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Short Notes :

in

Fevers

Internal medicine

+ pneumonia : chest

C.S. fever : N.S.

Rh. F. : C.V.S

Enteric Fevers

Typhoid fever

AE : caused by salmonella typhi.

Mode of infection : Ingestion of infected water, drinks or food.

Organisms come from a patient or a carrier either directly or by flies which play a very important role in transmission.

Route of organism after ingestion and pathology : the organisms penetrate the small intestine and then reach the mesenteric lymph nodes where they multiply for certain time and then reach the blood (bacteraemia) through the thoracic duct. From the blood, they localize in the liver, gall bladder, spleen and again to the Peyer's patches where they re-multiply and re-invade the blood stream and reach the bones, vertebral column and joints. The Peyer's patches will be inflamed and ulcerate. Hemorrhage and perforation may occur.

I.P. : 1 – 3 weeks.

C/P : Typhoid fever occurs in summer and autumn (flies). In both sexes, commonly 10 – 30 years old. Onset of symptoms is usually insidious with headache and lassitude. The course can be classified into 4 weeks (if not interrupted by treatment; as after the advent of chemotherapeutics, the natural history of different fevers is not usually seen).

First week :

1- Pyrexia rising gradually (by steps) with sore-throat and stiff neck. At the end of this week temperature may be 39 – 40 °C. it is remittent. Frontal headache is characteristic.
2- G.I. symptoms are few and the abdomen is tender (it corresponds to the stage of invasion).

Second week :

1- Pyrexia is more or less continuous at its high level. Delirium, muscle twitches and even unconsciousness may occur (typhoid state). The pulse is rapid but still relatively slow (for each 1 °C, the pulse increases 10/min. normally).
2- Spleen becomes enlarged, soft and tender.
3- G.I. symptoms are severe with the characteristic pea soup stools. More commonly obstinate constipation is present. The abdomen is distended (tympanitic).
4- Typical macular eruption may appear which is pink (rose spots) and lenticular in shape. It appears in crops on the sides and back of the chest and upper abdomen.

Third week (the week of complications) :

The most dangerous period is the end of the 2nd week and beginning of the 3rd week but in favorable cases the pyrexia starts to decline gradually (by lysis), toxaemia and appetite improves.

Fourth week (convalescence) :

The patient gradually becomes normal. This may take 1 – 3 weeks.

Complications :

A) Abdominal :

1. Perforation : results in severe abdominal pain. The temperature falls rapidly with pallor, sweating and collapse. There is localized rigidity and tenderness on palpating the abdomen. If left, generalized peritonitis will result and the temperature rises again.
2. Hemorrhage : it results in rapid drop of temperature with shock and melaena. There are rapid pulse, of small volume and low blood pressure. A previously palpable spleen may disappear.
3. Acute or chronic cholycystitis : and the gall bladder may be responsible for a carrier state.
4. rarely; rupture spleen.

B) Cardiovascular : myocarditis and venous thrombosis.

C) C.N.S. : meningitis, polyneuritis and nerve deafness.

D) Others : bronchitis, bronchopneumonia, pleurisy, otitis media, osteomyelitis (bone abscesses) and spondylitis (typhoid spine).

Diagnosis :

1- Blood picture : leucopenia with relative lymphocytosis (leucocytosis is seen with complications as hemorrhage).

2- Bacteriological diagnosis : the salmonella is detected in culture : +ve blood culture in the 1st, 2nd, 3rd weeks.

3- Serological diagnosis : by Widal agglutination test :
   - Typhi 0 : 1/125 or over is diagnostic especially with a rising titre (from the 2nd week).
   - Typhi H : is not of value as it is high in persons previously vaccinated and is liable to non-specific stimulation to any infection.

Paratyphi Fever :

Similar in every aspect to typhoid fever but :

- Shorter I.P., more acute onset, which may be atypical (simulating gastro-enteritis or Influenza).
- Duration of the illness is shorter with wide remissions of the temperature.

- Toxaemia and complications are less.
- Caused by salmonella para-typhi (A, B, C).
- Widal test is +ve with agglutination at para "H" A, B 1/250 while "H" C 1/50.

Treatment of enteric fevers : (the scheme for all fevers)

1. **General measures** : (for all fevers).
   - Bed rest up to the 4th week (convalescence).
   - Good nursing : keeping the bowels open by enemata, sponging and care of the back and pressure points and mouth toilet.
   - Diet : start by a fluid diet until the fever subsides (water, juice, milk, glucose, light tea.....) and then a highly nutritious well balanced diet is given (semisolid, low residue, non-flatulent diet with adequate proteins, fats, carbohydrates, salts and vitamins).

2. **Specific treatment : one of 2 drugs :**
   - Chloramphenicol : 50 mg/kg body-weight is given for adults as divided doses 6 hourly until the evening temp. reaches 37°C and then half this amount is continued for up to 10 days.
     - *Advantages* : specific & highly effective.
     - *Disadvantages* : may cause agranulocytosis and dose not kill the intra-cellular organisms. (relapses may occur if drug is not given for a long period after the temp. is normal).
   - Ampicillin : about 4 gm/day (as chloramphenicol) as capsules, used in the same way. It is a broad spectrum semi-synthetic penicillin.
     - *Advantages* : doesn't cause agranulocytosis and kill intra-cellular organisms, so diminish the relapse rate and is more suitable in eradication of carriers.
     - *Disadvantages* : less effective than chloramphenicol. It is more expensive.
   - Use of corticosteroids : rarely in highly febrile patients and in severe typhoid state, prednisolone can be given as 60 mg/1st day, 30 mg/2nd & 3rd days and 20 mg on the 4th day.

3. **Symptomatic treatment : (as for all fevers) :**
   - For the pyrexia : sponging (avoid anti-pyretic drugs).
   - For the headache and insomnia : cloral hydrate.
   - For the diarrhea : omit milk from the diet, give bismuth, chalk and Tr. Opii.

4. **Treatment of complications :**
   - Of hemorrhage : add blood transfusion + nothing by mouth, only fluids + may be morphia. Chloramphenicol is continued by the intramuscular route.
   - Of perforation : better treated surgically but other broad spectrum antibiotics + suction + fluids + morphia may be given a trial while the patient is under observation in the hospital.

5. **Prophylaxis :**
   - General : health measures.
   - Individual : T.A.B. vaccination 0.5 , 0.75 and 1 cc given at weekly intervals. It gives immunity for 2-3 years.

Typhoid relapses : all the symptoms and signs sometimes occur again after the temp. has been normal by about 10 – 14 days, treated by the same way.

Brucellosis (Malta or Undulant Fever)

AE : caused by *Brucella* organism, mainly *Br. Melitensis* (goats) rarely *Br. Abortus* (cows) and *Br. Suis* (pigs).

Mode of infection :

by ingestion of infected milk from goats or cows. It is originally a disease of these animals. Rarely by contact.

Route of the organism and pathology : the organism reach the blood stream and some of them localize in the spleen, lymph nodes and the other organs of the R.E.S. causing inflammation and granuloma formation.

I.P. : (1 – 3 weeks)

C/P :

It is more common in Mediterranean countries.

In typical cases the presentation is insidious with gradually rising temp. (up to 40°C), headache, malaise, sweating with nausea, vomiting, constipation (or rarely diarrhea).

On examination the spleen is ++, soft and tender and maybe also the liver, with generalized lymphadenopathy esp. the cervical lymph nodes.

The pulse is rapid but relative slow. A non-specific rash may occur (apart from the generalized lymphadenopathy; it is similar to typhoid fever clinically).

After 1 – 3 weeks pyrexia comes to normal with improvement. The patient remains afebrile for about 1 – 2 weeks then the fever relapses again for a shorter period (7 – 10 days), to be followed by a longer free period. A 3rd relapse for few days may occur and rarely more. This is the origin of the word "undulant".

Other atypical forms :

1. continuous type with no free periods for 1 – 3 months or even years (D.D. of P.U.O.).
2. ambulatory or mild type.
3. malignant or severe type.

Complications : may be bronchitis, bronchopneumonia, pleurisy, orchitis, arthritis, osteomylitis, spondylitis and abortion.

- Emaciation and anemia if prolonged.

Diagnosis : (same steps as in typhoid fever) :

1- Blood picture : as in typhoid.
2- Bacteriological diagnosis : blood and urine cultures as in typhoid but not stool cultures (show the coccobacilli).
3- Serological diagnosis : by an agglutination test similar in principle to Widal test. 1/100 dilution is diagnostic. Rising titres are more significant.

Treatment :

1- **General measures** : (as for any fever).
2- **Specific treatment** :
   Tetracyclines 50 mg/kg body weight along with Streptomycin 1 gm IM twelve hourly, are given for 2 – 3 weeks. Supha-trimethoprim (septrin or bactrim) 2 tablets 12 hourly are also very effective.
3- **Symptomatic treatment** : as usual.
4- Treatment of **complications** : if any.

Malaria

AE : Protozoa; Plasmodium *vivax* and *Pl. oval* for benign tertian malaria, *Pl. falciparum* for malign. malaria and *Pl. malariae* for quartan malaria.

Mode of infection :

by the bite of an infected female anopheles mosquito.

Route of organism after inoculation and pathology :

The sporozoites of the plasmodium are present in the salivary glands of the infected mosquitoes. When they are injected during the bite they disappear from the peripheral blood after a short time to the liver cells, spleen and bone marrow where they multiply.

After 7 – 10 days the liver cells rupture and liberate merozoites which enter the blood and infect the RBCs (this is called exo-erythrocytic phase).

In the erythrocytic phase i.e. inside the RBCs they form a signet ring → trophozoite → schizont → many merozoites. This is called schizogony.

The RBCs rupture and liberate their merozoites which infect new RBCs and the cycle is repeated. The period required for schizogony determines the frequency of the clinical attacks. It is 48 hours for benign tertian and malign. malaria and 72 hours for quartan malaria. But more than one set may mature at the same time and the clinical attacks may be irregular.

After sometime (about 7 – 10 days) gametocytes are formed (micro- and macro-gametocytes). When a mosquito becomes infected by such a blood, the micro- and macro-gametocytes unite to form a zygote then an ookinete (motile) is formed which penetrate the stomach wall and under its outer layer it develops into an oocyst which liberates many sporozoites. The sporozoites reach the salivary glands and remain there ready to infect other persons during biting. This part of the cycle in the mosquito is called "sexual phase" while in the body it is called "asexual phase".

I.P. : (1 – 2 weeks).

C/P :

Clinical picture of benign tertian malaria : the attack consists of :
Cold stage : with sudden onset of rigors and sense of being cold with rapid rise of the temp. up to 39 - 40°C.
Hot stage : after 0.5 – 1 hour, the sensation of cold disappears and there is severe headache and sense of hotness. Profuse sweat follows after 2 – 3 hours with fall of the temp., the "**Sweating stage**". The spleen may be enlarged, soft and tender and also the liver. The attack at first may occur daily but soon it repeats itself every 48 hours.

There are anorexia, nausea and vomiting. Inbetween the attacks there are prostration, muscular pains and headache and herpes febrilis may occur.

* In quartan malaria : the attack repeats itself every 72 hours.
* In falciparum malaria : here the involvement of the RBCs is more marked; both the mature and immature RBCs (reticulocytes) are attacked. It is more severe and dangerous as it may interfere with the vascular supply of the different organs e.g.: the brain. In the usual type

it is similar to benign tertian malaria, but the attacks are more irregular. The fever may be even continuous. Rigors are not marked, sweating is minimal and the hot stage is more prolonged. Prostration is more marked.

Pernicious forms of falciparum malaria :

1- Cerebral malaria : interference with vascular supply of the brain with gradually increasing headache, drowsiness and maybe coma. Convulsions, psychic disturbances and hyperpyrexia may occur.
2- Algid malaria : there is interference with the vascular supply of the GIT e.g.: persistent vomiting (gastric), diarrhea (choleraic form) or dysentery (dysenteric form). Shock and subnormal temp. may be present.
3- Repeated attacks of epigastric pain + persistent vomiting (of bile) + jaundice with high fever is called bilious remittent fever.
4- Black water fever : an autohaemolysin results in marked intravascular haemolysis with shivering, loin pains, vomiting and haemoglobinuria. Haemolytic jaundice may appear and anurea may result. The spleen decreases in size (due to contraction). It may be precipitated by quinine therapy.

Diagnosis :

1. Blood picture : leucocytosis is present during the attacks. Leucopenia with relative monocytosis in-between.
   Anemia [normocytic normochromic (hemolytic)] develop after repeated attacks. The parasite may be seen inside the RBCs in an ordinary film or a thick drop at the beginning of the attack. If not seen it may be examined after provocation by
   0.5 – 1 mL inj. of Adrenalin subcutaneous (spleen contracts).
2. therapeutic tests : e.g.: by resochin.

Treatment :

1- **General measure :** (as for any fever).

2- **Specific treatment :** consists of :
   a. Control of the clinical attack :
      The best is chloroquine phosphate (4 amino-quinoline) or resochin : it is a schizonticidal, so can control the acute attack of the parasites. It also result in a radical cure of falciparum malaria (because the exo-erythrocytic forms e.g.: in the liver doesn't release other parasites and relapses don't occur). In *vivax* and *malariae* malaria the exo-erythrotic forms remain up to 2 – 3 years with relapses.

Given as 10 tablets course as follows; 4 tablets initially , 2 tablets 6 hours later and 2 tablets daily for 2 successive days (or 1 x 2 x 5). Each tablet contains 150 mg active base. For cerebral and other forms of pernicious malaria, chloroquine HCl 40 mg injection can be given IM or even IV. Some cases of malaria resistant to chloroquine are sometimes encountered "chloroquine resistant malaria".

- Camoquine (another 4-amino-quinoline) : can be given as a single dose of 3 – 5 tabs each contain 200 mg. it is not effective in falciparum malaria.
- Quinine is rarely used now. May still have a place in the treatment of chloroquine resistant malaria.

b. For radical cure of *vivax* malaria :

we need a drug to control the acute attack as above + another drug to kill the exo-erythrocytic forms (merozoites ± sporozoites). These are the 8-aminoquinolines; primaquine and pamaquine, given as tablets 7.5 mg twice daily for 14 days.

c. Other anti-malarial drugs as :

- Pyrimethamine (daraprim): schizonticidal, 25 mg once a week, can be used by adults living in a malarial area as a suppressive treatment to guard against clinical attacks.
- Gametocidal : a drug acting on the gametes to prevent transmission of the disease by the mosquitoes e.g.: atebrin.

N.B.:

A true causal prophylactic is a drug which will kill the sporozoites and prevent them from establishing an infection. They are to be given in malarious areas to prevent the infection. No drug is known to produce this effect. Only biguanides (as paludrine) are known to kill the pre-erythrocytic forms (merozoites) and can be used as causal prophylactic in falciparum infection. Also a schizonticidal e.g.: resochin (2 tabs) or pyrimethamine (1 tab.) per week can be used to suppress any attack to those living in malarial areas "suppressive treatment".

3- **Symptomatic treatment** : as usual.

4- Treatment of **complications** :

Corticosteroids may be given in cerebral malaria and in black water fever. Measures for the diarrhea, dysentery, severe haemolysis, acute renal failure or liver failure are taken if they occur.

Chronic malaria :

with repeated attacks of malaria, anemia and huge splenomegally with result. This, along with the chronic ill health present and the irregular bouts of fever may lead to erroneous diagnosis e.g.: of lymphomas. Differentiation is made by blood film after provocation, blood picture and may be even sternal puncture. In *Pl. malariae* infection a nephrotic syndrome may occur due to an immunological reaction involving the glomeruli of the kidneys.