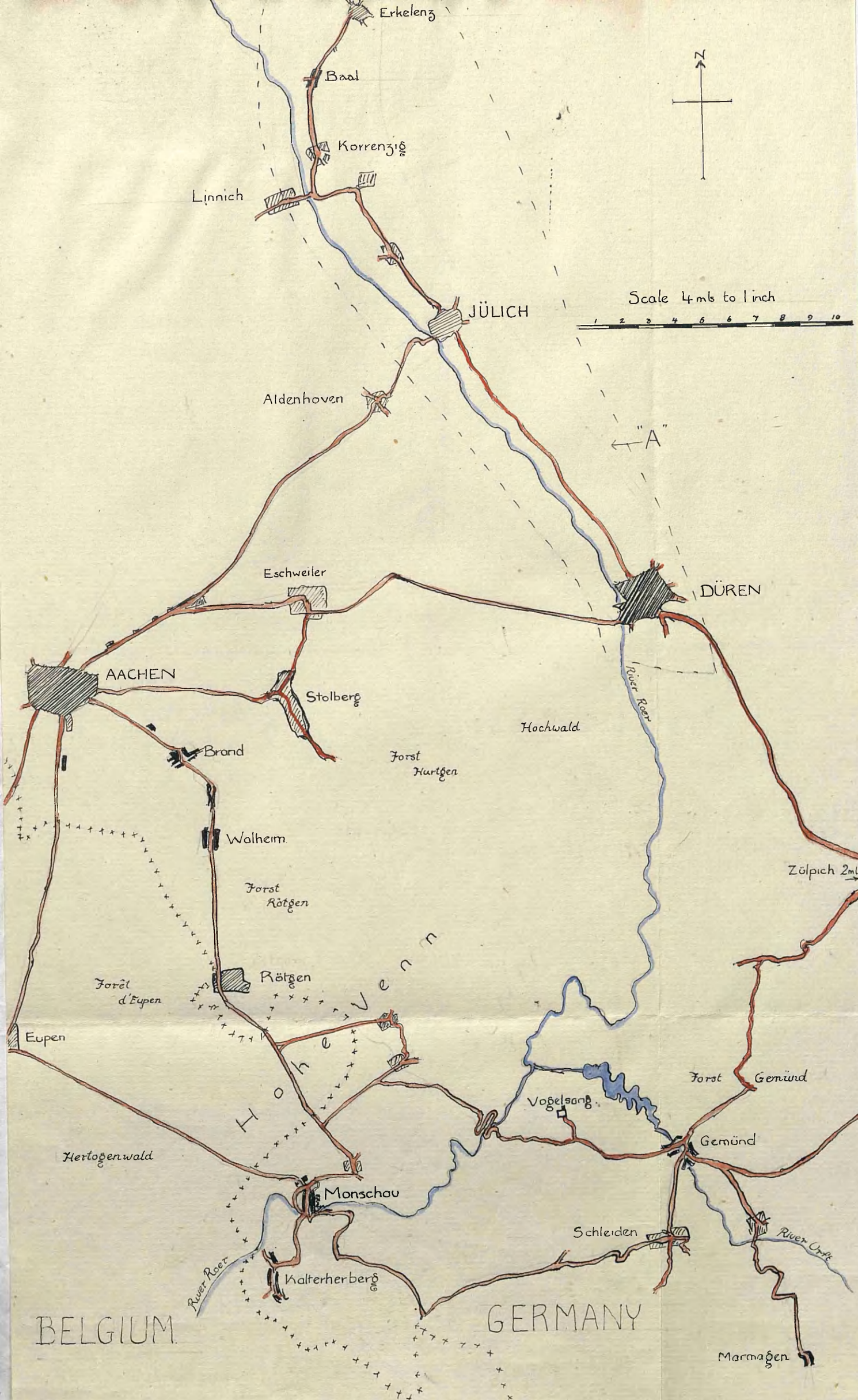
APPENDIX.

Map of the area affected in the epidemic.


Erkelenz
Baal
Korrenzig
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JÜLICH
Scale 4 mls to 1 inch
1 2 3 4 5 6 7 8 9 10
N
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DÜREN
AACHEN
Stolberg
River Roer
Hochwald
Brand
Forst Hurtgen
Walheim
Zülpich 2ml.
Forst Rötgen
Rötgen
Forêt d'Eupen
Hohe Venn
Eupen
Forst Gemünd
Vogelsang
Gemünd
Hertogenwald
Monschau
Schleiden
River Urft
River Roer
Kalterherberg
BELGIUM
GERMANY
Marmagen