After these important recommendations of principle it is perhaps unfortunate that the committee has concerned itself at this stage with the detailed layout of individual records. Thus the suggestion that a single record should serve both as an identification sheet and for abstracts of repeated episodes of both in-patient and out-patient treatment implies so many radical changes in procedure and format that it might be more suitable for a pilot study than for national use. There are also coding ambiguities and errors of layout in the proposed form, and it might well be withdrawn for further study.

A striking feature of the field of medical records is the almost complete absence of data on which to base future policy. We hope that the permanent body which the committee recommends should be set up will encourage the basic operational research which is so badly needed.

Sonne Dysentery

In the last 15 years Sonne dysentery has established itself as one of the most prevalent infectious diseases in this country. During the 1950s the average number of notifications in England and Wales was just over 30,000 per annum, but this represents only a fraction of the total number of infections with *Shigella sonnei* in the community, for many cases go unrecognized. The highest figure recorded was 49,009 notifications in 1956. Food-borne outbreaks are now rare, and the disease spreads mainly by contact. Patients suffering from an acute diarrhoeal attack are more infectious than symptomless excreters. Young children are the chief sufferers and probably also the main spreaders of the disease. The infection is therefore a problem in nurseries, nursery schools, and the infant departments of schools. When introduced into a family it tends to spread widely, particularly in the younger members.

Outbreaks of Sonne dysentery have proved very difficult to control. Trials of chemoprophylaxis in nurseries failed to show any clear benefit.[1] During outbreaks it is usual to attempt to control spread by paying increased attention to washing of hands and to hygiene in the lavatory. There are some who believe that this disease is so trifling, and control so difficult, that to remain inactive while the outbreak runs its course is the only sensible course. Admission to hospital for treatment is seldom justified, but circumstances do sometimes call for isolation in hospital.

Treatment, which at one time appeared to be fairly simple, has become more complicated since the appearance of drug-resistant strains of *Shigella sonnei*. To have any effect on the spread of infection treatment must be started as soon as possible, because it is the early stages of the disease that appear to be the most infectious. But the single sporadic case may be difficult to diagnose without laboratory examination, which takes time. However, Sonne dysentery has a well-defined seasonal maximum in late winter and early spring, and within this period an epidemic in any one locality may be intense and of fairly short duration. Once its existence is recognized a presumptive diagnosis can often be made on the occurrence of suspicious symptoms, allowing the appropriate treatment to be begun while waiting for bacteriological confirmation.

During the last few years the most popular form of treatment has been a combination of sulphonamide and oral streptomycin.[2 3] Although strains of *Shigella sonnei* resistant to either or both of these drugs are being detected with increasing frequency, the finding that the strains in a district are resistant does not mean that they will remain so permanently. A report from Drs. P. J. Moorhead and H. E. Parry in this issue of the *B.M.J.* (page 913) of their experience in Liverpool illustrates the point. Whereas in 1963 26% of the strains tested were resistant to streptomycin, in 1964 only 8% were resistant, and there were corresponding changes in the results of treatment with streptomycin. The conclusions of Moorhead and Parry on the choice of drugs for treatment may or may not be relevant to conditions elsewhere, but their description of the benefits that can come from close collaboration between clinicians and the laboratory should be studied by all who wish to obtain the best results in the treatment of this troublesome disease.

[1] Group Report, *Brit. med. J.*, 1955, **2**, 939.
[2] Stoker, D. J., ibid., 1962, **1**, 1179.
[3] Ibid., 1964, **1**, 825.

Haemorrhagic Fevers

Widespread interest in haemorrhagic fever originated around 1951 when reports began to appear of its occurrence in epidemic form among United Nations troops fighting in the central sector in the Korean war. The first account of the outbreak in English literature was that of N. M. Kater,[1] and many others followed. Several hundred cases were reported in the campaign. The condition was first mistaken for a new disease, but later study showed that Japanese troops had met with it in Manchuria in 1935 and it had been known by a variety of local names such as Songo fever. Russian workers had also encountered this and similar fevers.[2 3] From Russia too about 1950 came reports of similar but clinically distinguishable haemorrhagic fevers—in the Crimea,[4] in Turkmen (bordering on northern Iran),[5] in the Carpathian foothills,[6] and elsewhere.

A. A. Smorodintsev and his colleagues[2] showed that the fevers in this group are caused by a filter-passing virus present in the blood and urine of patients during the first five days of their illness. The disease was reproduced in monkeys and human volunteers by injecting material containing the virus, but intranasal, intragastric, and intrapharyngeal inoculation was not followed by infection. The evidence suggested that the reservoirs of infection were various field rodents and that from these the disease was transmitted to man by certain ticks and mites. Clearly military operations afford greater opportunities for such transmission than usual peacetime conditions.

In the years that have followed these studies similar haemorrhagic fevers have been reported from widely spaced regions—in the Philippines and Thailand,[7] Calcutta,[8] South India, as Kysanur forest disease,[9] the Argentine,[10 11]

[1] Kater, N. M., *Med. J. Aust.*, 1951, **2**, 824.
[2] Smorodintsev, A. A., ed. *Etiologia i klinika gemorragicheskogo nefrozonefrita*. Moscow. 1944.
[3] Bilibin, A. F., "*Semiotika i diagnostika infektsionnykh boleznei*, p. 197. Moscow, 1950.
[4] —— ibid., p. 200. Moscow, 1950.
[5] Semyatkovskaya, Z. V., and Sidtdykova, N. K., *Klin. Med.* (*Mosk.*), 1950, **28**, Part 8, 69.
[6] Kolachev, A. R., and Kosovskii, Iu. Iu., ibid., 1949, **27**, Part 8, 42.
[7] Hammon, W. McD., Rudnick, A., and Sather, C. E., *Science*, 1960, **131**, 1102.
[8] Chaudhuri, R. N., Chatterjee, J. B., Saha, T. K., and Chaudhuri, A. D., *Bull. Calcutta Sch. trop. Med.*, 1964, **12**, 1.
[9] Work, T. H., and Trapido, H., *Ind. J. med. Sci.*, 1957, **11**, 341.
[10] Greenway, D. J., *et al.*, *Publ. Hlth. Rep.*, 1959, **74**, 1011.
[11] Molteni, H. D., Guarinos, N. C., Petrillo, C. O., and Jaschek, F., *Sem. med.* (*B. Aires*), 1961, **118**, 839.
[12] Chew, A., *et al.*, *Lancet*, 1961 **1**, 307.
[13] Rudnick, A., Eu Tan, E., Lucas, J. K., and Bin Omar, M., *Brit. med. J.*, 1965, **1**, 1269.

Singapore,[12] and most recently from Malaya.[13] The Kysanur forest outbreak was preceded by an epizootic among monkeys in the district. In that disease, as in the one in Korea and Russia, the virus is probably transmitted by the bites of mites, but the evidence suggests that the other Asian outbreaks are transmitted by mosquitoes, probably by *Aëdes aegypti*.

In general, the clinical features of these fevers are of a severe illness of abrupt onset after an incubation period of 7–14 days. The patient has severe chills, pains in the back and limbs and at the back of the orbit, and in some cases cough, vomiting, and abdominal discomfort. Vomiting and abdominal pain were particularly severe in the recent Malayan series. Pyrexia of 102–105° F. (38.9–40.6° C.) usually lasts 4–5 days, and it is as the temperature drops that haemorrhages usually appear. The patient then enters an apyrexial but dangerous phase marked also by increased prostration, abdominal pain, and hiccough. The kidneys are frequently involved in the haemorrhagic process, and haematuria and albuminuria followed by oliguria and renal failure were common in the Manchurian and Korean cases; bleeding gums, melaena, and epistaxis were more common in India and Malaya. Petechial haemorrhages in the skin are usually seen. If the patient survives the twelfth day of illness the prognosis is good. The mortality has been as high as 44% in some series, but about 10% is more generally recorded. Leucopenia and thrombocytopenia are common during the febrile phase; later leucocytosis is usual.

The infecting agents so far identified belong to the group of arthropod-borne viruses. In Thailand a group-A virus very similar to that of Chikungunya fever was responsible for severe disease and a group-C virus was isolated from patients in Brazil; the virus of the Argentinian disease has not been specified. The other identified viruses have belonged to group B and are members of the dengue complex.

Inevitably there has been much speculation on whether these fevers are "new" and extending or have been long present but overlooked in regions where they are now encountered. The work of A. Rudnick and colleagues[13] indicates that in Malaya, for example, haemorrhagic fever was not recorded before 1962 and that it was newly introduced to Penang about that time, though it occurred in Singapore in 1960. The sporadic incidence of cases in the outbreak which these and most other workers have studied suggest that it is either being spread by scattered vectors—some birds may be responsible—or that it is a zoonosis with a reservoir of infection in animals such as rodents. From the latter the opportunity for transmission to man would be expected to occur only sporadically.

Much has yet to be learnt about this group of diseases—their incidence, epidemiology and modes of spread, their causation, and the means whereby they may be prevented. It seems likely that much more will be heard of them in the future, and it is important that practitioners throughout both the tropics and the temperate zones should be on the alert to detect them.

Safety of Drugs

The ready co-operation of both the medical profession and the pharmaceutical industry has helped the Committee on Safety of Drugs to a good start. Its first annual report,[1] published this week, pays tributes to the work of medical men in keeping it informed of the actions of drugs and to the readiness of manufacturers in seeing that no new drug is put to clinical trial or released for marketing without the Committee's consent.

The year 1964 was the first in which the Committee carried out its full range of duties. These come under three headings: "to advise whether a new drug should be submitted for clinical trial; to advise whether a drug should be released for marketing; and to study adverse reactions to drugs already in use." During the year details of 600 new drugs were submitted. The Committee raised no objection to the clinical trial or marketing of 386 of them, but for 15 of them it did not agree with the manufacturer's proposals. The rest were in various stages of being considered except for 32 which the manufacturers had voluntarily withdrawn. It is a comment on the great rapidity of advance in medicinal therapeutics that "the number of entirely new chemical substances included among the new products submitted to the Committee was 55." And some idea of the price that has to be paid for discovery in preparing and reading papers is contained in the Committee's observation that "a submission containing over 1,000 pages of reports, drafts, and tables was not unusual." Nor was this the end, for supplementary questions and answers customarily flowed between the Committee and manufacturers. Some of these are reported to have entailed "robust but usually good-humoured encounters." It appears that such exchanges of view with the manufacturers had their main effect not in leading to outright rejection of a drug but in encouraging the manufacturer to formulate it in a different way or for a different purpose. Co-operation of this kind is clearly of great value to all concerned—and not least to the patients who will benefit from it—so that much praise is clearly due to the members of the Committee, and notably its chairman Sir Derrick Dunlop.

The monitoring of adverse reactions in clinical practice is a particularly valuable function of the Committee. It is being carried out in both general and hospital practice. The "yellow cards" for notification of suspected adverse reactions by all practising doctors and dentists have been providing up to 100 reports a week. A procedure is now being developed to relate the numbers of such reports to the numbers of prescriptions of the drug concerned. The Committee has also arranged for selected hospitals to report on a "list of specially monitored drugs." This will include all the drugs introduced in the previous two years and some older drugs still considered to need observation.

The Committee on Safety of Drugs came into being largely in consequence of the thalidomide tragedy. Medical opinion found formal expression in a motion from Professor H. W. Rodgers, of Belfast, carried without dissent at the Annual Representative Meeting of the B.M.A. there in 1962,[2] on the establishment of an "independent and representative organization to supervise the introduction of new drugs." But it is worth bearing in mind that there are limits to what the new Committee can do. The practising doctor, for instance, will never be able to assume that a drug passed by the Committee is safe in all circumstances, for there will probably always be drugs whose benefits must be balanced against risks, however slight. Indeed, is there a substance with a pharmacological action which has never had alarming effects? The Committee's reports on toxicity, however, of which one appeared recently,[3] will surely help the clinician to reach a more exact view than he could formerly on the relative merits and drawbacks of a drug.

[1] *Committee on Safety of Drugs*. Report of the Committee on Safety of Drugs for the Year Ended 31 December 1964. H.M.S.O. 1965. (1s. 3d. net.)
[2] *Brit. Med. J. Suppl.*, 1962, **2**, 44.
[3] *Brit. med. J.*, 1965, **2**, 465.