August, 1945

I am grateful for the opportunities I have had of associating myself in thyroid work with the late Cecil Joll, Sir Thomas Dunhill and Geoffrey Kaynes, and for the benefit derived by me from their vast experience.

I wish to thank Miss E. M. Dean, Laboratory Technician to New End Hospital, for her careful compiling of statistics and records; Mr. J. E. Andrews, L.C.C. Medical Photographer and finally Dr. J. W. Linnell for his kindness in criticising this paper.

REFERENCES
2. RUSSELL, P. M. G., and DEAN, EDNA M., The Lancet (July 18, 1942).

PRACTICALITIES

CLINICAL OBSERVATIONS ON MALARIA

By P. G. Shute, F.R.E.S.
(Assistant Malaria Officer, Ministry of Health)

The disease malaria in man is caused by a specific, pathogenic organism known as the human malaria parasite, of a very primitive type belonging to the lowly animal kingdom, the *Protozoa*.

There are at least four separate species of human malaria parasites, each having morphological characters. By appropriate staining the microscopist is enabled to identify accurately the species involved.

The four species are:

1. *Plasmodium vivax* (Benign tertian).
2. *Plasmodium falciparum* (Malignant or sub-tertian).

A definite diagnosis of malaria can be made only by microscopical examination of the blood and recognition of the parasites. In certain cases, however, especially in relapses, the occurrence of fever every third day is indicative of Benign tertian malaria, while the occurrence of fever every fourth day is suggestive of Quartan malaria. Yet even when the fever presents this classical picture, diagnosis can be clenched only by finding the parasite in blood films.

It is probably no exaggeration to say that, until a few years ago, very few practitioners in this country were called upon to diagnose a primary attack of malaria. The reason, of course, was that it was almost impossible for people who were infected in tropical countries to arrive in England before the end of the normal incubation period of the disease. Now, however, with speedy air travel on an ever-increasing scale, it is possible for a person to be infected with malaria in the tropics one day, arrive in England on the following day, and develop malarial fever a week or two later.

In the knowledge of the writer there is the case of a man who spent only one night at a West African Station, returned to England by air a couple of days later, and developed Malignant tertian malaria nearly two weeks after his arrival. The diagnosis of malaria was not made for several days after fever had begun, because this disease had not been suspected and the fever chart was atypical.

It is generally agreed that, at least in non-immune Europeans infected with M.T., it is the primary attack and the first two or three relapses which, if not recognised and promptly and adequately treated, may lead to a fatal result. Unfortunately, in primary infections, and this applies to all four species of malaria parasites, the illness seldom begins with characteristic symptoms and signs. It may be worth while, therefore, to describe in detail the history of the fever as it occurs in each of the four species of human malaria parasites.

**Plasmodium vivax** = Simple or Benign tertian malaria.

The asexual parasite completes its cycle of multiplication in 48 hours.

**Common features of this species of parasite**

1. The normal incubation period is between nine and fourteen days but may be as long as one year.
2. The whole of the life cycle of the parasite takes place in the peripheral blood.
3. Parasites, if present, are about equal in numbers both during the fever and in the fever free period.
4. The host cell of the parasite is swollen and if correctly stained is seen to be heavily studded with fine granules (Schuffner's dots).
5. Temperature frequently rises to 105°F. or over.
6. Rigors, which nearly always precede the onset of an attack, usually last about an hour.

This is followed by the hot stage, the skin is hot and dry, the face flushed and headache and vomiting are often severe. This stage lasts about four hours.

Lastly, there is the sweating stage which is one of profuse perspiration. The temperature falls
rapidly, the headache disappears and the paroxysm is over. This stage lasts about two hours.

The duration of a complete attack lasts about eight hours (see Chart I).

If a non-immune individual infected with Benign tertian malaria is followed to the stage when he has acquired immunity it will be seen that there are five distinct phases.

**Stage I.**—The fever is usually remittent for a period of from two to five days (see Chart II).

**Stage II.**—The fever is quotidian and continues to be so for many days, or even for some weeks, unless anti-malarial drugs are given (see Chart III).

**Stage III.**—The fever is true tertian (see Chart IV).

**Stage IV.**—The fever has disappeared spontaneously but parasites (often quite numerous) are present in the blood.

**Stage V.**—The patient is immune to reinfections with the same strain of the same species.

In Stage I there are numerous small rises of temperature over 3 days. It is believed that each is due to segmentation of a group of parasites. In the absence of any degree of immunity, each group of parasites, even in very small numbers,
In all cases such as these, parasites in every stage of development, from young ring forms (merozoites to pre-segmenting forms, i.e. mature schizonts) are present in the peripheral blood at the same time. In an untreated attack of quotidian \( P. \) \textit{vivax} malaria the number of parasites per c.mm. may exceed 25,000, but seldom 50,000, on or about the 4th day of untreated fever, excluding the already mentioned initial phase (Stage I).

Stage III. This is the stage common in relapses. Parasites are numerous on the first day of the recognised attack (contrast Stage I). In a large number of cases, probably in most, there is a history of feeling “off colour” several days before the attack develops. This is probably due to the degree of tolerance established as the result of a previous attack, especially in those cases who, in the primary attack, were untreated for several days. A much larger number of parasites is necessary to produce clinical symptoms in a relapse than when the patient first develops the disease. The “off colour” stage preceding the frank attack was caused by the parasites, but it is not until they reach a certain density that they succeed in incapacitating the patient.

Usually all the parasites are of the same stage of growth. Occasionally two age groups may be present but if a differential count is made it will be seen that one group of parasites is much larger than the other, and it is only the large group which is capable of producing clinical symptoms—evidence that the patient has acquired some degree of tolerance to his parasites.

Stage IV.—The number of relapses necessary to produce sufficient acquired immunity which will prevent future clinical symptoms, depends on several factors, but probably the most important is the amount of fever and subsequent saturation of the blood with parasites. In a very large number of cases who have been infected with a single strain of a single species of Benign tertian malaria and who have had some relapses, the tendency is towards a spontaneous recovery (see Chart V).

The fever peters out, but parasites may be numerous in the blood and often exceed 5,000 per c.mm. The disease has now reached the chronic stage, and, although the patient’s parasites are still virile and developing and segmenting normally, there is no fever.

The parasites of these chronic cases produce an acute attack when they are injected into a susceptible host.

In this stage the disease malaria is absent, even though parasites are present in the blood in fairly large numbers. This is an important point to remember because a patient reporting sick with a temperature may be considered to be suffering from malaria because parasites have been found in his blood. It is the opposite of the picture as seen in Stage I, where there is severe malaria fever in the absence of detectable parasites. In other words, despite the fact that the malaria parasites are the cause of the disease, in very chronic cases the existence of parasites may not be the cause of fever. The patient has now reached this chronic stage.

Stage V. Little need be said about this stage. As the result of the previous attacks complete immunity has been established, and repeated reinfections by the same strain of the same species fail to cause clinical symptoms, and parasites cannot be found in the blood.

Stage I to Stage V may be completed in from one to three years, the period depending to a large extent on the frequency of relapses and the amount of fever at each attack before treatment is begun.

A fairly common feature in Benign tertian malaria is the phenomenon of latency. Individuals who are infected by the bites of mosquitoes may remain free of all malaria symptoms (clinically and parasitologically) for several months or even for one year. This latency period has nothing to do with acquired immunity and when eventually the disease develops it is as severe as the average attack is when the incubation period is 10–14 days. This suggests that there is a resting stage of the parasite in this type of malaria. Some believe it is the infective organism injected by the mosquito (sporozoite), others that it is a form of the parasite between the sporozoite and the red blood cell parasite (trophozoite).

Latent Benign tertian is common in endemic countries \textit{in the absence} of drug prophylaxis, and where drug prophylaxis is carried out throughout a malaria season, \textit{latency is the rule}. Therefore, among troops who are not operating in areas where Benign tertian malaria is common, and where the troops are being protected by drug prophylaxis, many of them may, and probably will, develop their first attack of malaria after returning to their homes. Here, clinical guidance may be of
some value. Those who experience quotidian fever and who claim not previously to have suffered from malaria are, in all probability, cases of true latency and they should be treated as primary cases. It may not be out of place here to mention that after the war there may arise cases of indigenous malaria in the civil population, brought about by English Anopheles mosquitoes (in which this country abounds) biting returned troops who have gametocytes (sexual parasites) in their blood, and subsequently passing on the infection. If, however, a member of the community develops his first attack between the months of November and May, it is fairly certain that he acquired his infection in the previous summer or autumn.

Untreated Benign tertian malaria results in progressive anaemia and debility. The spleen becomes enlarged. Icteric haematogenous jaundice is not uncommon and frequently there is herpes, especially of the lips. After several attacks the patient becomes exhausted rapidly if the fever is quotidian but less so if the fever is tertian.

**Plasmodium falciparum** = Malignant or sub-tertian malaria.

The asexual parasite completes its cycle of multiplication in 36 to 48 hours.

**Common features of this species of parasite**

1. The normal incubation period is between 8–14 days.
2. So far as is known protracted incubation periods of several months do not occur.
3. The developmental cycle takes place in the internal circulation and only ring forms (merozoites) are seen in the peripheral blood.
4. The host cell of the parasite is not swollen but a type of stippling may be present, consisting of small numbers (seldom more than 12) composed of dots, streaks and loops (Maurer’s dots).
5. Even in very severe cases the temperature may not exceed 103° F. to 104° F.
6. Very heavy infections are sometimes seen and parasites may exceed 500,000 per c.mm.

Rigors seldom occur, but if they do they should be considered as a serious manifestation. It often indicates that developmental forms of the parasite are present in the peripheral circulation and when this occurs the prognosis is grave.

In a primary attack of Malignant tertian there is the same type of fever as is seen in Stage I of Benign tertian malaria, but unlike this species, the fever does not settle down to a definite quotidian rhythm. It persists for many days and may end fatally if untreated (see Chart VI).

Because of the long-continued fever, the patient may remain in the hot stage for a day or two and experience great discomfort. Despite this, personal experience enables the writer to state that 48 hours of Malignant tertian fever causes less discomfort than 48 hours of Benign tertian fever, if in the latter rigors are severe.

Malignant tertian malaria is a dangerous disease, especially the primary attack. The absence of a rigor in Malignant tertian may fail to draw attention to the true nature of the disease, because rigors are so closely associated with malaria that it may be considered that the rigor-less paroxysm cannot be malaria. An important point to remember is that, even in severe attacks, parasites may be difficult to find in the peripheral blood, especially at the height of an attack. Blood films should be examined at the earliest possible moment whether there is fever or not. But if parasites cannot be found in films taken at the height of the fever, further films should be examined a few hours later, preferably after the temperature has fallen, because it is in the fever-free period of Malignant tertian that parasites are most numerous in the peripheral blood. It cannot be emphasised too strongly that in Malignant tertian malaria, treatment should be started as soon as possible, especially when a patient reports that he has been feeling unwell for several days. Unlike the relapses of Benign tertian malaria, those in Malignant tertian, when they do occur, follow closely one upon the other, and only very rarely do patients continue to relapse (fever and parasites) for more than six to eight months after the last infection. We have seen that in Benign tertian relapses the fever is nearly always true tertian. In Malignant tertian relapses the fever may also be tertian, but it is
just as frequently quotidian and may even be intermittent (see Chart VII).

Unless the primary Malignant tertian infection is properly treated, a relapse usually occurs within a few weeks. Repeated relapses follow one another in quick succession if each one is inadequately treated, and these will continue over a period of several months. The first and second relapse may be almost as severe as the primary attack, but the subsequent relapses are usually mild, affording proof that the disease is becoming chronic. Although Malignant tertian infections are much more dangerous to life than the other species, it is the easiest of all to terminate, providing efficient treatment is given (sterilisation of the infection).

In Malignant tertian malaria, unlike the other three species, the red cells containing parasites tend to stick to each other and to the lining of the capillaries, thereby blocking the lumen of the small blood vessels. This is likely to occur in non-immunes who have had several days of fever without treatment, and in such cases pernicious symptoms are frequent, depending on the site of the damaged capillaries. In some very severe forms of Malignant tertian the skin may be cold and fail to register a high temperature. In these cases, rectal temperatures should be registered.

The clinical picture of Malignant tertian malaria is well summed up by Dixon in Medical Diseases of War.* The following are extracts:

Pernicious Attacks

A special feature is the dramatic suddenness of the attack which is frequently fatal.

Cerebral Malignant tertian

The gradual onset of coma is generally preceded by premonitory symptoms, drowsiness, twitchings,

patient has been suffering from attacks for at least ten days, or else during the month before his present attack suffered from a relapse. In this type of malaria, gametocytes do not appear in the peripheral blood for at least ten days following the first day of an attack, but when they do appear they survive for several weeks. Neither quinine or mepacrine causes their destruction and their ultimate disappearance from the blood is due to natural causes. Therefore blood in which both ring forms (merozoites) and gametocytes (crescents) are found, is of clinical significance.

Anaemia is more rapid in Malignant tertian infections than in all other types of malaria. This is attributable partly to the greater parasite density compared with that of the other species, but also to the attack made by the parasites on erythrocytes of all ages; in Benign tertian the parasites are believed to have a predilection for reticulocytes. The anaemia in malaria does, however, clear up rapidly after the destruction of the parasites by treatment. In malaria it is hypochromic in type and since the iron stores are unaffected by the destruction of parasitised red cells, the restoration of the blood is rapid after adequate treatment of the disease.

Although Malignant tertian infections often lead to a fatal issue, deaths from this type of malaria are usually due to delayed or inadequate treatment, or, as often happens, to attempts at self medication. As shown above, the fever chart in Malignant tertian frequently fails to conform to a tertian periodicity; one might almost say generally fails to do so, at least in primary cases.

PLASMODIUM MALARIAE = Quartan.

The asexual parasite completes its cycle of multiplication in 72 hours.

Common features of this species of parasite
1. The minimum incubation period is one month.
2. The whole of the life cycle of the asexual parasite takes place in the peripheral blood.
3. Parasites, when present, are about equal in numbers both during the fever and in the fever-free interval.
4. The host cell of the parasite is not enlarged and very rarely shows any stippling (Zieman's dots).
5. True latency as observed in Benign tertian infections is not known.
6. Rigors may, or may not, precede an attack.

As with Benign tertian, there is a well-marked hot and sweating stage, but it is generally much less severe and therefore less exhausting. The onset of an attack is sudden and the initial phase as seen in Benign tertian and Malignant tertian is rare. The duration of an attack is approximately the same as in Benign tertian but may be longer—even 12 hours is fairly frequent. The life cycle of the asexual parasite is completed in 72 hours. Therefore, when only a single group of parasites is present in the blood, fever occurs every fourth day (Classical Quartan) (see Chart VIII).

However, as with the other species, in primary infections the parasites are in various stages of development, with the result that the fever is atypical. Often there is quotidian fever which clinically, cannot be distinguished from either Benign tertian or Malignant tertian (see Chart IX).

In the absence of treatment or acquired immunity, fever may continue over a period of many weeks or even months. In Malignant tertian most non-immune Europeans would die of the disease if left untreated for such long periods, according to the strain of Malignant tertian parasite involved. In Benign tertian most otherwise healthy subjects would run to a spontaneous recovery. But in Quartan malaria, attacks often persist for very long periods without showing any tendency to cure spontaneously, and without apparent danger to life. Hence it is to be deduced that immunity in Quartan is exceedingly slow in developing. This is borne out by the length of life of the Quartan
species as an active organism in man. Genuine relapses (parasites and fever) have been reported in patients infected twenty years previously, who have not during the interval been in an area where they could have been reinfected. Even in the developed stage of a primary attack parasites are usually rare compared with those in Benign tertian and Malignant tertian infections and seldom exceed 10,000 per c.mm. of blood. In some of the observed relapses which have occurred many years after infection, parasites may be extremely rare, and in one relapse which occurred more than twenty years after infection, parasites were less than one per c.mm. of blood. The ordinary thin film examination is not of much use in these cases; only the special thick film examination is likely to reveal parasites.

It is believed that throughout the whole length of infection in Quartan malaria, even during the afrebrile period (which may be over a period of years), a few parasites are present in the peripheral blood, without apparently interfering with the health of the victim. If, however, the patient acts as a blood donor, the recipient will contract malaria. Some years ago a London policeman served as a donor for his infant daughter. A month after the transfusion the child developed fever and subsequently died. The post mortem revealed a Quartan malaria infection. The father had been in this country for more than 12 years, having lived previously in Ceylon. He had no knowledge that he was infected with malaria, but said that every few months he experienced night sweats when he would have to change his pyjamas two or three times a night over a period of a week or two. Many thick films of his blood were examined for long periods before even a single parasite could be found. Had it not been for the blood transfusion it is unlikely that this case of Quartan would ever have been brought to light. It is therefore unwise to allow old malaria cases to act as donors. It is, too, advisable to examine the blood of recipients for malaria parasites in the event of fever, especially when the fever begins several days after transfusion. Several cases of Quartan malaria have occurred among drug addicts in the United States. Here infection was induced by using the same syringe and needle a number of times before cleaning it.

While victims of Quartan malaria may have attacks of fever over a period of several weeks without losing weight or becoming very anaemic, a common incident in the clinical course of an infection is the development of an albuminuria which, it is considered, represents a nephrosis rather than a nephritis. This condition usually clears up rapidly with the termination of the malaria infection.

**PLASMODIUM OVALE** = Ovale tertian.

The asexual parasite completes its cycle in 48 hours.

**Common features of this species of parasite**
1. The incubation period is usually between ten and fourteen days but, as in Benign tertian, protracted incubation periods of one year or more have been recorded.
2. The whole of the life cycle of the asexual parasite takes place in the peripheral blood.
3. Parasites, when present, are about equal in numbers both during the fever and in the fever-free interval.
4. The host cell of the parasite is enlarged and shows prominent stippling.

Fever due to this species of parasite is just as severe as in Benign tertian, at least during the primary attack, but it is the mildest of all species. In untreated attacks, the disease usually cures spontaneously after a few days of fever, and, although relapses have been reported, they are not frequent, probably because the length of life of the parasite in man is of short duration. In many respects the parasite closely resembles that of Benign tertian, but because it is so mild and the
disease is so easily cured by anti-malarial drugs, from the clinical angle, it is not to the detriment of the patient if an Ovale infection is mistaken for that of Benign tertian. Even in the primary attack the fever is generally tertian in character, unlike the other three species (see Chart X).

Until recently it was believed that Ovale was essentially a type of malaria to be found only on the continent of Africa, but during recent years it has been reported from New Guinea, South America, the Caucasus, and elsewhere. It is probable that in the past, cases of Ovale have been diagnosed as Benign tertian and even Quartan.

**MIXED INFECTIONS**

While it is true that malaria is widely distributed throughout more than half of the inhabited world, not all the species of malaria parasites are equally distributed. For example, in many parts of the tropics, West Africa and elsewhere, Malignant tertian infections greatly outnumber all other species. On the other hand, in some temperate regions (e.g. Holland, North Spain and North Italy) only Benign tertian is found. In many areas, however (Eastern Europe and elsewhere) Benign tertian and Malignant tertian are present in about equal numbers with Quartan present, but rare by comparison. The incidence of all cases varies according to the season of the year. Therefore after the war is over and the troops return home, many, if not most of them, will have been infected with at least two, and possibly three, species of malaria. The greatest number of acute relapses will be with Benign tertian, but some Malignant tertian will occur, especially among troops who were not stationed for long periods in the tropics and who returned home soon after being infected. A patient who is ill with fever and states that he was diagnosed as suffering from Malignant tertian one or two years previously, is not likely to be having severe relapses caused by the same species of parasite. The relapses are most likely to be Benign tertian, or in rare instances Quartan. Immunity to one species of parasite does not confer significant immunity to the other species, although it may prolong the incubation period, especially when the first infection is due to Malignant tertian. The reason for this lack of immunity is unknown.

**Brief Notes on the Preparation and Staining of Thick and Thin Blood Films for demonstrating Malaria Parasites**

**Choice of slides**

Use new slides whenever possible; scratched or foggy slides are unsuitable. Slides should be quite free from grease.

Use a grease-free cloth for polishing slides. The edge of the slide used to spread a thin blood film should be quite smooth.

**Thin blood films**

Puncture the pad of the middle finger with a straight triangular surgical needle. See that the finger is clean. The drop of blood should not be larger than the head of a pin, otherwise the blood smear will be too thick. Hold the spreader at an angle of 45° to the slide and allow the drop of blood to spread evenly along its lower edge. Make the films by gently spreading along the slide. See that the slide used as a spreader has a smooth edge. In a satisfactory film there are no gaps or holes and red cells almost touch, but do not overlap each other.

**Leishman's stain for thin films**

Pour 100 c.c. of methyl alcohol into a clean, dry, narrow-necked bottle. Add to this 0.15 gm. Leishman's powder and shake for a few minutes. Repeat the shaking a few times daily for a couple of days. The stain is ready for use in within 24 hours of preparing it. Never heat or filter Leishman's stain. Leishman's stain gives very much better results if the water is slightly alkaline. All distilled water is acid, especially when it is stale. This can be rectified by adding a few drops of strong alkali, e.g. lithium carbonate, a pH of 7.2-7.4 should be aimed at. If staining is poor it is usually because the distilled water is acid. A slightly alkaline distilled water is the secret of successful staining with Leishman's stain and, in point of fact, all the Romanowsky stains. Leishman's stain will keep in good condition for at least 6 months.

**Technique of staining**

1. Four drops of the stain on the film and allow it to act for 15 seconds.
2. Add twelve drops of distilled water and mix thoroughly.
3. Leave specimen staining for 15 minutes.
4. Flush off with distilled water but do not wash for more than 5-6 seconds.
5. Dry film without artificial heat.

**Thick blood films**

One drop of blood, a little larger than for a thin film, is placed in the centre of a clean slide. With the pricking needle distribute the blood by circular movements until it covers about three times its original size. Lay the slide on a flat surface to dry. Blood films, whether thick or thin, must be covered before staining, otherwise flies will quickly eat all the blood.
If a thick film is too thick the blood, when dry, will crack and peel off during staining. Newspaper which is just readable through a thick film is a good indication of a satisfactory thick film. Before staining thick films the blood must be quite dry, and it is a good plan to apply gentle heat to a freshly made thick film before staining it.

Staining thick films

Leishman’s is not satisfactory. Dilute Giemsa gives better results but Field’s stain* is probably the best of all for thick films.

Note

Detection and classifying malaria parasites in thick films is much more difficult than in thin films. Not until one is fully familiar with parasites in thin films should one undertake the responsibility of diagnosing with thick films. But when films are being sent for examination to a laboratory where specialists are available a thick film should always be included.

1. Sprained Ligaments

The internal lateral ligament is the ligament most frequently damaged. Usually a few of the upper fibres are torn away from the periosteal attachment at the lower end of the femur. Occasionally, however, the deep fibres which are attached to the internal semilunar cartilage are partially torn without the cartilage being damaged. Occasionally, the external lateral ligament is injured. With more severe violence the anterior cruciate ligament may be torn. It should be borne in mind that in relatively small injuries these ligaments are not completely torn across or pulled from their bone origins, but only a few fibres are torn away. In gross injuries, however, which are often accompanied by dislocation of the joint, the whole ligament may be torn across or the ligament will pull off a flake of bone at its base attachment. The commonest ligament to do this latter is the anterior cruciate, which pulls away a flake from the upper surface of the tibia.

2. Traumatic Synovitis

Any over-use of a knee, any sudden twist or contusion to the knee may be sufficient to either bruise, tear, or nip the synovial membrane of the joint, giving rise to a traumatic synovitis which is accompanied by an exudate of fluid and hypertrophy of the whole synovial membrane. Adhesions may follow.

3. Nipped Local Villi of the Synovial Membrane

Often a sideways twist or a direct blow, as in football, on to the knee will cause one villous process of the membrane to get nipped between two bone surfaces, giving rise to a localised synovitis. In this case the nipped process will have exudate of blood inside it, which blood will organise and clot, giving rise eventually to a pedunculated tag. This pedunculated tag gets repeatedly nipped, leading to a more diffuse synovitis; and eventually may drop off and become a loose body.

4. Internal Derangements of the Knee Due to Fracture—Dislocations of the Semilunar Cartilages

With various types of twist the semilunar cartilage may get forcibly detached from its synovial attachment and become either torn or partially loose inside the joint.
Clinical Observations on Malaria

P. G. Shute

Postgrad Med J 1945 21: 253-261
doi: 10.1136/pgmj.21.238.253

Updated information and services can be found at:
http://pmj.bmj.com/content/21/238/253.citation

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/