TROPICAL AND TRAVEL MEDICINE IN GENERAL PRACTICE.

ALAN. S. MELTZER.

Physician, Health Unit, Carleton University, Ottawa.

FIRST EDITION
1976.
ACKNOWLEDGEMENTS

I would like to acknowledge the help and encouragement that Dr. J. Casselman and the Staff of the Health Unit, Carleton University, have always given. Dr. R. Dupuis and the Staff of the Tropical Disease Clinic, National Defence Medical Centre, Ottawa, have always been more than willing to offer advice on all aspects of parasitic disease. The section on Antimalarials is reproduced from the author's article in Modern Medicine of Canada (March 1975) by kind permission of the Editor. The typing was very kindly done by Mrs. P. Davey.

The Tropical Medicine and International Health Division of the Canadian Public Health Association has done much to encourage the pursuit of tropical disease in Canada and is always more than willing to offer expert advice on all aspects of the problem. The Table of International Immunization requirements is reproduced from the Immunization Supplement (January 1976) published by Health and Welfare Canada.

Alan S. Meltzer,
Health Unit,
Carleton University,
Ottawa, Ontario
CHAPTER 1. PREPARING FOR THE TROPICS.
CHAPTER 2. RETURN OF THE TRAVELLER.
CHAPTER 3. MALARIA.
CHAPTER 4. DIARRHEA ?? AMEBIC INFECTION.
CHAPTER 5. P.U.O. / EOSINOPHILIA/OVERLANDER SYNDROME.
CHAPTER 6. WOBBLY WORMS.
CHAPTER 7. NOTES ON SOME TROPICAL DISEASES.
CHAPTER 8. CHEMOTHERAPY OF PARASITIC INFECTIONS.
CHAPTER 9. CLINICAL CONSIDERATIONS.
INTRODUCTION

Most physicians are now seeing patients who have travelled in many parts of the world, and although the essentials of medical practice are the same in different global zones, some aspects of travel and tropical medicine are worthy of further consideration. This brief volume is not intended to be a complete guide to travel or tropical maladies, but rather to serve as an introduction to the subject, particularly as it concerns the general practitioner, and it is hoped that further reading on the subject will be encouraged.

The concept of "Exotic" diseases is an important one and Maegraith defines these as being acquired outside the area in which the physician works. These notes are mainly confined to subjects who usually live outside the tropical zones, but who visit such areas in the course of their work or pleasure. It is pertinent to ask how common are imported tropical and parasitic diseases, but for most countries we have no exact figures. Reported cases of such diseases as amebic dysentery suggest that this malady is not a significant problem in such a country as Canada, but it would appear that many cases are not being diagnosed. The cases which are reported may well be the tip of the iceberg, particularly as some infections can remain asymptomatic, and the problem is more than an academic one as amebic infection may have a fatal outcome and amebic hepatic abscesses are often associated with much debility.

The spectrum of tropical and parasitic diseases is a broad one and only a few aspects of the problem are considered here. Thus a fair number of subjects consult their local family physician for advice on antimalarials and it is important for the physician to be aware of the different drugs used in the chemoprophylaxis of malaria. Again diarrhea ranks high on the list of symptoms which patients bring to their physician on returning from the tropics and an approach to the problem is presented. As this is not a textbook of tropical diseases, only a handful of such conditions are discussed and for further details it is essential that the practitioner turn to one of the excellent books covering this field. For in these days of stress, where psychosomatic disease reigns king, it is very satisfying to identify a parasite and then to be able to treat the patient, knowing that with modern chemotherapy we can be sure of a cure in many instances.
CHAPTER 1

PREPARING FOR VISITS TO THE TROPICS.

Personal Interview (?? Exclusions).
Propaganda (Food/drink etc.).
Prophylactic Immunizations.
Prophylaxis Against Malaria.

IS EVERYONE FIT TO TRAVEL TO THE TROPICS ??

The answer to this question is an emphatic no, but at the same time every case must be assessed on its own merits, and any contraindications to life in the tropics are usually relative ones rather than absolute exclusions. The following examples are merely quoted to give some idea of the extent of the problem. The tropics pose various physical and mental stresses to all subjects and in some instances such an environment may be a real threat to the well-being of the individual. Thus the executive who is promised a plum post overseas may find that the increased mental and physical strains to which he is subjected, become an overbearing problem to him. One factor to always take into account is the duration of the visit, and neurasthenic states are not uncommon in the long stay visitor. The elderly should be warned to take life slowly in such areas, but in general tolerate the warmer climates fairly well. Subjects with a history of a significant mental disorder would be best advised to keep away from tropical zones and in particular this applies to those with depression. Alcoholics often deteriorate rapidly where the normal social life in warmer regions encourages an excessive intake of alcohol. Life in the tropics tends to encourage the formation of renal calculi and if those with such a history must go, they should certainly watch their intake of fluids with care. Obviously life in the larger towns and cities carries less risk than a rural existence for those with "unstable" diseases, and thus the diabetic should not wander too far off the beaten track. Hepatitis is prevalent in these areas and those with a history of previous hepatitis should travel warily before exposing themselves again, and if it is imperative that they go then the use of gamma globulin is strongly recommended (as it is for all visitors to these areas). Although the effect of sunlight is beneficial for some skin disorders, other dermatological conditions do not fare so well with this exposure, and fungal infections of the skin, for example, may flare up in hot humid climates. These same climatic factors also tend to upset some asthmatics, though a dry warm surrounding may ameliorate the condition of others with this illness. Subjects with certain gastrointestinal disorders should
avoid the tropics if they can e.g. in ulcerative colitis repeated attacks of tropical diarrhea may lead to the disease becoming more severe. Uncontrolled hypertension can also be associated with problems in the tropics.

In general the following conditions should be taken as relative contraindications to travel in the tropics.

1. Old age.
2. Mental disease. (especially depression).
3. Alcoholism.
4. Renal calculi.
5. "Unstable" diseases e.g. diabetes.
6. Hepatitis.
7. Severe skin disorders (particularly fungal).
8. G-I disorders e.g. ulcerative colitis.
9. Hypertension (unstable).
10. Travellers with a history of significant tropical illness e.g. those who have had severe amebic infections of the liver.

PERSONAL INTERVIEW.

The physician should aim to see all those intending to visit the tropics, for this initial interview represents an excellent opportunity for the physician to practice some preventive medicine and to inform the traveller of simple measures which may help him to avoid some disabling parasitic disease and an example of this may be seen in the case of malaria. For clinical experience soon reveals that many travellers, if not the majority, do not take their antimalarials correctly, usually stopping too early, and if we can persuade them to take these chemoprophylactics as directed, then this alone is well worth while. This initial consultation can also be used to drive home the importance of commonsense precautions relating to food and water. All must be warned that sufficient time must be set aside to allow for acclimatization. Again the hazards of acute sunburn should be stressed. As has been mentioned some diseases constitute a contraindication to travel in the tropics, but if the visitor to the tropics must make his journey, then certain organizations can be of great use. Thus "IAMAT" (International Association For Medical Assistance To Travellers-Empire State Bldg. 350 Fifth Ave., Suite 5620 New York, N.Y. 10001) issues useful literature for the traveller to the tropics. Those on long term medication should carry adequate supplies of any medication which they may need.
PARADISE - THE THREE "P"S.

PROPAGANDA - (FOOD/DRINK/CLOTHING).
PROPHYLACTIC - IMMUNIZATIONS.
PROPHYLAXIS - AGAINST MALARIA.

DO BE CAREFUL WITH FOOD & DRINK.
DO TAKE ANTIMALARIALS.
DO ACCLIMATIZE PROPERLY.
DO WEAR SENSIBLE CLOTHING.

DO NOT SWIM IN RIVERS/LAKES.
DO NOT WALK BAREFOOT.
DO NOT OVEREXPOSE (SUN/HEAT).

"YOU ARE WHAT YOU EAT"
In general the main facets of the problem are covered by the following points.

1. **ACCLIMATIZATION.** On arriving in the tropics, all should allow several days to adapt to the local conditions. This will allow recovery from the "time" barrier. Initial exposure to the sun should be short and increased gradually over the next few days. In high altitude areas several days should be allowed for acclimatization. Hot climates demand sensible clothing and cotton materials are preferable to synthetic ones. Changes in diet also take their toll and most travellers have episodes of travellers diarrhea.

2. **FOOD.** Milk and dairy products are best avoided and vegetable, meat or fish dishes must be well cooked. Salads are dubious, unless the visitor prepares them himself (care water). Where fruit is concerned, it is advisable to stick to items which can be peeled by the traveller. If milk is to be taken it must be boiled before use.

3. **WATER & DRINK.** Care must be taken with water supplies, and where these are of poor quality, tablets such as Halazone can be used to render the water safe for drinking. Filtration methods are not usually satisfactory. In general all water should be boiled before use. Bottled beer is usually safe, but the label "bottled" water means little. Ice-cubes must not be made with unsafe water, and it must be remembered that if the local water is unsafe for drinking, then it is not suitable for dental use. Fluid input should be generous in the tropics, but extra salt is only needed if hard physical work is being undertaken.

4. **SWIMMING.** In some tropical zones e.g. parts of Africa and the Middle-east, it is best not to swim in fresh water as there is a risk of contracting schistosomiasis.

5. **BAREFOOT WALKING.** In most tropical regions it is not a good idea to walk barefoot on the ground as some parasitic infections e.g. hookworm can be acquired in the way.

6. **ANTIMALARIALS.** (also see notes on malaria). The initial interview represents a supreme opportunity for the physician to drive home the importance of taking antimalarials correctly, for after a spell in a hot climate many subjects take the medication incorrectly or not at all.

7. **DIARRHEA.** After venturing into the tropics most people experience diarrhea.
and although this is often brushed off as being innocuous, all travellers should seek medical aid if the diarrhea persists, or is accompanied by a high fever or by the passage of blood (in particular it is important to rule out amebic infections).

8. A MEDICAL ARMENTARIUM FOR ALL ?? Many subjects consult with their physician because they wish to travel with medication for each and every illness. All cases must be assessed on their own merits, and the following items represent a basic list, additional items being added as necessary.

A. ANTIDIARRHEAL PREPARATION. Diphenoxylate-atropine preparations are useful in controlling diarrhea, or alternatively kaolin mixtures can be taken. Some preparations e.g. iodochlorhydroxyquin, are best avoided for they have little efficacy and may mask amebic infections, and significant adverse reactions are sometimes associated with their use.

B. ANTIFUNGAL PREPARATIONS. Fungal infections of the skin are by no means rare in the tropics and a good antifungal cream should be taken on the trip. (e.g. tolnaftate).

C. ANTIHISTAMINES. Systemic antihistamines are preferable to local preparations as far as allergic reactions to insect bites etc. are concerned.

D. WATER DECONTAMINANT PREPARATIONS. Where water supplies are unsafe water decontaminant tablets (e.g. Halazole) are useful.

E. ANTIBIOTICS ?? The place of these compounds in the travellers medical kit is a vexed one, but where the individual can be trusted to use a modicum of commonsense, there is no valid reason why the subject cannot be informed as to the correct indications for these drugs, particularly when the itinary takes in isolated areas.

F. OTHERS. Depending on the type of travel involved other items may be indicated e.g. analgesics.

IMMUNIZATIONS
Though the health risks of travel in the tropics are appreciated by some, many visitors to these areas travel in woeful ignorance, for travel agencies and airlines paint the tropics in glowing romantic colors and do little or nothing to warn their patrons of the potential hazards. Often the traveller is led to believe
that if he has all the prophylactic immunizations, then no parasitic infection will trouble him. With reference to the various immunizations, the requirements for these vary from time to time and it is not possible to draw up comprehensive lists for each and every region. Subjects must realise that they have to allow plenty of time in which to receive the various procedures. All visitors to the tropics should be immunized against smallpox, poliomyelitis, typhoid, tetanus and cholera, but some areas warrant other preparations also (e.g. typhus). The doses given below are only examples and different preparations may need different doses.

1. SMALLPOX.
Both primary vaccination and revaccination, are valid for 3 years, the primary procedure being valid 8 days after vaccination and the revaccination being valid at once. Contraindications to vaccination include:
A. Eczema.
B. Acute illness.
C. The administration of another live virus vaccine during two weeks before or after the vaccination.
D. Gamma-globulin abnormalities and blood dyscrasias.
E. Women in the first trimester of pregnancy.
F. Corticosteroid therapy or immunosuppressive therapy.

2. YELLOW FEVER VACCINATION.
This is valid 10 days after the primary vaccination and remains valid for 10 years, the revaccination being valid at once. The vaccine should not be given to children below the age of 9 months. The vaccine is needed for such areas as tropical Africa, South and Central America. If smallpox vaccination is first performed there should be an interval of at least 21 days before yellow fever vaccine is administered. If yellow fever vaccination is carried out first, at least 14 days should elapse before smallpox vaccine is given. (This period can be shortened if necessary, but should be at least 4 days).

3. CHOLERA.
Whereas smallpox and yellow fever vaccines offer good protection against the respective diseases, cholera prophylaxis is not so efficient. The vaccination is valid for 6 months, beginning 6 days after the primary procedure, and where revaccination is concerned it is valid from the date given and again lasts 6 months. Reinforcing doses are given every 6 months.
The vaccine is given subcutaneously.

**ADULTS.**
First dose of 0.5 ml. followed by 1.0 ml. 3-4 weeks later. A third dose of 1.0 ml. is desirable (3-4 weeks after the second dose).
Children under 5 years of age; first dose 0.1 ml. Then second and booster doses are of 0.3 ml.
Children 5-10 years; first dose of 0.3 ml. Then second and booster doses of 0.5 ml.
Children over 10 years should receive the adult dose.

The disease can appear in most parts of the world, as the recent outbreaks have shown, and the vaccine is recommended for all visitors to the tropics.

4. **POLIOMYELITIS.**
This infection is prevalent in many tropical areas, and all visitors to these zones should have appropriate protection.

5. **PARATYPHOID-TYPHOID.**
Although this vaccine offers some protection against the above enteric infections, these diseases still pose a risk to the subject, particularly when there is exposure to constant infection. Different strength vaccines are available, but typical doses are; (given subcutaneously)

**ADULTS.**
Initial course- First dose-0.25ml.  
Second dose - 0.5 ml; given 3-4 weeks after the first dose.
Third dose - 1.0 ml; given 3-6 months after the second dose.
When time is at a premium the intervals can be decreased to 10-14 days.
Children under the age of 10 years are given half of the adult dose.
Reinforcing doses of 0.5 ml. are given at least every 3 years. Where special risk factors are involved, booster doses can be given every 1-2 years. Smaller doses of the vaccine can be given by the intradermal route.

6. **TETANUS.**
Visitors to the tropics should have adequate protection against tetanus. However it should be noted that although the administration of any biological preparation carries the potential risk of a severe allergic reaction, special care should be
taken with tetanus toxoid products as severe local and systemic reactions are not uncommon in those who have had repeated tetanus toxoid injections.

7. **TYPHUS VACCINE.**
This is not generally recommended for all travellers to the tropics, but rather for those at special risk (e.g. in Vietnam or Laos). It is used to prevent typhus of the endemic type.

**ADULT DOSE** - given subcutaneously. Initial course of 2 doses of 1.0 ml. at intervals of 10 days. Reinforcing doses of 1.0 ml. annually are given at the commencement of the typhus season.

**Precautions;** the vaccine should not be given to those with a history of hypersensitivity to egg protein.

8. **PLAGUE VACCINE.**
Most travellers to the tropics do not require this vaccine. Even when it is used only partial protection against the disease is offered and local and general reactions may be severe.

9. **GAMMA GLOBULIN.**
Infectious hepatitis is common in many tropical regions, and it would appear that human immune serum globulin can offer some protection against the disease for about 6 months. After that length of time it is likely that the individual has some active immunity. Repeated use of gamma globulin can sensitize the subject to the protein components of the injection. Gamma globulin should be given fairly near the departure date and at least some 12-14 days after the last of any other vaccination or immunization.

Adults can be given 5.0 ml. I.M.

**IMMUNIZATION SCHEDULE.**
Several routines have been recommended, but the following will serve as a guide and are based on the guidelines of Cannon.

A. This is used where the subject has plenty of time available before his journey. Cholera vaccine can be given at the end of the course.

Week 1. Yellow Fever vaccine.
Week 4. Smallpox vaccination.
Week 7. Tab(I). Tetanus (I)
Week 10. Polio vaccine.
Week 13. Tab (2). Tetanus (2)
Week 16. Polio vaccine.
Week 22. Polio vaccine.
Week 39. Tab (3). Tetanus (3).
B. This routine is for those who have less time available,
Day 1. Yellow fever/Cholera (1)/Polio (1).
Day 5. Smallpox/Tab/Tetanus (1).
Day 11. Cholera (2).
Day 28. Polio (2)/Tab/Tetanus (2).
Any further doses are given later as required.

REINFORCING DOSES.
Smallpox vaccine - every 3 years.
Yellow Fever vaccine - every 10 years.
Cholera vaccine - every 6 months
Polio vaccine - every 3-5 years.
T.A.B. - every 3 years (every 1-2 years where special risks involved).
Typhus vaccine - annually (at beginning to the typhus season).
N. B. WHERE ANTIMALARIALS ARE INDICATED THE PHYSICIAN SHOULD STRESS THE IMPORTANCE OF TAKING THESE CORRECTLY AND OF CONTINUING TO TAKE THEM AS DIRECTED AFTER LEAVING THE TROPICS (please see notes on malaria).
Although Ethiopia appears to be the only country where there is a continuing transmission of smallpox, some countries still require vaccination for entry. All travellers should verify the situation for each country to be visited.
"SOUVENIRS FROM THE TROPICS"

EDEMA - FILARIASIS/TRYPANOSOMIASIS/TRICHINOSIS.
NODULES - ONCHOCERCIASIS/LEPROSY/LEISHMANIASIS.
"SPOTS" - TYPHOID/TYPHUS/S<small>MA</small>LLEPOX.
ULCERS - LEISHMANIASIS/LEPROSY.

EYES - TOXOCARA/FILARIASIS/TRACHOMA/LEPROSY.
R.<small>S.</small> - "ASTHMA" (=WORMS)/TUBERCULOSIS.
LIVER - HEPATITIS/AMEBIC ABSCESS/LIVER FLUKE/SCHISTOSOMIASIS/
LEISHMANIASIS.
LYMPHADENOPATHY - TUBERCULOSIS/LYMPHOGRANULOMA/TRYPANOSOMIASIS/
LEISHMANIASIS.
"SPLENOMEGALY - ALWAYS RULE OUT MALARIA.
C.N.S. - TRYPANOSOMIASIS/LEPROSY.
C.V.S. - S. AMERICAN TRYPANOSOMIASIS.
V.D.
CHAPTER 2.

THE RETURN OF THE TRAVELLER.

A. TAKING THE HISTORY.

UNDE VENIS ?? ("WHERE HAVE YOU BEEN?")

DID YOU HAVE A FEVER?

DID YOU TAKE ANTIMALARIALS?

DID YOU HAVE SEVERE DIARRHEA?

DID YOU WALK BAREFOOT OUTDOORS?

DID YOU SWIM IN FRESH WATER?

ETC.

Most subjects who return from the tropics feel well on their homecoming, but it is still advisable that they consult with a physician on their return. Some parasitic diseases may remain dormant for many years and are only detected when routine screening tests are instituted. Thus it is essential to take a good history, perform a physical examination and carry out basic screening tests on all those who have been to the tropics, whether they have symptoms or not. Certain points in the case-taking are worthy of emphasis.

A full geographical history is a necessary pre-requisite for the diagnosis of any tropical disease and Maegraith's master words "Unde Venis" (where have you been?) must now be directed at all who return from the tropics, and the countries visited and the duration of each visit should be noted, for often the itinerary will suggest the probable diagnosis. Thus for example a prolonged stay in West Africa would bring the possibility of such infections, amongst others as malaria, amebic dysentery or filariasis to mind. Many who have had a fever are usually vague about the exact details but as far as endemic zones for malaria are concerned, any traveller who returns from such an area with history of unexplained fever SHOULD BE ASSUMED TO HAVE MALARIA UNTIL PROVED OTHERWISE. All subjects should be questioned as to whether antimalarials were taken, and if so were they taken as directed. The fact that the subject states that these drugs were taken does not rule out the possibility of the malaria parasite being present (see notes on malaria).

Visitors are often unaware of the fact that only one bite from the relevant infected mosquito is needed to contract the disease, and even a short stay at an airport in a malarious zone might raise the possibility of this disease being present. Thus exact details of the itinerary must be obtained, and in particular the physician has to be aware of all stopover visits. Again the examiner should keep in
mind the fact that although many global regions are now said to be free from malaria, the disease does not follow any clear-cut geographical boundaries.

Diarrhea remains a common complaint for many who return from the tropics. Amebic infections, asymptomatic or otherwise, are by no means rare and because this infection can be associated with much disability if untreated, the physician should always keep the disease in mind whenever there is a history of diarrhea. Details of any self-medication are useful since tetracyclines and iodochohydroxyquin may mask the presence of an amebic infection.

In locations where the hookworm thrives a history of walking barefoot outdoors would incline one to suspect the presence of this parasite. Urinary tract symptoms should alert the examiner to the possibility of schistosomiasis, especially when the visitor admits to a history of swimming in fresh water in such areas as tropical Africa. A history of hematuria obviously demands a full investigation, but it is worth noting that renal calculi are not uncommon in the person who makes his stay in the tropics a lengthy one. A history of respiratory symptoms may be associated with some helminthic infections, and thus ascarsis can produce an asthma-like episode, particularly in the early stages of the infection.

Medical histories for all the members of the family must be obtained and no temporal limits should be placed on the history as some parasitic conditions can make their presence felt many years after the initial exposure (e.g., amebic infections).

THE RETURN OF THE TRAVELLER - THE PHYSICAL EXAMINATION.

A full physical examination should be carried out on all who return from the tropics. Sometimes the elicitation of a specific physical sign will suggest a possible diagnosis. It is not proposed to cover all the possibilities here, and only a few examples are mentioned. Localized edema may be observed in filariasis, trypanosomiasis, trichinosis and some intestinal helminthic infections. In South American trypanosomiasis the characteristic unilateral facial edema which is sometimes seen is known as Romana's sign. Calabar swellings are painful edematous areas, often near joints, and are seen in infections caused by the filarial worm, Loa loa (seen in tropical Africa). The well defined zones of edema observed in association with parasitic disease are often fleeting in nature. Skin nodules are associated with onchocerciasis, leprosy and leishmaniasis. The manifestations of leprosy are protean and include macules, ulcers and anesthetic hypopigmented areas of skin, in addition to the wide range of other clinical presentations. Fungal lesions of the skin are not uncommon in this group of travellers.
"Creeping" cutaneous eruptions can indicate the presence of such parasites as strongyloides or hookworm. Skin ulcers are not commonly observed in this group of subjects, and such entities as tropical ulcer are commoner in the indigene rather than in the visitor to the tropics. Cutaneous leishmaniasis may scar the skin. Erythematous and other rashes may be associated with a wide range of parasitic infections including filariasis and schistosomiasis.

Tuberculosis is prevalent in many tropical areas and must always be kept in mind when discussing the differential diagnosis of respiratory illness in this group of subjects. Respiratory signs suggestive of asthma raise the possibility of such parasites as ascaris, visceral larva migrans or schistosomiasis being present, particularly where there is an associated eosinophilia. Bouts of coughing are sometimes seen in the Katayama syndrome (fever/urticaria/eosinophilia) due to schistosomiasis. Paragonimiasis may also produce severe coughing and hemoptysis. Amebic pulmonary abscess may cause significant pulmonary changes. Although localized lymph node enlargement is a fairly non-specific finding it may herald tuberculosis, filariasis, trypanosomiasis or leishmaniasis. Enlargement of the liver or spleen brings a host of potential causes to mind, and all the usual "Commoner" causes must be eliminated. Clinical jaundice would bring to mind such tropical entities as falciparum malaria, hepatitis, liver flukes (clonorchis) and visceral leishmaniasis. Hepatomegaly can be observed in many tropical conditions including:

1. Malaria.
2. Amebic infections.
3. Visceral larva migrans.
4. Hepatitis.
5. Visceral leishmaniasis.
7. Liver fluke infections.

Again the causes of splenomegaly are legion, but malaria must always be on the top of the list of suspected culprits. Parasites can invade most of the body tissues. Thus the eye may be involved in leprosy, trachoma, onchocerciasis and loiasis. Various worms and their eggs may involve the C.N.S. and if coma is present then trypanosomiasis, cerebral malaria or hepatic coma in later schistosomiasis should be considered as far as "exotic" diseases are concerned.

RETURN OF THE TRAVELLER - LABORATORY INVESTIGATIONS.

As has been mentioned it is highly desirable that all visitors to the tropics have basic screening tests for parasitic disease on their return. The temple of truth for most tropical diseases remains the laboratory, and the high priest is to be found in the person of the experienced laboratory technician, for
however careful we are in our history taking and physical examination, we are dependent on efficient laboratory techniques for the detection of most parasites. The history and physical findings dictate the extent of any investigations, but in general the following basic tests should be considered:

1. Examination of fresh stool samples. (minimum of three).
2. Examination of the blood.
3. Urinalysis.
4. Biochemical tests as indicated.
6. Other tests (e.g. skin testing & tests for V.D. etc).

A thorough examination of the stools ranks high on the list of priorities and a minimum of three fresh stool samples must be obtained. Ideally the samples should be produced at the laboratory itself, but if this is not feasible then the samples must reach the laboratory within one hour after being passed. Preserved stool specimens which are mailed to the laboratory are very much a second best and should not be relied upon to exclude such infections as amebic dysentery. Often patients do not take kindly to the prospect of producing several stool samples, but they must be informed that a single negative report does not rule out parasitic disease. Parasites identified by examination of the stools include:

1. Entameba histolytica.
2. Hookworm.
3. Ascaris.
4. Schistosomiasis.
5. Trichuris trichuria.
7. Clonorchis.
8. Tapeworm.

Sometimes the identified organisms are non-pathogenic e.g. Entameba coli, iodoameba butschlii and endolimax nana. In cases of persistent diarrhea bacterial culture and sensitivity studies are also indicated, particularly to rule out salmonella and shigella infections.

Blood studies vie with examinations of the stools in importance as far as diagnosis is concerned, and in some instances a solitary abnormal finding, such as a persistent eosinophilia, may be the only finding to show the presence of a parasite. The field of tropical anemias is a subject in itself, but when reviewing
the etiology of anemia in a subject who has returned from the tropics, the physician would do well to keep malaria, hookworm and schistosomiasis in mind. Also where applicable the various hemoglobinopathies would need to be considered as well. Occasionally antimalarials can produce anemia e.g. pyrimethamine and primaquine. Although the raison d'être of doing a blood film in those returning from the tropics is the detection of malaria, such a technique is useful in screening for trypanosomiasis and the microfilariae of filariasis. Day films should be done and where the traveller has taken in such an area as the Pacific Islands, late night films (the blood being taken between the hours of 10 p.m. and 2 a.m.) are required to identify microfilariae. Sometimes blood culture methods are useful e.g. for the diagnosis of typhoid or brucellosis.

Serological tests have a place also e.g. latex reactions for extra-intestinal amebic infections, complement fixation tests for trichinella spiralis or schistosomiasis. A leucocytosis is too non-specific to be of much use but the presence of a leucopenia is a little more helpful and may be associated with kala-azar, typhoid or brucellosis. An eosinophilia is always a significant finding and parasites producing such a change include filariasis, schistosomiasis, ascariasis, hookworm, larva migrans, trichinosis and tropical eosinophilia. Biochemical investigations remain non-specific but liver function abnormalities often reflect the relatively common viral hepatitis of the tropics.

Examination of the urine is used to detect the eggs of schistosoma hematobium. Examination of the sputum may occasionally reveal the trophozoites of E.histolytica, the eggs of paragonimus or the larvae of ascaris. The possibility of TB. must always be kept in mind.

Intradermal tests can be utilized to demonstrate some infections e.g. schistosomiasis. A chest x-ray and suitable blood test for V.D. should always be part of the routine check-up.

X-ray examination can be useful in the diagnosis of imported diseases. Thus screening of movement of the diaphragm may assist in the detection of an amebic hepatic abscess, though a liver scan would be needed to confirm the diagnosis. Intestinal amebic infections can produce evidence of intestinal ulceration, a conical cecum, and spasm of the ascending colon. Sometimes amebomas are mistaken for neoplasms. Giardiasis can be associated with irregularities of the second portion of the duodenum. Rim calcification in the bladder wall and lower ureters is a sign in schistosomiasis (S. hematobium). Schistosomiasis (S. mansoni) sometimes causes changes similar to Crohn's disease. Although rare in the visitor, Chaga's disease (South American trypanosomiasis) may be associated with ventricular aneurysms, paralysis of the esophagus and a
dilated colon and x-rays are useful in confirming the diagnosis. X-ray of the chest, in subjects with tropical eosinophilia, may reveal a diffuse mottling. Calcified cysts of Cysticercosis or encysted larvae of trichinosis may show on chest x-rays.
EXCLUDE??

1. MENTAL DISEASE (DEPRESSION).
2. ALCOHOLICS.
3. RENAL CALCULI.
4. UNSTABLE DISEASES (DIABETES).
5. HEPATIC DYSFUNCTION (HEPATITIS).
6. SKIN DISEASE (FUNGAL).
7. SEVERE ALLERGIES.
8. ULCERATIVE COLITIS etc.

HISTORY.

1. EXAMINATION.
2. STOOLS (FRESH! x3).
3. BLOOD (FILM)
5. URINE.
6. V.D.R.L.
7. X-RAY CHEST.
CHAPTER 3

MALARIA.

This disease is worthy of consideration by most physicians, not only because it is a fascinating entity, but because it is also of great significance as far as world travel is concerned. It is a vast subject in itself, and only a few aspects of the problem as they relate to the field of general medicine are reviewed here. Although the majority of people exposed to this infection (estimated at over 350 million subjects) are obviously indigenes of tropical zones, it is clear that more and more citizens from temperate climates are penetrating malarious regions. The usual form of transmission of the parasite is by the female anopheline mosquito, and the parasite, a protozoon of the genus Plasmodium, is present in many tropical areas. Infection may be associated with one or more species of the parasite, but the main clinical forms of the disease can be classified:

A. Malignant malaria (caused by P.falciparum).
B. The vivax group (caused by P.vivax, P.ovale or P.malariae).

It is worth noting that the parasite can be transmitted by blood transfusions or by use of contaminated syringes.

As P.falciparum represents the main hazard to human health, this is the parasite which is mainly considered here, but it should be remembered that mixed infections may occur. As untreated malaria may have a fatal outcome, it should be a golden rule for all physicians to assume;

THAT IF A SUBJECT GIVES A HISTORY OF PYREXIA AFTER RETURNING FROM A MALARIOUS AREA, THEN MALARIA SHOULD BE DEEMED TO BE PRESENT UNTIL PROVED OTHERWISE.

The following aspects of the disease are now considered,

1. CHEMOPROPHYLAXIS.
2. CLINICAL FEATURES AND DIAGNOSIS.
3. TREATMENT OF MALARIA.
1. CHEMOPROPHYLAXIS

Clinical experience soon shows that many visitors to the tropics take antimalarials incorrectly and the physician is in a good position to advise on this point when the traveller first presents himself for the various immunizations required for visits to the tropics, for travel agents and airlines do little to warn of the risk of malaria. The following notes mainly relate to the non-immune subject i.e. one who usually resides outside an endemic malaria zone, but it is worth noting that when the indigene from a malarious area spends a significant time in the Western world he may forfeit part of his protection against the malaria parasite and when he eventually returns home he may well need to be regarded as a non-immune who merits chemoprophylaxis.

Which travellers should be provided with these drugs? In some instances there is little doubt that protection against the disease is indicated e.g. where the itinerary takes in West Africa, but some zones are not so obviously associated with the parasite and the WHO publication "Information on malaria risk for international travellers"(reprinted from the WHO Weekly Epidemiological Record No. 3, 1973 pp. 25-45) provides useful information on this point. The visitor to the tropics must be carefully questioned as to the exact details of his proposed journey and should be warned that only one bite from the relevant mosquito is needed to contract the disease, and thus even a short stay at an airport in a malarious region would warrant the use of a antimalarial. The parasite still reigns supreme in such areas as tropical Africa, most of South-East Asia, much of South America, some of Central America, parts of the Middle East and certain South Pacific regions.

When considering the choice of preparation one obvious prime factor to take into account is the possibility that the parasite may be resistant to a particular drug. Thus P.falciparum is resistant to chloroquine in parts of South-East Asia and South America, but so far this problem does not extend to Africa. Where there is some doubt as to whether a drug resistant parasite is contained in a certain region, a good case can be made out for using a combination of drugs. In some highly malarious zones e.g. parts of West Africa, efficient chemoprophylaxis may only be achieved when the drugs used are taken in doses which are larger than those usually recommended. The absent-minded individual may be better suited with a "once-a-day" rather than a "once-a-week" preparation. Chemoprophylaxis should be commenced prior to entering the malarious area and must be taken regularly throughout the stay. On leaving the endemic region the drugs are required for
at least a further four weeks, and preferably should be continued for a period of six to eight weeks. The administration of an antimalarial is no guarantee that the traveller is fully protected against the disease, and significant attacks of malaria may occur even when chemoprophylaxis is instituted because:

1. The parasite may have been resistant to the drug used (particularly with P.falciparum infections).
2. The drug may have been taken incorrectly, or severe diarrhea could lead to impaired absorption of the medication.
3. "Breakthrough" infection can occur.
4. In some forms of malaria (involving P.vivax, P.malariae or P.ovale), cessation of a suppressant drug may be followed by a relapse at a later date (see notes on primaquine).

All subjects should be warned about the potential adverse reactions of these drugs, but it would appear that in the usual antimalarial doses serious adverse effects are rare. However, the increasing use of combinations of agents and the administration of larger than the usual doses in some zones might change our ideas in this respect. As has been mentioned the ideal antimalarial is still only a concept, and the physician must convince the traveller that such entities as unexplained fever or malaise in a person who has visited an endemic area should be assumed to be due to malaria until proved otherwise. Even in present times cases of malaria are still being missed. Although fever remains the commonest present feature, the illness can present with the signs and symptoms of any acute infection, and in some instances the complications dominate e.g. acute hemolytic anemia, cerebral malaria, hyperpyrexia, algid malaria, renal failure, hepatic dysfunction or dysenteric states. In all cases a rapid diagnosis is mandatory and treatment must be instituted with alacrity.

With reference to malaria, the term chemoprophylaxis is really a misnomer, for at present we have no safe and efficient preparation capable of destroying the sporozoites i.e. the infective forms of the parasite, and in practice the drugs we employ are mainly used for their suppressant effect. Before discussing some of the more commonly used antimalarials it is useful to review a few of the terms involved.

Causal prophylactic drugs.
(Primary tissue schizontocides)

These act on the preerythrocytic stages of the parasite i.e. the infection
of the erythrocytes is prevented. Pyrimethamine and chloroguanide are good causal prophylactics against P. falciparum. Primaquine is also effective in this respect, but it is too toxic for routine use.

Suppressive drugs.
(Blood schizontocides)

These inhibit the asexual erythrocytic stages of the parasite i.e. the subject has no significant clinical symptoms. The exoerythrocytic stages of the parasite remain intact, and at a later date the subject may have attacks of malaria long after the drug has been discontinued (this does not apply to P. falciparum infections where efficient suppression eliminates the infection). In order to eradicate the exo-erythrocytic stages a drug such as primaquine must also be administered.

Radical curative drugs. (Secondary tissue schizontocides)

These compounds act on the secondary exo-erythrocytic stages of the parasite. Primaquine, an 8-aminoquinoline drug is used for this purpose, and is given to prevent relapses in infections due to P. vivax, P. malariae or P. ovale.

Gametocytocidal drugs.

These act on the sexual forms of the parasite, some destroying the gametocytes in human blood, whilst others prevent the development of the gametocytes in the mosquito. They have little clinical application.

It is worth noting that there is a basic difference between P. falciparum and the other parasites associated with human malaria, viz. in P. falciparum infections there is no obvious re-invasion of the liver cells, and because there is no secondary tissue stage, efficient suppression of the parasite results in a complete cure.

Some common antimalarials

1. Chloroquine.

This 4-aminoquinoline compound was first synthesized in 1934 and has been used in both the chemoprophylaxis and therapy of malaria. Because of its efficacy in the acute attack, and taking into account the problem of the drug resistant parasite, some are of the opinion that the drug should be reserved for treating the acute malarial episode. In view of its potential for serious toxic effects on the eye, chloroquine must always be administered with care. The drug has an effect on the asexual erythrocytic forms of the parasite. However it should be noted that it does not prevent relapses in subjects with P. vivax, P. malariae or P. ovale infections. When given as a suppressive for P. falciparum the drug results in a complete cure being obtained (providing the parasite is not resistant). It should not be given to those with retinal disease or visual field defects and is
contraindicated in those with a history of a hypersensitivity to the 4-aminoquinolines. In an effort to prevent, and overcome, the problem of the resistant parasite the compound has been given in combination with other antimalarials e.g. pyrimethamine, primaquine and dapsone. 

Dose (for suppressive effect) 

Adults (Chloroquine phosphate)

An oral dose of 300 mg of the base is given once a week (on the same day each week). The medication is commenced two weeks before entering the malarious zone and must be taken for at least four weeks after leaving the endemic area (preferably taken for six to eight weeks). In high risk areas 300 mg of the base should be taken twice a week.

Although it is well tolerated in the usual antimalarial doses, the compound is not without potential adverse effects. It may produce severe reactions in those with psoriasis or porphyria and should be given with care to those with hepatic dysfunction. In general the most serious adverse reactions have been reported in association with the long term administration of the preparation. Eye changes remain the most significant threat and include retinopathies, corneal deposits, macular lesions and optic atrophy. Now that antimalarials are sometimes employed in relatively high doses, it would seem prudent to advise all subjects who are likely to be on chloroquine for any length of time to have regular ophthalmic examinations, particularly as retinal changes may be asymptomatic. Eye changes can also occur after the drug has been discontinued. Other reported adverse reactions include headache, pruritus, gastro-intestinal upsets, psychotic episodes, convulsions, neuromyopathies, blood dyscrasias and skin changes. Amodiaquine is a 4-aminoquinoline compound and has similar properties to those of chloroquine.

2. Chloroguanide (Paludrine)

This acts as a causal prophylactic for P.falciparum and has a suppressive effect on the other parasites associated with human malaria. When given in the usual antimalarial doses it is relatively non-toxic. Some strains of the parasite are resistant to the drug, and there may be cross resistance with pyrimethamine. It is very suitable for use in children.

Dose – Adults

The oral dose is 100 mg daily. In high risk areas 200 mg of the drug should be taken daily.

The drug should be started just prior to entering the endemic zone and continued
for at least four weeks after leaving the endemic area (preferably taken for six to eight weeks).

3. **Pyrimethamine**

Pyrimethamine acts as a causal prophylactic for *P. falciparum* infections and has a suppressive effect on the other parasites causing human malaria. The preparation is well absorbed and need only be taken once a week. In the usual doses it has few adverse effects, but larger doses can produce a macrocytic anemia. Resistance to the drug occurs and there may be cross resistance with chloroguanide. The drug prevents maturation of the gametocytes in the mosquito. Pyrimethamine has been given in association with other antimalarials e.g. dapsone and chloroquine.

**Dose - Adults**

The usual antimalarial dose is 25 mg to 50 mg given orally once a week.

The drug is commenced just prior to entering the malarious zone and continued for at least four weeks after departing from such an area (preferably taken for six to eight weeks).

4. **Quinine and mepacrine**

Although quinine has been used as an antimalarial, its present role is mainly in the therapy of acute malaria, particularly in *P. falciparum* infections which are resistant to chloroquine. Mepacrine has also been used as a suppressant for malaria, but it is now mainly indicated for the therapy of such diseases as giardiasis and tapeworm infections.

5. **Primaquine**

Although this toxic 8-aminoquinoline drug is essentially used for the radical cure of *P. vivax*, *P. malariae* and *P. ovale* malaria, it has been given in association with other drugs for the chemoprophylaxis of malaria (e.g. with chloroquine and dapsone). It has a causal prophylactic effect, but in view of its potential toxicity it is not used for routine chemoprophylaxis. Drugs such as chloroquine or chloroguanide will not prevent relapses in *P. vivax*, *P. malariae* or *P. ovale* malaria, and as these relapses are due to the secondary exo-erythrocytic stages of the parasite in the liver, in order to prevent relapses and provide a radical cure of the disease, a course of primaquine is given. These secondary exo-erythrocytic phases do not apparently take place in *P. falciparum* infections. Adverse effects associated with the drug include abdominal pain, methemoglobinemia, hemolytic anemia (in subjects with a glucose - 6 - phosphate dehydrogenase deficiency a severe hemolytic crisis may be induced) and granulocytopenia. The drug should not be administered to
those who have been recently on mepacrine as severe toxic reactions may be produced. In adults an oral dose of primaquine 15 mg of the base is given daily for 14 days.

6. Other drugs.

Dapsone and other sulfones have been used as antimalariais for some time, but they are not satisfactory when given alone and are usually given in association with other drugs. Thus dapsone has been given in combination with pyrimethamine on a weekly basis, and has also been used with chloroquine and primaquine. With reference to P. falciparum, dapsone has a schizontocidal effect, but is less effective against P. vivax. It does not act on the tissue stages of the parasite. As the sulfones can produce severe adverse reactions including hemolytic anemia (especially in those with a glucose - 6 - phosphate dehydrogenase deficiency), agranulocytosis or methemoglobinemia, they are not recommended for routine use.

The antimalarial activity of the sulfonamides has been known for many years, but although they have been given in association with other chemoprophylactic drugs, their main indication is the therapy of the acute attack, particularly where the drug resistant parasite is involved. The combination of sulfadoxine and pyrimethamine has been used for suppression of the parasite, but the place of such combinations in the chemoprophylaxis of the disease is not yet fully established. Also the long term use of sulfonamides carries a significant risk of adverse reactions, and in addition to the emergence of drug resistant parasites, bacteria may become resistant as well.

Cycloguanil has a long lasting effect against some strains of the parasite and is given as a single intramuscular dose. It is effective for several months, but there have been reports of parasite resistance.

Antimalarials and pregnancy.

With reference to the use of antimalarials in pregnancy, the physician must assess the benefit to risk ratio for each individual subject, but it is generally accepted that the potential risk of malaria justifies the use of these drugs in the pregnant subject. Combinations of drugs are probably best avoided, but on the whole the usual doses of antimalarials appear to be relatively safe when given during pregnancy.

The drug resistant parasite.

The drug resistant parasite remains a significant problem as far as the chemoprophylaxis of malaria is concerned and even now we are unaware of all the areas where this hazard exists. The resistance of the parasite to chloroquine
Sites of action of antimalarials (Simplified)

Radical curatives (Primaquine)
- Liver
  - Secondary (persistent) tissue schizonts
    - NOT for *P. falciparum*
- Liver
  - Primary tissue schizonts

Schizontocidal drugs (Chloroquine, quinine, mepacrine and amodiaquine)
- Trophozoite
- Schizont

Gametocytes
- Merozoite
- Asexual erythrocytic cycle

Gametocytocidal drugs (Primaquine)
- Causal prophylactics (Pyrimethamine and chloroguanide)
  - True prophylactic would act here
  - Sporozoites injected by mosquito into human

Human cycle

Mosquito cycle
- Taken up by mosquito

Sporontocidal drugs (Pyrimethamine, chloroguanide and primaquine)
was first described in 1960 and essentially relates to *P. falciparum*. It poses a problem in such zones as South America and South-East Asia, but at present it is not a significant entity in Africa. However mass chemoprophylaxis may well lead to a spread of the phenomenon. Some strains of the parasite which are resistant to chloroquine may also have a cross resistance to other antimalarials. In parts of Africa (e.g. Tanzania) *P. falciparum* has been found to be resistant to chloroguanide and pyrimethamine, and similar findings have been described in South-East Asia and South America. With reference to these two latter drugs resistance involving *P. vivax*, *P. malariae* and *P. ovale* has also been noted.

In an effort to prevent the emergence of resistant strains of the parasite, and provide efficient chemotherapy when the subject encounters the drug resistant parasite, combinations of drugs have been employed, particularly in such areas as Vietnam where drug resistant *P. falciparum* has been a problem. Many permutations have been tried, including the following combinations:

- Chloroquine 300 mg. of base plus primaquine 45 mg. of base - once weekly. (This routine has also been combined with daily doses of dapsone 25 mg.).

- Pyrimethamine 12.5 plus dapsone 100 mg. - once weekly.

- Pyrimethamine 15 mg. plus chloroquine 150 mg. of base - 1-2 tablets weekly.

- Pyrimethamine 12.5 mg. plus sulfadoxine (125-250 mg.) - once a week.

Some of the sulfonamides (e.g. sulfalene) are of interest from the point of view of antimalarials, but at present their role in chemoprophylaxis is not fully established, and they have mainly been used in the treatment of the acute attack. In view of the potential toxicity of the sulfonamides, there is some concern about their routine long term use.

It should be noted that in areas where *P. falciparum* is resistant to chloroquine, chloroguanide may still be effective and combinations of drugs may not always be required.
**Summary of antimalarial dosage (For chemoprophylaxis)**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Below 1 year</th>
<th>1-4 years</th>
<th>5-8 years</th>
<th>9-12 years</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroquine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>weekly</td>
<td>37.50-50 mg</td>
<td>50-100 mg</td>
<td>150-200 mg</td>
<td>200-300 mg</td>
<td>300 mg base</td>
</tr>
<tr>
<td></td>
<td>base</td>
<td>base</td>
<td>base</td>
<td>base</td>
<td>base</td>
</tr>
<tr>
<td></td>
<td>(N.B. In highly malarious areas, adults should take 300 mg of the base twice a week).</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloroguanide</td>
<td>25-50 mg</td>
<td>50 mg</td>
<td>75 mg</td>
<td>100 mg</td>
<td>100 mg</td>
</tr>
<tr>
<td>daily</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(N.B. In highly malarious areas adults should take 200 mg daily).</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrimethamine</td>
<td>6.25 mg</td>
<td>6.25-12.50 mg</td>
<td>12.50 mg</td>
<td>12.50-25. mg</td>
<td>25-50 mg</td>
</tr>
<tr>
<td>weekly</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amodiaquine</td>
<td>50 mg</td>
<td>50-100 mg</td>
<td>150-200 mg</td>
<td>200-300 mg</td>
<td>300-400 mg</td>
</tr>
<tr>
<td>weekly</td>
<td>base</td>
<td>base</td>
<td>base</td>
<td>base</td>
<td>base</td>
</tr>
<tr>
<td></td>
<td>(N.B. In highly malarious areas adults should take 300 mg of the base twice a week).</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2. MALARIA-CLINICAL FEATURES AND DIAGNOSIS.

A. CLINICAL FEATURES.
"INCUBATION PERIOD".
P.falciparum - about 12 days.
P.vivax - 13-15 days (may be much longer)
P.malariae - upto 1 month.

FEVER.
P.falciparum - primary attack is potentially the most threatening. In visitors to malarious areas, usually a quotidian fever is seen. Later a tertian fever may present, accompanied by a cold stage - lasting upto 2 hours, followed by a hot period (3-4 hours) and then a stage of sweating (2-4 hours). P.vivax can produce high fevers and there may be severe malaise. Episodes of pyrexia on every fourth day occur in P.malariae infections (quartan malaria). The classical stages of the disease are not always seen.

COMMONEST PRESENTING SIGN IS FEVER.

In severe P.falciparum infections accompanied by shock, the temperature may be subnormal. Sometimes the subject may notice headache, backache or limb pains before the fever is obvious.

OTHER CLINICAL FEATURES.
The spleen is usually palpable by the second week and there may be some hepatomegaly. Jaundice may be observed in cases with significant liver involvement. Nausea and vomiting are present in some instances.

COMPLICATIONS OF FALCIPARUM MALARIA.
These can develop at any stage in the infection.

(A) ALGID MALARIA.
There is acute shock and death can occur with little warning. Adrenal failure may play a part in the syndrome.

(B) CEREBRAL MALARIA.
Cerebral involvement can produce coma. Also there may be hyperpyrexia. Convulsions are sometimes the presenting sign.

(C) RENAL FAILURE AND BLACKWATER FEVER.
Renal insufficiency can take place at any stage. In blackwater fever hemoglobinuria is seen, and this may be accompanied by vomiting and abdominal pain. The syndrome is not common now but was essentially observed in non-immune
subjects who had taken quinine. Treatment of the condition involves the routine chemotherapy for the malaria parasite and treatment of the renal failure. Corticosteroids and dialysis have also been employed.

(D) **SPLENIC RUPTURE.**

Spontaneous rupture of the spleen may occur in acute primary episodes of the disease.

(E) **HEPATIC FAILURE.**

With this complication the patient may complain of abdominal pain, nausea and vomiting and the prognosis is usually poor.

**MALARIA-LABORATORY FINDINGS.**

The blood findings show evidence of a hemolytic anemia. The sedimentation rate is usually increased. There may be a leucocytosis with a increase in the monocytes, but sometimes a leucopenia is seen. Plasma albumin is decreased but there is usually an increase in globulin levels. There may be evidence of impaired hepatic and renal function. The urine findings are usually normal but in cases of blackwater fever there may be hemoglobinuria. In episodes of pyrexia there is sometimes an increase in plasma potassium and blood sugar levels. **DIAGNOSIS IS DEPENDENT UPON FINDING THE PARASITE IN BLOOD FILMS.**

**MALARIA DIAGNOSIS.**

This aspect of the illness can be considered as having three components.

1. **HISTORY "UNDE VENIS?"** (Where have you been).
2. **BLOOD FILMS.** (Thick and Thin)
3. **PHYSICAL EXAMINATION AND OTHER INVESTIGATIONS.**

The history is supremely important, and the master words of Maegraith, "Unde Venis" must be directed at all who return from the tropics. Many parts of the globe remain malarious, including much of tropical Africa, parts of North Africa, South America and some of Central America, much of Asia, parts of the Middle-east and some South-Pacific regions. If the traveller has visited such an area it should be determined whether antimalarials were taken as directed. It is worth stressing that;

Only one bite from an infected mosquito is needed to acquire the parasite. The ideal antimalarial does not yet exist.

Even if the subject took antimalarials the disease may still be present (please see notes on chemoprophylaxis).
IF ANY SUBJECT WITH A PYREXIA, OR HISTORY OF PYREXIA, HAS RETURNED FROM A MALARIOUS AREA, THEN THE PHYSICIAN SHOULD ASSUME MALARIA TO BE PRESENT UNTIL PROVED OTHERWISE.

With reference to the diagnosis of the parasite, the only certain way of confirming the disease is to detect the erythrocytic forms of the parasite in a suitable blood film and repeat films may be necessary. (Both thick and thin films being done). Rarely sternal marrow samples are needed. Parasites are most numerous in the peripheral blood during or soon after the paroxysm. In primary falciparum infections the fever may be very irregular and at times the parasites may be very scanty in the blood.

Although the infection can appear under several guises, fever is usually the main clinical pointer and the combination of fever, splenomegaly and a history of a sojourn in a malarious area should always raise the possibility if this disease. Besides the blood film other diagnostic tests include complement fixation, hemagglutination tests, and fluorescent antibody tests.

TREATMENT OF ACUTE MALARIA.

The acute attack usually responds to chloroquine.

ADULTS.

Initial dose is 1.0 gm. (600 mg. of the base) of chloroquine phosphate, followed by an additional 500 mg. (300 mg. of base) some 6-8 hours later. Then a single dose of 500 mg. (300 mg. of the base) is given on each of two consecutive days. All doses given orally.

INFANTS AND CHILDREN. (oral chloroquine phosphate).

First dose of 10 mg. base/kg. (not exceeding a single dose of 600 mg. of base)
Second dose of 5 mg. base/kg. (not exceeding a single dose of 300 mg. of base)
-six hours after the first dose.
Third dose of 5 mg. base/kg 18 hours after the second dose.
Fourth dose 5 mg. base/kg 24 hours after the third dose.
All doses expressed/kg. of body weight. Supportive therapy is also needed including:
1. Bed rest.
2. Fluid balance & correction of electrolyte imbalance.
3. Treatment of complications - renal failure and hyperpyrexia etc.

The above regimen refers to the acute uncomplicated attack and should result in a radical cure for P.falciparum infections (where there is no drug resistance).
N.B. FOR A RADICAL CURE OF VIVAX, OVALE OR MALARIAE MALARIA CONCOMITANT THERAPY WITH AN 8-AMINOQUINOLINE DRUG IS NEEDED.

Thus adults should be given Primaquine orally for 14 days (15 mg./day), but this is a toxic drug and must be given with care, and may produce a severe hemolytic anemia (especially in subjects with a glucose-6-phosphate dehydrogenase deficiency) and methemoglobinemia.

In children the dose of Primaquine is:
- 4-8 years of age-total oral dose of 5.0 mg.-7.5 mg. once a day for 14 days.
- 8-15 years of age-total oral dose of 10.0 mg.-15.0 mg. once a day for 14 days.

Above doses refer to the base.

The patient who is severely ill may have some of the complications already mentioned, and in addition to chemotherapy each complication will need its own specific therapy. Where the subject is unable to tolerate oral medication, chloroquine can be given intramuscularly but must be given with great care. Thus adults are given chloroquine hydrochloride 250 mg. (200 mg. of the base) I.M. every 6 hours (maximum dose being 1.0 gm. daily-as soon as possible a change should be made to oral therapy). In emergency use quinine dihydrochloride can be given intravenously, adults receiving 600 mg. in normal saline (300 ml.) given slowly over half an hour. The dose can be repeated in 8 hours (maximum dose being 1800 mg. in 24 hours). Oral therapy should be substituted as soon as possible. Intravenous quinine may be associated with severe adverse reactions (especially on the C.V.S. system). I.V. steroids are indicated in cerebral malaria (e.g. dexamethasone 4-6 mg. being administered every 4-6 hours).

Intravascular coagulation may occur with cerebral malaria.

P.falciparum malaria-resistant to chloroquine.

1. Where the attack is not severe. - Adults are given:
   - Oral quinine sulfate - 650 mg. t.i.d. for 14 days-plus;
   - Oral pyrimethamine - 25 mg. b.i.d. for 3 days - plus;
   - Oral sulfadiazine - 500 mg. q.i.d. for 5 days
     (or oral dapsone, 25 mg. daily for 28 days can be used instead of sulfadiazine).

   Where the patient is severely ill the following is given;
   - Quinine dihydrochloride - 600 mg.in 300 ml. normal saline, given intravenously slowly over half an hour. Dose is repeated after 8 hours. As soon possible oral therapy is substituted.

Other drugs have been used to treat the drug-resistant parasite e.g. sulformethoxine a single dose of 1.0 mg. being given with a single dose of pyrimethamine 50 mg. Tetracyclines and trimethoprim have also been tried.
CHAPTER 4.
THE PATIENT WITH DIARRHEA - ? AMEBIC INFECTION.

Diarrhea ranks high on the list of symptoms for which the traveller seeks medical aid on his return from the tropics, and this complaint can be the presenting symptom in a wide range of tropical maladies. Advice is usually sought because the bowel upset persists or recurs at frequent periods after the return from the tropics. Although one can distinguish between diarrhea and dysentery (diarrhea plus blood and mucus) such a distinction is often academic. Amebic infections are not the commonest cause of diarrhea in these subjects, but the condition should receive some extra attention, for if untreated the infection can have grave sequelae. In order that no parasitic disease is overlooked in the patient with diarrhea, the physician should adopt a systematic approach consisting of:

1. HISTORY - UNDE VENIS?
2. PHYSICAL EXAMINATION.
3. FRESH STOOL EXAMINATION.
4. OTHER INVESTIGATIONS.

The history is useful, for although no one geographical area can claim the monopoly on any given parasitic disease, the travellers itinerary may indicate some possible culprits. Although it is a somewhat grandiose assumption, it is a safe rule to regard all subjects who have returned from the tropics and who give a history of bloody diarrhea accompanied by abdominal cramps after visiting such countries as India, Vietnam, Phillipines and areas of South America and tropical Africa, as having an amebic infection until proved otherwise. It is useful to know if the subject took prophylactic drugs for compounds such as iodochlorhydroxyquin may mask amebic infections. Occasionally early schistosomiasis can produce diarrhea and there might be a history of swimming in fresh water. In all instances it must be ascertained whether the individual had any previous history of diarrhea before going to the tropics, for such conditions as ulcerative colitis have a high risk of relapse in tropical climates and of course in all cases it is essential to rule out other causes of diarrhea, for parasitic infections may co-exist with a wide range of other diseases. (e.g. neoplasms).

A physical examination has little chance of pin-pointing the exact cause of any diarrhea in these subjects, but sometimes it yields suggestive clues. Thus the presence of "rose spots" would raise the possibility of typhoid, and amebic
"TROPICAL" DIARRHEA—??? CAUSE.

THINK:
AMEBIC DYSENTERY.
GIARDIASIS.
BACILLARY DYSENTERY.
TYPHOID.
SCHISTOSOMIASIS.
TRICHURIS.

STOOLS—FRESH SAMPLES.
-? OVA/PARASITES.
-BACTERIOLOGY.

BLOOD—?ANEMIA.
-EOSINOPHILIA
-?PARASITES.
-CULTURE.
- SEROLOGY.

URINE— BACTERIOLOGY.
- ETC.

WHERE INDICATED— X-RAY INVESTIGATIONS/INTESTINAL BIOPSY/MALABSORPTION STUDIES/LIVER SCAN (HEPATIC ABSCESS)/ETC.)

SIGMOIDOSCOPY AND OTHER INVESTIGATIONS ARE ALSO INDICATED TO ELIMINATE "NON-TROPICAL" CAUSES (e.g. NEOPLASMAS OR ULCERATIVE COLITIS).
infections may be associated with tenderness over the hepatic area (amebic liver abscess). Falciparum malaria sometimes produces a watery diarrhea and the presence of splenomegaly would support this diagnosis.

A thorough examination of the stools must be done. At least 3 FRESH samples should be obtained i.e. the sample should be examined at the laboratory and this should be done immediately after the stool have been passed. If this is not feasible then the samples must reach the laboratory within one hour after being passed. Often patients do not take kindly to the prospect of producing several fecal samples, but they must be told that a single negative report does not rule out parasitic infection. Preserved stool samples are very much a second best procedure.

In all cases bacteriological studies should be carried out, particularly to rule out shigella and salmonella infections. Occasionally culture methods are useful in isolating amebic infections.

Sigmoidoscopy is useful in confirming amebic infections and radiological examination of the gastrointestinal tract may reveal other causes of diarrhea such as ulcerative colitis. Long standing giardiasis can produce malabsorption syndromes and in some travellers, particularly "overlanders" malabsorption syndromes may be found in the absence of any parasites. In these subjects fat, xylose and vitamin B 12 malabsorption is present and low levels of serum folate and vitamin B 12 confirm the diagnosis. Sometimes intestinal biopsy methods are used to confirm such disease as schistosomiasis or malabsorption. On occasions blood culture and serological techniques are of use e.g. in the diagnosis of typhoid. Radiological investigations are often needed, especially to exclude non-parasitic causes of diarrhea.

AMEBIASIS.

Entameba histolytica usually exists in the large bowel, as a commensal, but it is capable of invading the bowel wall and spreading to other organs. In some tropical areas over three-quarters of the population harbour the parasite. TRANSMISSION - Humans become infected by swallowing the cysts of the parasite. CLINICAL FEATURES.- The incubation period is often long, and symptoms can occur many years after the initial exposure. In most instances the onset is insidious, and the main complaints are of abdominal discomfort and diarrhea (with or without blood and mucus). In more severe cases tenderness over the sigmoid colon is found and there may be 10-12 stools/day, accompanied by abdominal cramps. Pyrexia is unusual, but there is sometimes a moderate leucocytosis. The disease is capable of
appearing in several different forms, and the W.H.O. classification is useful.
1. Asymptomatic.
2. Symptomatic - (A) Intestinal Amebiasis.
   - Dysentery.
   - Colitis.
   - Ameboma.
   - Amebic appendicitis.
(B) Extraintestinal amebiasis.
   - Hepatic
   - Cutaneous
   - Other organs.
Many subjects who excrete the cysts remain symptomless i.e. the presence of cysts in the stools is not synonymous with amebic disease.

COMPLICATIONS. (of intestinal amebiasis).
1. Hemorrhage.
2. Perforation.
3. Intussusception.
4. Stricture.
5. Abscess formation.

DIAGNOSIS.
1. History of diarrhea, abdominal cramps, blood and mucus in the stools.
2. Acute stage - the motile trophozoites of Entameba histolytica are found in a FRESH stool sample.
3. In the chronic stage the diagnosis is made by observing the cysts in the stools.
4. Culture methods are also available, but they are not reliable for routine use.
5. Endoscopy may reveal the characteristic ulcers associated with this parasite, and this can be combined with a biopsy.
6. Serological methods are available (e.g. Indirect hemagglutination test, complement fixation test and indirect fluorescent antibody test).

DIFFERENTIAL DIAGNOSIS.
1. Bacillary dysentery.
2. Ulcerative colitis.
3. Diverticulitis.
4. Giardiasis.
5. Tropical sprue.
7. Intestinal TB.
AMEBIC LIVER ABSCESS.

The commonest extraintestinal form of the disease is hepatic involvement, and this can present many years after the original exposure with such varied symptoms as pyrexia, abdominal discomfort, general malaise and pain over the right costal margin. There may be a leucocytosis and increased sedimentation rate. Liver function tests are not usually affected. Clinical examination sometimes reveals a tender enlarged liver. To confirm the diagnosis a liver scan, screening of the diaphragm and serological tests for extraintestinal amebiasis are often required. X-ray examination is used to demonstrate elevation of the right diaphragm.

TREATMENT OF AMEBIC INFECTIONS.

1. Patient who passes cysts, but has no symptoms. (Adult doses)
   Diiodohydroxyquin - given orally. 650 mg. t.i.d. for 20 days
   (This drug should be given with care because of the risk of optic neuritis).
   or;
   Metronidazole - given orally. 750 mg. t.i.d. for 7-10 days
   or;
   Diloxanide furoate - given orally. 500 mg. t.i.d. for 10 days.

2. Patient with intestinal disease (not severe).
   Metronidazole - given orally. 750 mg. t.i.d. for 7-10 days.

3. Patient with intestinal disease (severe).
   Metronidazole (as in 2).
   or;
   Dehydroemetine - 1.0-1.5 mg./kg. daily. Given intramuscularly or subcutaneously for up to 5 days.

N.B. With reference to the above it should be noted that;

A. Originally metronidazole was considered to be effective at all sites of amebic infection, but recent evidence suggests that amebic liver abscesses can develop when metronidazole is used alone to treat the intestinal form of the disease. However many still consider this compound to be the drug of choice.

B. Emetine and its derivatives can have highly toxic effects on the cardiovascular system, and such drugs should only be given to subjects who are hospitalized. Patients should have regular electrocardiographic monitoring during therapy.

Other drugs have also been used for the treatment of amebiasis including tetracyclines, paromomycin and niridazole.
4. Treatment of amebic liver abscess.

Larger abscesses may require surgical drainage. Drugs used include.

Metronidazole - given orally, 750 mg. t.i.d. for 7-10 days
or;
Dehydroemetine - 1.0-1.5 mg./kg. daily. Given intramuscularly or subcutaneously for up to 5 days.
Plus;
Chloroquine phosphate. Given orally - 1.0 gm. daily for 2 days then 500 mg. daily for 21 days.

N.B. All patients who have been treated for intestinal amebiasis should have follow-up stool examinations for one year.
AMEBIASIS-CLINICAL FEATURES

AMEbic Dysentery
Long Incubation Period
Insidious Onset
Diarrhea (Blood/Mucus)
Fever
Leucocytosis
Abdominal Pain
Peritonitis
Ameboma

Amebiasis
Diagnosis

Amebiasis

Hepatic Abscess
Fever
Abdominal Discomfort
Hepatomegaly
Rupture of Abscess

Stools (Fresh)
Sigmoidoscopy
Liver Scan
SEROLOGY

Undevenis?
"P.U.O."

"P.U.O." / EOSINOPHILIA/OVERLANDER SYNDROME.

Sometimes subjects returning from the tropics state that they feel well except for periodic bouts of fever, and in all these cases after it has been ascertained that none of the "usual" causes of fever are present then one is left with a list of "tropical" entities which may present as a P.U.O. IF ANY SUBJECT WITH A PYREXIA, OR HISTORY OF PYREXIA, HAS RETURNED FROM A MALARIOUS AREA, THEN THE PHYSICIAN SHOULD ASSUME MALARIA TO BE PRESENT UNTIL PROVED OTHERWISE.

Often the zone visited provides a clue to the likely causes. Thus with reference to U.S.A. troops in South Vietnam the following diseases were found to be common causes of pyrexia; malaria, leptospirosis, typhus and arbovirus infections (including dengue and Japanese B encephalitis).

1. HISTORY-UNDE VENIS?
2. PHYSICAL EXAMINATION.
3. EXAMINATION OF FRESH STOOL SAMPLES.
4. BLOOD FILM EXAMINATION.
5. OTHER INVESTIGATIONS.

Did you take antimalarials as directed? Where did you travel? Did you swim in fresh water? Did you have all the recommended prophylactic immunizations before travelling? These are some of the main questions to be directed at all who admit to episodes of pyrexia after returning from tropical climates. As has been mentioned even though antimalarial drugs were taken correctly, malaria can still be present. The physical examination sometimes yields a pointer to the etiology of any unexplained fever. Thus typhoid produces a typical rash. Possible jaundice should be looked for, Splenomegaly and fever would raise the possibility of such infections as malaria, typhoid or leishmaniasis being present.

Hepatomegaly is associated with hepatitis, malaria, leishmaniasis or amebic liver abscess. Fresh stool samples must be examined for ova and parasites to exclude conditions such as amebiasis and bacteriological culture studies are required to detect bacillary dysentery and typhoid. Urinalysis may reveal the eggs of schistosomiasis (S. hematobium).

Malaria, trypanosomiasis or filariasis can be detected on a suitable blood film, and an eosinophilia would lead one to suspect the presence of some parasitic
disease. Blood cultures are useful (typhoid and brucellosis) and marrow samples may reveal leishmaniasis. Serological tests are useful in confirming some infections e.g. Widal test, Weil-Felix reactions, the various complement-fixation reactions (e.g. trichinosis and filariasis), and other tests (e.g. latex agglutination test for extraintestinal amebiasis—Serameba test). Liver function investigations would confirm the presence of hepatitis. Intradermal sensitivity tests are also available for brucellosis, lymphopathia venereum (Frei test), and hydatid disease as well as other infections. Tuberculosis must never be forgotten and all subjects are advised to have a chest X-ray on returning from the tropics.

Radiological techniques are also of use for other infections e.g. I.V.P. investigation can sometimes reveal genito-urinary schistosomiasis, screening of the diaphragm may reveal abnormalities due to amebic liver abscess and liver scans are taken to confirm the presence of such abscesses.

The following are some of the causes of fever to be considered in subjects returning from abroad. (Points relating to diagnosis are given in parenthesis).

1. MALARIA. (Blood films—thick and thin/bone marrow/fluorescent antibody).
2. AMEBIASIS. (Stools/Sigmoidoscopy/Serology—Liver abscess—Liver Scan/X-ray).
3. BACILLARY DYSENTERY. (Stools).
4. TYPHOID. (Serology/Blood & Stool culture/Urine culture).
5. FILARIASIS. (Blood films—day & night/Serology).
6. SCHISTOSOMIASIS. (Stools/Urine/I.V.P./Biopsy/Serology).
7. TRICHINOSIS. (Muscle Biopsy/X-ray/Serology/Skin tests).
8. HEPATITIS. (Liver Function Tests).
9. BRUCELLOSIS. (Blood culture/Serology).
10. TYPHUS. (Weil-Felix).
11. TUBERCULOSIS. (X-ray).
12. ARBOVIRUSES. (e.g. Dengue/Yellow Fever).
13. TRYPANOSOMIASIS. (Blood films/Lymph node smears/Cultures/Serology).
14. LEISHMANIASIS. (Blood films/Bone marrow/Splenic puncture/Cultures/Serology).
15. LASSA FEVER. —rare (Serology).
"PALM TREE" P.U.O.

ALWAYS RULE OUT "EVERYDAY" CAUSES. (e.g. urinary tract infections).
ALWAYS RULE OUT MALARIA.
NEVER FORGET TB.

FEVER ?—THINK MALARIA.
HEPATITIS.
FILARIASIS.
BRUCELLOSIS.
TYPHOID.

EOSINOPHILIA—THINK "WORMS"

BLOOD FILMS

?MALARIA.

?FILARIASIS.

?TRYPANOSOMIASIS.

SPOTS?
TYPHOID.
SMALLPOX.
TYPHUS.

BLOOD CULTURES/SEROLOGY.

TYPHOID.
BRUCELLOSIS.
AMEBIASIS (HEPATIC).
LEPTOSPIROSIS.

STOOLS.
SALMONELLA.
E. HISTOLYTICA.
ETC.

EOSINOPHILIA-THINK "WORMS"

BLOOD FILMS

?MALARIA.

?FILARIASIS.

?TRYPANOSOMIASIS.

RARE BUT "DEADLY"—LASSA FEVER.

URINALYSIS.
C&S.
PARASITES.
(?S. HEMATOBUM).
"EOSINOPHILIA" - ON RETURN FROM THE TROPICS AND THE "OVERLANDER" SYNDROME.

A. EOSINOPHILIA.

Sometimes a routine physical examination in patients who have returned from the tropics reveals no significant abnormality, the subject states that they feel to be in good health, but laboratory tests reveal a single isolated abnormality and the physician is left to decide whether further investigation is warranted. One such example is the patient who is found to have a persistent eosinophilia, and this finding always merits an extensive search for parasitic disease. Potential parasites and conditions to be considered in such cases are listed below, but it should be remembered that not all of these infections are found in all zones and in all instances a full geographical history must be obtained from the subject.

1. FILARIASIS.
2. SCHISTOSOMIASIS.
3. ASCARIASIS.
4. ANCYLOSTOMIASIS.
5. TRICHINOSIS.
6. LARVA MIGRANS.
7. STRONGYLOIDES.
8. TROPICAL EOSINOPHILIA.

Filariasis can sometimes be difficult to diagnose, particularly as "occult" forms can occur. The microfilariae of W. bancrofti show a nocturnal periodicity (appearing in the blood between 10 p.m. and 2 a.m.). The infection is found in such areas as tropical Africa, West Indies, South America and some South Pacific zones (where the microfilariae may appear in the blood in the day and at night) and parts of Asia. The microfilariae of B. malayi also show nocturnal periodicity and the parasite is found in Indonesia, Malaysia, parts of China and India and the clinical picture is similar to that of W. bancrofti. The filarial worm Loa loa occurs in well defined zones in tropical Africa and the microfilariae appear in the blood in the largest numbers in the day. The eosinophilia can be very high (up to 90%). Occasionally the adult worm is to be observed crossing the eyelid or conjunctiva. The filarial worm Onchocerca volvulus can produce subcutaneous nodules and the parasite is present in tropical Africa and South America. The eye lesions are the main danger from the worm but mainly appear in the indigene and are not often seen in the visitor. The microfilariae
are found in the skin nodules. Suitable blood films remain the main diagnostic test for filariasis, but intradermal, complement fixation tests and other serological tests are also used.

With reference to schistosomiasis, the history may show that the traveller spent some time in an endemic region and indulged in fresh water swimming. In S. hematobium infections the diagnosis is confirmed by finding the eggs of the parasite in the urine and the subject often admits to painless hematuria. In some cases an I.V.P. demonstrates involvement of the urinary tract. S. mansoni and S. japonicum infections are confirmed by observing the eggs of the fluke in the stools. Rectal mucosal biopsy is also used. Intradermal and various serological tests are available for the detection of filariasis. Ascariasis is capable of producing a high eosinophilia, and is confirmed by finding the ova of the worm in a stool sample. Ancylostomiasis is common in tropical countries and can remain symptomless, but examination of the blood often shows an eosinophilia to be present and sometimes there is evidence of an iron-deficiency anemia. Diagnosis is by finding the eggs of the hookworm in suitable fecal preparations. Trichinosis is associated with high eosinophil counts, but it should be noted that stool examinations are only helpful in the early stage of the infection and diagnosis usually depends upon muscle biopsy, X-ray examinations (calcification in soft tissues), intradermal tests and serological investigations. The persistent eosinophilia of visceral larva migrans (v.l.m.) on occasions is accompanied by such clinical finding as hepatomegaly, asthma-like syndromes and pyrexia and a similar pulmonary picture can be observed in strongyloidises infections where the presence of the nematode is confirmed by finding the adult worm or larvae in the stools. In tropical pulmonary eosinophilia there may be fever, splenomegaly, cough, hemoptysis and ill-defined mottling on chest X-ray films. It is present in such areas as Sri Lanka, India and Malaysia and is probably a reaction to the incomplete maturation of a filarial worm, for often the syndrome yields positive serological tests for filariasis, yet no microfilariae are to be observed in the blood and the symptoms respond to diethylcarbamazine.

THE OVERLANDER SYNDROME.

This entity has been well described by Knight and is of particular interest to the physician who sees students on their return from the tropics. The syndrome usually relates to the 18-25 year old traveller whose journey lasts from some 12 week to 2 years and takes in such areas as India, Turkey, Afghanistan and various
parts of Europe. Many of these subjects now travel across the various exotic areas of South and Central America. Often the going is rough and for financial considerations the diet is poor and the life style adopted brings the visitor into contact with many potential hazards. On their return these patients commonly give a history of loss of weight, general malaise and diarrhea, and although the diarrhea is often due to Shigella organisms, the possibility of other parasites being present must never be ignored. Amebic infections, giardiasis and hepatitis are by no means rare in the overlander and where recurrent or persistent diarrhea is present the following possibilities must be kept in mind:

1. Amebic dysentery.
2. Giardiasis.
4. Tropical sprue.
5. Various other parasites—especially ascaris, trichuris trichuria, hookworm and strongyloides.

Amebic infections may be masked by the self-medication which the overlander takes as a panacea. Giardiasis is sometimes associated with vague abdominal discomfort, anorexia and malabsorption syndromes. Tropical sprue is not common but can sometimes be observed in subjects who have spent time in India or South-east Asia and who complain of diarrhea, malaise, loss of weight and glossitis. Vague abdominal symptoms are common in the overlander and are often functional, but repeated fresh stool examinations must always be carried out to exclude parasitic infections. Tomkins has recently described 34 cases of malabsorption in a group of overlanders going to India and symptoms included diarrhea, abdominal distension and weight loss. Investigations revealed fat, xylose and Vitamin B12 malabsorption with mucosal changes. Low levels of serum folate and Vitamin B12 were seen in those with long standing diarrhea, but no anemia was observed. Most subjects responded to a course of tetracyclines for two weeks followed by sulfadimidine for two weeks. Most subjects also received folic acid.

Viral hepatitis remains a constant threat to the overlander in his travels, and abnormal liver function tests are not rare. One of the paradoxes of the syndrome is that although many of the subjects wander through malarious zones, few develop overt malaria, even though antimalarials were not taken. Fungal skin infections, various ectoparasites and V.D. are not uncommon in this group of global travellers.
PERSISTENT EOSINOPHILIA—PARASITES PROBABLY PRESENT.

???
ASCARIS.
HOOKWORM.
SCHISTOSOMIASIS.
TRICHURIS.
TRICHINOSIS.
LARVA MIGRANS.
TROPICAL EOSINOPHILIA.

ABSOLUTE COUNT 600/CU.MM.

EOSINOPHILIA ?

"THINK—PARASITES."
CHAPTER 6

WOBBLY WORMS

Most Family Physicians are now seeing an increasing number of "imported" diseases, and often a routine investigation (e.g. a stool examination done for immigration purposes) will reveal the presence of some unsuspected parasite. The following notes relate to some of the helminthic infections which are essentially detected by fecal examinations. Some infections (e.g. ascaris, tapeworms and pinworms) are by no means rare in subjects who have never been in the tropics. The physician interested in seeking out the various worms which trouble the human host should keep the following points in mind.

1. In all cases it is mandatory to make a positive identification of the worm before treatment is initiated. Fresh stool examination yield the richest harvest and tests involving preserved samples are very much a second best. Unfortunately a "negative" result does not mean too much as far as the average commercial laboratory is concerned, and facilities for the efficient diagnosis of parasitic disease are sadly lacking in most areas.

2. Because of the potential adverse reactions involved, antihelminthic drugs should not be used in the pregnant subject.

3. Serological and skin tests are available for the detection of some worms, but as far as the family Physician is concerned, such investigations are best carried out in tropical disease clinics or similar units. (The National Reference Centre for Parasitology, Montreal, carries out a wide range of tests for parasitic disease).

4. After therapy it is essential to perform follow-up investigations before the patient can be pronounced "cured".

1. ASCARIS (Roundworm).

Ascaris lumbricoides lives in the small intestine. Infections due to the worm are widespread throughout the world and some say that 1 in every 4 of the human race is host to the helminth. The parasite is acquired by ingestion of the fertile eggs and food and drink are the common vehicles involved. Often there are no symptoms, but the migration of larvae in the early stages of the infection is sometimes-associated with pulmonary signs (Loefflers syndrome consists of the pulmonary manifestations, eosinophilia and adenitis). The adult worms may produce pruritus ani, intestinal colic, acute appendicitis, and occasionally there may be hepatic complications. Larval forms can be responsible for episodes of
convulsions or epilepsy. Some patients "vomit" the worm. Diagnosis is dependent upon observing the ova or adult worms in the stools. An eosinophilia supports the diagnosis and occasionally the helminth may be detected in barium meal examinations. With reference to therapy it should be stressed that where mixed infections occur, ascaris must always be treated first. Piperazines are the drugs of choice.

**Piperazine citrate.** (Antepar).
Given orally (syrup).
Up to 30 lb. of B.W. - 1.0 gm. for 2 consecutive days.
30-50 lb. of B.W. - 2.0 gm. for 2 consecutive days.
50-100 lb. of B.W. - 3.0 gm. for 2 consecutive days.
Over 100 lb. of B.W. - 3.5 gm. for 2 consecutive days (maximum daily dose).

Piperazines are usually well tolerated but are contraindicated in those with a history of seizures or renal dysfunction. Adverse effects include dizziness, tremors, vomiting and skin rashes.

Pyrantel pamoate (Combantrin) can also be used. (Not in those below the age of one year). A single oral dose is administered. (As suspension or tablets).

**DOSE.** (per B.W.)
11 Kg. or less - 125 mg.
11 Kg. - 22 Kg. - 250 mg.
22 Kg. - 45 Kg. - 500 mg.
45 Kg. - 70 Kg. - 750 mg.
Over 70 Kg. body weight - 1000 mg. (maximum daily dose).
Potential adverse drug effects include vomiting, headache and dizziness.

2. **HOOKWORM** (Ancylostomiasis).

The nematodes *Ancylostoma duodenale* and *Necator americanus* live in the human small intestine (mainly in the jejunum). The larvae enter the human host via the skin, and the infection is usually acquired by walking barefoot on contaminated soil. An itchy dermatitis sometimes appears at the site of entry of the larvae and migration of the larvae through the pulmonary tissues is associated with eosinophilia, asthma and blood-stained sputum in some subjects. A clinical history of a short unexplained episode of asthma in a patient returning from the tropics would raise the possibility of a helminthic infection being present. The main pathological effects depend upon the worm load and often there are no clinical symptoms, but heavy infections result in anemia (iron-deficiency type) and
epigastric discomfort (mimicking an ulcer). Eosinophilia is common.

Diagnosis rests upon detecting the eggs of the worm in the stools, and therapy consists of administering an antihelminthic drug and correcting any anemia which is present. The drug of choice is Pyrantel Pamoate (but not given to children under the age of 1 year). For A. duodenale infections a single oral dose is given (in the same amounts as for ascaris). For N. americanus infections the same daily doses are used but the drug is given for 3 consecutive days. Bephenium hydroxynaphthoate (Alcopar) may be used as an alternative drug.

A. duodenale infections—Adults and children over 2 years of age are given an oral dose of one 5 gm. sachet b.i.d. for 1 day.
Children under 2 years of age or under 10 Kg. in body weight should receive half the above dose.

N. americanus infections—the above doses are given daily for 3 consecutive days.
The drug is best taken on an empty stomach and food should be withheld for 2 hours after taking the drug. The preparation must be given with care to hypertensive patients but is usually well tolerated. Adverse reactions include vomiting and diarrhea. Thiabendazole (Mintezol) has also been tried in ancylostomiasis. The tablets are given orally at a dose of 25 mg./Kg. of body weight b.i.d for 2 days (given after food). The maximum daily dose is 3 gm. Adverse effects include headache, dizziness, vomiting, drowsiness and leucopenia.

3. STRONGYLOIDES.
The nematode Strongyloides stercoralis usually infects the small intestine. Most infections are symptomless. The larvae enter the skin and are carried to the lungs where they are sometimes associated with pulmonary signs and symptoms. Other clinical features include diarrhea, eosinophilia and skin rashes (creeping eruptions and urticaria). Debilitated subjects have been known to succumb to "massive" infections with the worm. Diagnosis is by finding the adult or larval forms of the nematode in the stools or in a duodenal drainage specimen.
Treatment is with Thiabendazole (given in the same doses as for hookworm infections).
Pyrvinium Pamoate (Vanquin) has also been used at an oral dose of 5 mg./Kg. of body weight; given for 5-7 days. (maximum daily dose being 250 mg).
The drug should not be given to children under 1 year of age. Pyrvinium pamoate stains the stools red. It should be noted that in Canada the indications for use of the drug do not include strongyloides.
4. **TRICHURIASIS. (Whipworm).**

Trichurus trichiura infects the cecum and colon and infection occurs through ingestion of the embryonated eggs (from contaminated soil). Usually there are no symptoms, but diarrhea, blood in the stools or rectal prolapse (in children) are manifestations of heavy infections. The presence of the eggs of the worm in the stools confirms the diagnosis. The drug of choice is Mebendazole. The drug is very well tolerated, but should not be given to children below the age of 2 years. For other subjects the dose is; Mebendazole—given orally—100 mg b.i.d. for 3 days.

Thiabendazole can also be used but it is not always effective in trichuriasis. The oral dose is that used for hookworm infections.

5. **CLONORCHIS. (Clonorchis sinensis)**

This liver fluke is essentially found in the Far East (Japan, China and Korea). It is acquired by consuming raw contaminated fish. Often the worm produces no symptoms, but fever, jaundice and cholangitis are occasionally present. The parasite has also been associated with adenocarcinoma of the liver. As with many other helminthic infections ectopic larvae can produce damage in a wide range of tissues (e.g. in the CNS and lungs). The typical eggs of the parasite can be seen in the stools or on examination of aspirates of duodenal contents. Therapy is unsatisfactory. Oral doses of Chloroquine phosphate (250 mg. t.i.d. for 6 weeks in adults) may diminish egg production by the fluke, but the drug has significant adverse effects and does not kill the worm. Bithionol, Dehydroemetine and Emetine are other preparations which have been given for the parasite, but none is completely satisfactory.

6. **SCHISTOSOMIASIS. (Blood Flukes).**

The therapy of these trematodes is best carried out at a Tropical Disease Unit and as the worm produces a wide variety of pathological and clinical changes, only a few brief details are covered here.

S. hematobium (lives in the veins of the bladder)—is found in Africa and the Middle East. A few other foci also occur.

S. mansoni (lives in the veins of the mesentery)—is found in Africa, Middle East, S. America and the Caribbean.

S. japonicum (lives in the veins of the small intestine)—is found in the Far East.
Infection is acquired in endemic zones by swimming in contaminated fresh water. Clinical features include skin rash (early stages), fever, eosinophilia, dysentery, hematuria (S. hematobium), hepatic damage and C.N.S. involvement. Genitourinary symptoms predominate in S. hematobium infections. S. mansoni may be associated with intestinal signs and symptoms. Severe infections may mimic a carcinoma and polypi are sometimes present. Late stages lead to hepatic fibrosis and portal hypertension. S. japonicum produces a similar clinical picture. The Katayama syndrome may be present in S. mansoni and S. japonicum infections (fever/skin rash/eosinophilia/cough). For the diagnosis of S. hematobium the eggs of the fluke should be sought for in the urine (terminal portion), feces or biopsy (bladder/rectum). I.V.P. and cystoscopy are useful. For S. mansoni and S. japonicum the eggs may be present in the stools or in biopsies of intestine or rectum. Serological and skin tests are also available.

Niridazole (Ambilhar) has been used for S. hematobium and S. mansoni infections. (at present the drug is only available from special units).

Dose: An oral dose of 25 mg./Kg. of B.W./day (Maximum 1.5 mg.) is given for 5-7 days. Adverse effects include dizziness, mental changes, seizures, vomiting, E.C.G. changes, skin rashes and hemolysis (G-6-PD deficiencies). The drug should not be used where there is hepatic dysfunction, portal hypertension or a history of seizures. Some prefer the use of Stibophen for S. mansoni infections. S. japonicum is difficult to eradicate and Antimony Potassium Tartrate has been used.

7. TAPEWORMS.
A. TAENIA SAGINATA (Beef tapeworm).

This cestode has a worldwide distribution and humans become infected by eating raw beef (a delicacy with a fair number of Canadians). Most subjects have no symptoms, but abdominal pain, vomiting and the observation of proglottides around the anus may be a feature of the infection. Diagnosis is by finding the eggs or proglottides in the stools. The drug of choice is Niclosamide (Yomesan), but the drug should not be given to children under the age of 2 years.

Dose—adults and children over the age of 6 years—a single oral dose of 2 gm. is given. Children between the ages of 2 and 6 years are given 1 gm. The drug should be taken after a light meal. The tablets should be chewed before being taken with water. Adverse reactions are rare (mainly gastrointestinal). Mepacrine has also been used.
B. TAENIA SOLIUM. (Pork Tapeworm).

This is acquired by eating raw or poorly cooked pork. The adult worm gives a similar picture to the beef tapeworm as far as the clinical picture is concerned. However the cysticerci may cause lesions in a wide range of tissues, and treatment is only symptomatic. The tapeworm is detected by detecting the ova in the stools. Niclosamide is used to treat the tapeworm infection, but is not without danger. (risk of auto-infection). The dosage is the same as that mentioned for the beef tapeworm, but in order to lesson the risk of causing cysticercosis, a purgative should be given 2 hours after the drug is taken.

C. DIPHYLLOBOTHRIUM (Fish tapeworm).

Man is infected by eating raw contaminated fish. It usually produces little in the way of symptoms, but can be associated with a B12 vitamin deficiency (megaloblastic anemia). Niclosamide is the drug of choice (same doses as for the other tapeworms).

D. DWARF TAPEWORM

The small tapeworm, Hymenolepis nana, rarely gives clinical signs or symptoms. Treatment is with Niclosamide.

Dose-Adults and children over 6 years of age-2 gm. on the first day, then 1 gm. daily for 6 days. Children between the ages of 2 and 6 years should be given 1 gm. on the first day and then 0.5 gm. daily for 6 days. For good results a second course can be given 3 week after the above therapy.

8. PINWORM (Enterobiasis).

This ubiquitous parasite is the commonest helminth with the worst "therapeutic" record. It is difficult to eradicate and occurs in all members of a family. Clinical features include pruritus ani, vulvitis, insomnia and enuresis. Diagnosis is by perianal swab. Mothers may observe migration of the worms (perianal) in their children at night. All the family should be treated. General hygiene is important (particularly to remove eggs from under the finger nails). Pyrantel pamoate is the drug of choice. Given orally as a single dose, the dosage is the same as that used for ascaris, and the same precaution should be observed. The dose should be repeated after 2 weeks.

Or Piperazine citrate can be given:

Daily dose - Up to 15 lb. of B.W. - 250 mg.
15 - 30 lb. of B.W. - 500 mg.
30 - 60 lb. of B.W. - 1 gm.
Over 60 lb. B.W. & Adults - 2 gm.

The drug is given for 7 days, withheld for 7 days and then given for another 7 days.
Pyrvinium pamoate is also used.

**Dose**—single oral dose of 50 mg./22 lb. B. W. This can be repeated after 2 weeks.

In summary the family physician can expect to see an increasing number of patients who are hosts to an unwanted helminth. A good medical history will help to narrow down the list of possible culprits (Unde venis-Where have you been?/What have you eaten?). Good follow-up is essential, and it is worth mentioning that fact that post-therapy stool examinations should not be carried out straight after drug therapy as residual eggs of the worm will be present for some time after the cessation of therapy.
CHAPTER 7

NOTES ON SOME TROPICAL DISEASES.

(For notes on helminthic infections please see previous section on worms).

BALANTIDIOSIS.

This is relatively rare but on occasions may produce severe dysentery. Infection is acquired by ingesting the cysts (passed in the feces of pigs). In the acute case the parasite is found in the stools, but in chronic infections the cysts are present in the stools. Tetracyclines are effective therapy.

CHOLERA.

An acute infection due to the Vibrio cholerae presenting clinically with vomiting, cramps and watery diarrhea. Water or food are usually involved in the transmission of the disease. Incubation period is about 3-6 days and the vaccine does not offer total protection against the disease. Dehydration and shock are the main risks. Diagnosis is by finding the organism in the stools. El Tor cholera has been seen in many countries. Treatment is directed to correcting the dehydration and shock and correction of electrolyte imbalance and the administration of a suitable antibiotic (e.g. Tetracyclines for 3-5 days). At least three stool samples should be negative before the patient is declared free from the infection. Immunity, by vaccination lasts for some 3-4 months.

DENGUE FEVER.

This arbovirus has been associated with fever, rashes, muscle pains and hemorrhagic syndromes (which have a high death rate). The incubation period is 5-10 days. Treatment is essentially symptomatic.

DRACONTIASIS.

The guinea-worm is found in India and Africa. The infection is transmitted through water, via Cyclops. The female worm usually inhabits the connective tissues of the trunk and limbs. In over three-quarters of the cases the lower extremities are involved, the patient complaining of discomfort and blistering. Treatment involves extraction of the parasite and Hetrazan and Niridazole have also been used.

FILARIASIS.

Several nematodes of the family Filariidae are associated with human disease. The parasite is transmitted by the bite of infected insects (e.g. mosquitoes & Black flies) the adult worms usually inhabit the lymphatic tissues, skin or
connective tissues. Incubation periods are long (up to 12 months or longer) and the short-stay visitor is not commonly affected.

A. *Wuchereria bancrofti.*

This is found in many areas including tropical Africa, Asia, South America and some South Pacific zones. The adult worms usually lie in the lymphatic tissues, and the microfilariae can be observed in the peripheral blood at night (10 p.m. - 2 a.m.). Light infections are often symptomless but heavier ones may produce interference with lymph flow. Clinical presentations include pyrexia, lymphangitis and elephantiasis. Diagnosis is confirmed by detecting the microfilariae in suitable blood films. Complement-fixation and intradermal tests are also useful. There is often an associated eosinophilia. Diethylcarbamazine is used to treat the condition, but must be given with care because of the risk of acute "allergic" reaction.

B. *Brugia malayi.*

This worm is present in such areas as China, Malaysia and Sri Lanka. Essentially it resembles *W. bancrofti* infections. Diagnosis is by detecting the microfilariae in the peripheral blood (these may be nocturnal or present in the day). Treatment is with diethylcarbamazine.

C. *Loa loa.*

Loa loa is confined to West and Central Africa. The adult worm lives in the subcutaneous tissues. Clinical features include Calabar swellings (transitory edematous swellings in the skin), fever, eosinophilia and occasionally the movement of the worm in the skin or across the eye may be noticed. Diagnosis is by the detection of the microfilariae in the blood (day time sample). Treatment is with diethylcarbamazine.

D. *Onchocerciasis.*

This is found in tropical Africa, and parts of Central and South America. It is transmitted by flies of the genus *Simulium.* Clinical features include subcutaneous nodules (which contain the adult worm), skin rashes and eye lesions which remain the most dreaded complication of the disease, for these may lead to blindness. The conjunctiva may be involved and chronic iritis and cataract can develop. Diagnosis is by biopsy of the nodules. Microfilariae are sometimes seen in skin samples and occasionally in the anterior chamber of the eye. A high eosinophilia can be present. Diethylcarbamazine is effective but there is a risk
of allergic eye reactions, and the drug is best given with concomitant antihistamines or steroids. Other drugs have also been used e.g. Suramin.

GIARDIASIS.

Although this parasite is present throughout the world (it has recently been in the public eye after a good number of visitors to Russia became infected with it), it is commonly seen in visitors returning from the tropics and clinical features include abdominal discomfort, flatulence, diarrhea and malabsorption syndromes. It is common in overlanders. Giardia lamblia inhabits the upper part of the small intestine and duodenum and humans are infected by ingesting the cysts of the parasite. Many patients remain symptomless. Diagnosis is by finding the cysts in the stools. Drugs used to treat the infection include metronidazole and mepacrine.

LARVA MIGRANS.

In this condition larvae of nematodes enter the human subject and although the worm may develop no further, the subject sometimes experiences a wide range of clinical symptoms. Skin lesions may be produced by the larvae of Ancylostoma braziliensis or Strongyloides stercoralis. As there is usually no associated eosinophilia, the diagnosis is often made on clinical grounds. In treatment local freezing (ethyl chloride) may suffice. Thiabendazole has been used for strongyloides infections. Sometimes the larval forms of nematodes inhabit the viscera and produce severe signs and symptoms. Thus Toxocara canis and T. cati may be involved. A high eosinophilia can be present, along with hepatomegaly, fever and respiratory syndromes (cough and asthma). Sometimes retinal lesions are to be seen and investigations indicate hypergammaglobulinemia. Diagnosis is by finding the larvae in biopsy samples (e.g. liver). Diethylcarbamazine and thiabendazole have been tried in the treatment of the condition.

LASSA FEVER.

This is virus infection (probably originating in an animal reservoir) and was first noted in Nigeria. Clinical features include hemorrhagic fever, vomiting, diarrhea and abdominal pain, cough, chest pain, renal failure, myocarditis, and encephalopathy. It carries a high fatality rate. Although rare it constitutes a real hazard as far as "imported" tropical disease goes and strict precautions and isolation must be observed for suspected cases.
LEISHMANIASIS.
A group of disease due to infection with protozoa of the genus Leishmania, transmitted to humans by sandflies.

Visceral Leishmaniasis (Kala azar).
This is associated with L. donovani and found in India, tropical Africa and parts of the Middle-east. The parasite is seen in the reticulo-endothelial system and a leucopenia is sometimes present. The incubation period is long (up to several years) and clinical features include splenomegaly, anemia, lymphadenopathy and reversal in the A/G ratio. Some subjects develop a post Kala azar dermal skin lesion. Diagnosis is by finding the Leishman-Donovan bodies in marrow samples or lymph node biopsy or liver samples. Skin tests and fluorescent antibody techniques are also used. Culture methods are available as well. Drugs used to treat the condition include Sodium Stibogluconate, Meglumine antimonials and Pentamidine isethionate.

Cutaneous Leishmaniasis. (Oriental Sore)
This is caused by L. tropica and the incubation period ranges from several weeks to several years. The nodular lesions (usually face or limbs) may lead to ulcers. There is no systemic involvement and diagnosis is confirmed by finding the parasite in samples taken from the edge of the ulcer. Drugs used to treat the infection include Cycloguanil pamoate, metronidazole and dehydroemetine dihydrochloride.

Mucocutaneous Leishmaniasis.
This is present in South America and is caused by L. braziliensis. Different types of the disease are recognised and lesions involve the face or limbs. Diagnosis is by finding the parasite in aspiration samples of the lesion or in biopsy samples. Intradermal tests are also available. Treatment is similar to that of oriental sore.

LEPROSY.
This disease has a wide distribution in the globe, but is most common in tropical areas. It is caused by M. leprae. The incubation period is long, from 1-10 years. Several forms of the disease are recognised:
Lepromatous.
Tuberculoid.
Dimorphous.
Indeterminate.
This spectrum of different forms represents the subject's immune response to the disease.

If resistance is low, the lepromatous form is seen, and many body tissues are involved (e.g. nerves, skin, reticulo-endothelial system, testes, nose and eyes). The tuberculoid form is seen where resistance is high. Nerves are involved, becoming thickened and anesthesia or muscle weakness develop. In dimorphous infections the features are related to the subject's resistance, which lies between the first two types mentioned. Indeterminate leprosy is seen in those who give a clinical picture which may develop into the other three types or else clear up.

The disease can produce a vast range of clinical features including:

**Lepromatous leprosy**
- Macules, papules or nodules (usually on face or limbs).
- Destruction of nasal cartilage, ulceration of the legs and ichthyosis.
- Thickening of the peripheral nerves (great auricular, ulnar and lateral popliteal).
- Sensory impairment, muscle palsies and claw hand.
- Absence of corneal reflex.
- Atrophy of digits. Eye changes (keratitis, iritis and opacities)
- Atrophy of bones.
- Atrophy of the testes.
- Renal damage (nephritis and amyloidosis).

**Tuberculoid leprosy.**
- Dermal or neural symptoms are present. When nerves are involved, pain loss of sensation, paraesthesiae or muscle weakness may appear. Cranial nerves are sometimes involved. Dermal lesions are usually single (plaque) and local nerves can usually be palpated when thickened. Skin lesions are erythematous, scaly with well defined edges, and there is impairment of hair growth over the lesion.

**Dimorphous leprosy.**
- This is probably the commonest form of the disease and has features which lie between the previous two forms. There may be thickening of the nerves with muscle paralysis and anesthesia of the skin. Skin lesions are more numerous (macules, punched-out lesions and nodules).

**Indeterminate leprosy.**
- Seen in children and several hypopigmented macules and slight anesthesia may be present. The disease may heal or develop into one of the other forms.

**DIAGNOSIS.**
1. Skin smears.
3. Biopsy of nerves.
4. Biopsy of skin.
5. Histamine test.
The history might raise the possibility of the disease being present and in carrying out a physical examination loss of sensation should be looked for. Thicken nerves can be felt on palpation. Biopsy of the skin is useful for classifying the disease. In the differential diagnosis syphilis, yaws, fungal infections, leishmaniasis, filariasis and skin conditions such as lichen planus must all be considered. The lepromin test is non-specific and is used more for classifying the disease rather than diagnosis. False positive tests for syphilis may be obtained in leprosy and some tests for auto-immune conditions may yield a false positive. Several reactional syndromes have been described in leprosy (e.g. Lepra reaction and Lucio phenomenon).

Drugs used to treat the disease include Dapsone, Thiambutosine and Rifampicin. General medical and surgical care are of importance.

**LYMPHOGRANULOMA VENEREUM.**

This virus is related to the psittacosis-trachoma group of viruses. In males the initial primary sore is usually on the penis, but in females the primary lesion may pass unobserved. Later the infection involves the regional lymph nodes. Later complications include fistulae, strictures and an anorectal syndrome. Diagnosis is by demonstrating the virus in a smear from the lesion, lymph node biopsy, Frei skin test and complement fixation test. Sulfonamides and tetracyclines have been used to treat the infection. Sometimes surgical procedures are indicated.

**MALARIA—please see earlier notes on this infection.**

**MYIASIS.**

This denotes a group of conditions due to an infection with the larvae of various flies (e.g. Cordylobia anthropophaga or the Tumbu fly). The larvae are capable of invading open wounds, the intestines, eyes or ears. Treatment involves removal of the larvae and symptomatic measures.

**PARAGONIMIASIS.**

This is due to the trematode *P. westermani* in such areas as Korea, China, Japan and the Philippines. Infection is usually by humans eating raw crabs. The adult worm lives in the lungs and other tissues. Clinical features include fever, cough, hemoptysis, and a chest X-ray films may resemble Tb. Occasionally the C.N.S. is involved. To make the diagnosis the eggs of the parasite should be sought in the sputum and stools. Intradermal and complement fixation tests are available. Often there is a moderate eosinophilia. Bithionol is the drug used for treatment, but chloroquine has also been used.
SMALLPOX.
This infection represents one of the most significant risks of "imported" disease, and the physician should always keep this disease in mind.

TRYPANOSOMIASIS.
AFRICAN TRYPANOSOMIASIS.-This parasite is transmitted to man by the bite of infected tsetse flies. Two strains of trypanosomes are involved in man, T.gambiense and T. rhodesiense, and in the main these two parasites produce a similar clinical picture, but T. rhodesiense is associated with earlier involvement of the C.N.S. and is more difficult to treat. The disease is seen in many parts of tropical Africa. The parasite occurs in the blood, lymphatic system and C.N.S. The incubation period ranges from several weeks to several years and early clinical features include fever, rashes and areas of transient edema. Lymphadenopathy may be seen and as the C.N.S. becomes involved headache, drowsiness and personality changes can be observed. Speech difficulties, tremors and muscle weakness are also seen when the nervous system is involved. Diagnosis is by finding the parasite in blood films or in a fresh aspirate sample obtained from affected lymph nodes. In later stages of the disease the trypanosomes may be detected in the C.S.F., which then also shows an increase in cells and protein content. Serological tests are available as well. Pentamidine and Suramin have been used to treat the disease, and Pentamidine has been used for chemoprophylaxis.

AMERICAN TRYPANOSOMIASIS. (Chagas's Disease).
The parasite is transmitted to man by the bite of a reduviid bug and is present in South and Central America. Following the initial infection there may be swelling of the local lymph nodes and sometimes unilateral swelling of the tissues around the eye (Romana's sign). Other clinical features include pyrexia, tachycardia, enlargement of the liver and spleen and cardiac complications (arrhythmias and cardiomyopathy). Diagnosis is by finding T. cruzi in the blood or the leishmanoid forms in the tissues (e.g. muscles). Blood cultures, xenodiagnosis and complement fixation tests have also been used. Treatment is unsatisfactory, but primaquine and Bayer 2502 have been used.

YAWS. (Framboesia).
This infection is due to treponema pertenue and is a disease which mainly affects the indigene rather than the visitor. Primary, secondary and tertiary stages are recognised. Granulomatous lesions may involve many tissues. The disease should be differentiated from syphilis. Penicillin is effective in treating the disease.
CHAPTER 8
THE CHEMOTHERAPY OF SOME PARASITIC DISEASES.

Many of the drugs used to treat parasitic infections have potential adverse reactions and in all cases the "benefit to risk" ratio should be assessed. Examples of toxic drugs include emetine, niridazole, antimony compounds and the arsenicals. Sometimes the death of a parasite is associated with a violent "allergic" reaction in the host and steroids or antihistamines may be needed (e.g. in schistosomiasis or onchocerciasis). Antiparasitic drugs should not be used in pregnancy unless they are essential.

BEPHENIUM HYDROXYNAPHTHOATE.

This is used in ancylostomiasis and is usually well tolerated. Adverse reactions include nausea, vomiting and diarrhea.

DOSE (Adult).

Necator americanus- 5GM. b.i.d. for three days. This is taken in water 2 hours before food. Given orally.

Ancylostoma duodenale- 5 GM. b.i.d. for one day.

(N.B. When re-checking the feces for the presence of any eggs of the worm, at least 3 weeks should be allowed to lapse after treatment).

BITHIONOL.

The toxic effects include vomiting, diarrhea, skin rashes and albuminuria.

DOSE (Adult).

Paragonimus westermani infections-30-50 mg./kg. on alternate days for 10-15 doses, given orally.

Similar doses have been used for clonorchis infections.

CHLOROQUINE.

This is widely used as an antimalarial. It is effective against the asexual erythrocytic forms of the parasite. However it does not prevent relapses in subjects with P.vivax and P.malariae infections as it is not effective against the exo-erythrocytic forms of the parasite.

Indications. To suppress attacks of malaria due to P.vivax, P.malariae and P. falciparum (where the parasite is not resistant). It is also used in the therapy of amebiasis (extraintestinal) and clonorchis sinensis.
Contraindications. It should not be given to those with a history of hypersensitivity to the 4-aminoquinolines or subjects with significant ocular pathology (especially retinal or visual field changes).

Precautions. Some strains of P. falciparum are resistant to the drug. When the compound is given for long periods of time regular ophthalmological examinations should be carried out. If any visual signs or symptoms are noted the drug must be discontinued, and the subject followed up. The drug may exacerbate porphyria or psoriasis. The drug should be used with caution in those with hepatic disease or G-6-PD deficiency.

ADVERSE EFFECTS.

These include headache, vomiting, pruritus, GI upsets, convulsions, hallucinations, neuromyopathy and blood dyscrasias. Eye changes represent the most significant potential risk. Blurring of vision or difficulty in focussing may be seen but these are usually reversible and disappear on discontinuing the drug. Other more serious changes have been noted in association with long term therapy including corneal changes (edema and deposits) and retinal changes (including optic atrophy).

DOSAGE.

For use as an antimalarial please see notes on malaria.

Amebic Hepatic Abscess- Chloroquine phosphate-1 GM. daily is given orally for two days, then 500 mg. daily is given for 21 days.

Clonorchis sinensis infections- Chloroquine phosphate-250 mg. t.i.d. is given orally for 6 weeks.

Paragonimus westermani infections- Chloroquine phosphate is given orally-250 mg. t.i.d. for 6 weeks.

DAPSONE.

This drug has been used in leprosy and malaria. Toxic effects include fever, anemia, skin rashes, psychoses and methemoglobinemia. Subjects with G-6-PD deficiency may develop a hemolytic anemia.

Dose- Leprosy-doses of 25 mg.-100 mg./week have been used.

Malaria- In chemoprophylaxis daily doses of dapsone 25 mg. have been given in association with weekly doses of chloroquine (300 mg. base) and 45 mg. primaquine (base).

The drug has also been used to treat acute chloroquine-resistant P. falciparum malaria (25 mg. orally, daily for 28 days)
DEHYDROEMETINE.

This is a toxic drug with similar properties to emetine. The main toxic effects relate to the heart (arrhythmias) and patients receiving the drug should have cardiac monitoring.

Dose

Amebiasis (Severe intestinal disease) - Dehydroemetine 1.0-1.5 mg./kg. daily given I.M. or S.C. for 5 days.

Amebic Hepatic Abscess  - Dosage as above.

The drug has also been given orally (as dehydroemetine bismuth iodide or the resinate). It has also been used in the therapy of cutaneous leishmaniasis and schistosomiasis.

DIETHYLCARBAMAZINE.

This piperazine derivative is used to treat filariasis and pulmonary tropical eosinophilia. Toxic effects include vomiting and dizziness. The death of the microfilariae may be associated with severe allergic reactions and antihistamines and steroids have been used to cover these adverse effects. The drug must be used with great care in onchocerciasis. It may produce itching, lymph node enlargement, fever or a rash. If a patient has eye involvement with onchocerciasis then steroids should be given several days before therapy is initiated and during treatment. Both cortisone drops and systemic steroids have been used to prevent allergic reactions to anti-filarial drugs.

Dose.

Wuchereria bancrofti.
Brugia malayi.
Loa loa.
Tropical Pulmonary Eosinophilia.

For all the above infections, Diethylcarbamazine citrate (Hetrazan) is given orally at a dose of 2 mg./kg. t.i.d. for 14 days.

Onchocerca volvulus (River Blindness)

Diethylcarbamazine citrate is given orally-(Adults).

25 mg. daily for 3 days.
50 mg. daily for 5 days.
100 mg. daily for 3 days.
150 mg. daily for 12 days.
In order to kill the adult worm the above should be followed by a course of Suramin (see notes on the drug) which is very toxic. In adults a test dose of 100 mg. of Suramin is given intravenously. If this is tolerated then 1.0 gm. of the drug is given intravenously once a week for 5 weeks.

**DIODOHYDROXYQUIN.**

This have been used to treat asymptomatic cyst "passers" of Entameba histolytica. Toxic effects include skin rashes, nausea and thyroid enlargement. Optic neuritis has also been associated with use of the drug.

**Dose (Adults).**

650 mg. t.i.d. for 20 days given orally.

**DILOXANIDE FURATE.**

This is a well tolerated compound used to treat asymptomatic intestinal amebic infections and mild amebic dysentery.

**Dose (Adults).**

0.5 Gm. t.i.d. for 10 days.

**EMETINE.**

This toxic drug is used to treat amebiasis. Adverse effects include cardiac damage, hepatic and renal damage. Local reactions may be seen also (including myositis). Some 50% of subjects show E.C.G. changes. (flattening or inversion of T wave and prolonged QT interval). Vomiting and diarrhea may be produced by the drug. The drug must not be given to those with cardiac, renal or hepatic dysfunction and should be avoided in pregnancy.

**DOSE (Adults).**

It is given by the S.C. or I.M. route (maximum daily dose is 65 mg.) 1mg/kg./B.W. For normal adults a daily dose of 65 mg. is given for 10 days or less. The patient should have bed rest and cardiac monitoring is essential. Given by injection the drug has no effect on intestinal luminal infections and emetine bismuth iodide tablets have been used for luminal infections (Adults-oral dose of 200 mg./day for 10 days).

**MEBENDAZOLE.** (Vermox)

Because of limited clinical experience this drug should not be used in children under two years of age, and it is contraindicated in pregnancy. It has been used to treat Trichuris, Ascaris, Hookworm and Pinworm infections. Adverse effects include abdominal pain and diarrhea.

**Dose (Children and adults).**

(For trichuriasis, ascariasis and hookworm infections)-Mebendazole-100 mg. tablet-I tablet b.i.d. on three consecutive days. (For pinworm infections a single tablet is given).
Mepacrine.

As an antimalarial, mepacrine has a similar action to chloroquine and quinine, but it is now very little used as an antimalarial. It has a place in the therapy of tapeworm infections and giardiasis. Adverse effects include a yellow staining of the skin and urine. Headaches, vomiting, skin rashes and mental changes have also been reported. It should not be given with 8-aminoquinoline drugs as there is increased toxicity.

Dose
As a teniacide.
Mepacrine hydrochloride (Adult dose) given orally. Patient is put on a bland non-fat diet the day before. A saline purge is given, and the subject should fast from the previous evening. A total of 600-800 mg. of the drug is given. (200 mg. at 10 minute intervals). Sodium bicarbonate should be given with each dose to prevent vomiting. Another purge is given two hours after the last dose, and if possible the scolex of the worm should be identified. It should not be used for T. Solium infections. (Risk of cysticercosis).

Giardiasis.
Mepacrine hydrochloride-100 mg. is given orally t.i.d. for 7 days. (Adults).

Metronidazole.
This is effective in amebic dysentery and amebic hepatic abscess, and has been used to treat giardiasis. Adverse reactions include headache, vomiting, skin rashes and leucopenia. It darkens the urine and can produce a bitter taste in the mouth.

Dose (Adults).
(N.B. Alcohol is contraindicated several days before, during and several days after therapy).

Amebiasis.
Asymptomatic cyst passer-Metronidazole 750 mg. t.i.d. orally for 7-10 days.
Moderate intestinal disease-Metronidazole 750 mg. t.i.d. orally for 7-10 days.
Severe intestinal disease-Metronidazole 750 mg. t.i.d. orally for 7-10 days.
Hepatic Abscess-Metronidazole 750 mg. t.i.d. orally for 7-10 days.
(N.B. Cases of amebic hepatic abscess have been reported when the drug has been used as the sole therapeutic agent to treat intestinal amebic infections and the drug has been given in association with other compounds in an effort to prevent this (e.g. with chloroquine).
GIARDIASIS.

Dose (Adults)
Metronidazole-500 mg. t.i.d. orally for 5-10 days.

NICLOSAMIDE (Yomesan).
This is well tolerated and is used to treat tapeworm infections.

Taenia saginata
Taenia solium.

Diphyllobothrium latum
Niclosamide-2 gm. is chewed thoroughly and taken as a single dose after a light meal. (N.B. with T. solium infections the drug breaks up the segments of the worm and the release of the eggs may cause cysticercosis).

NIRIDAZOLE. (Ambilhar).
This compound is effective in schistosomiasis, the best results being obtained in S. hematobium infections. The drug is metabolized rapidly in the liver and its metabolites color the urine dark brown. Adverse effects include vomiting, headache, skin rashes, hemolytic anemia and C.N.S. changes (convulsions, psychoses and confusion). C.N.S. effects may be marked when the patient has hepatic dysfunction, and are due to the unmetabolized drug. Thus the drug must be given with caution to those with impaired hepatic function. Likewise it must be administered with caution to subjects with significant renal disease. E.C.G. changes which may be observed when the compound is given include flattening of the T waves and S-T depression.

Dose.
Schistosoma hematobium.
Niridazole-given orally-25 mg./kg. of body weight, daily. (maximum 1.5 gm.) for 5-7 days.

A similar dosage can be used for S. mansoni infections, but some prefer to use stibophen for that infection. Antimonyl potassium tartrate is given for S. japonicum infections.
N.B. Because of the toxicity of the drug, patients on the drug must be carefully observed.

PALUDRINE (Paludrine/Chloroguanide)-see notes on chemotherapy of malaria.

PENTAMIDINE.
This is used in early trypanosomiasis (Gambiense/Rhodesiense). It is of no use if the C.N.S. is involved. It has also been used in visceral leishmaniasis and in the prophylaxis of trypanosomiasis. Adverse effects include hypotension, hypoglycemia and vomiting.
Dose.
T.gambiense (hemolytic stage)-Pentamidine 4 mg./kg. of body weight I.M. daily for 10 days. A similar dose has been given for T. rhodesiense (hemolytic stage), but Suramin is preferable as a first choice.
(N.B. for T.rhodesiense and T.gambiense infections with C.N.S. involvement Melarsoprol is used. The dose is 2-3.6. mg./kg. of body weight I.V. daily for 3 doses. After one week 3.6 mg. is given I.V. daily for three doses.
Treatment may be repeated after 12-21 days. Adverse effects include cardiac damage, hypertension, albuminuria, encephalopathy, shock and peripheral neuropathy).
Chemoprophylaxis (African trypanosomiasis)
This may be considered for subject at "high" risk.
Pentamidine is given-4mg./kg. of body weight given I.M. every 3-6 months.
PIPERAZINE CITRATE.
This compound is used to treat ascariasis and enterobiasis (pinworm). Adverse effects include vomiting and headache, and the drug should be used with caution in children as larger doses can produce C.N.S. changes (tremors and vertigo). It should not be administered to those with a history of epilepsy or renal impairment.
Dose.
Ascariasis.
Up to 30 lb. of body weight.-I.0 Gm. daily.
30 - 50 lb. " -2.0 Gm. daily.
50 - 100 lb. " -3.0 Gm. daily.
Over 100 lb. " -3.5 Gm. daily.
The drug is given for 2 days. Both tablets and syrup are available.
Enterobiasis.
Up to 15 lb. of body weight.-250 mg. daily.
30-60 lb. " -1000 mg. daily.
Over 60 lb. " -2000 mg. daily.
The drug is given orally for 7 days, withheld for 7 days then given for another 7 days.
PRIMAQUINE PHOSPHATE.- see notes on malaria.
PYRANTEL PAMOATE. (Combantrin)
This preparation is indicated for the treatment of pinworm, hookworm and ascaris. Adverse reactions include vomiting, diarrhea and headache. It is given orally.
Dose.-see notes on "worms"
PYRIMETHAMINE-see notes on malaria.
PYRVINIUM PAMOATE.
A useful drug for the treatment of pinworm, but has the disadvantage of staining the stools red. Usually well tolerated.
Dose.
50 mg/22 lb. of body weight, given as a single dose.
QUININE.
This toxic drug has a place in the therapy of malaria and its toxic effects include visual changes, cinchonism, hypotension and cardiac arrhythmias. For dosage see notes on malaria.
SULFONAMIDES.
Sulfonamides have been used for the chemoprophylaxis of malaria, but in view of the potential risks of long term administration of these compounds, they are not recommended for routine prophylaxis. However they have a place in the treatment of chloroquine-resistant malaria. (see notes on malaria).
SURAMIN.
This is used in the therapy of trypanosomiasis and onchocerciasis. It is very toxic (adverse reactions include shock, neuritis, albuminuria, hepatic damage and photophobia). It should be noted that the drug is not effective when the C.N.S. is involved in trypanosomiasis.
Dose.
Trypanosomiasis (T.gambesiense/T.rhodesiense)-100-200 mg. test dose I.V. then 1.0 Gm. IV on days 1,3,7,14 and 21.
It is not effective in South American trypanosomiasis.
(In onchocerciasis suramin 100-200 mg. test dose IV, then 1 Gm. IV at weekly intervals for 5 weeks is given in association with a course of diethylcarbamazine).
TETRACYCLINES.
Tetracyclines have been used to treat amebic infections (always in association with other drugs), balantidiasis and in addition they have some antimalarial effects.
THIABENDAZOLE. (Mintezol)
This drug is a broad spectrum antihelminthic, but used mainly in trichuris trichuria infections (though mebendazole is more effective) and cutaneous larva migrans. It has also been used in trichinosis and hookworm infections. Adverse effects include dizziness, headache, vomiting, skin rashes and leucopenia.
Dose.
Trichuris trichuria-25 mg./kg. of body weight b.i.d. for 2 days.
Trichinosis. -25 mg./kg. of body weight b.i.d. until symptoms are reduced or toxic effects are present.
Hookworm infections-25 mg./kg. of body weight for 2 days. B.I.D.
The drug is given orally.

GENERAL CONSIDERATIONS.
1. When ascaris is present in association with other intestinal helminths, ascaris should always be treated first.
2. Where possible follow up tests should be done after treatment of any parasitic disease. Sometimes these should be done for many months after therapy. (e.g. in amebiasis).
3. Where the drugs concerned are highly toxic, the physician must assess the benefit to risk ratio for each individual case.
CHAPTER 9.

SOME CLINICAL CONSIDERATIONS.

A. PARASITE NEUROSIS.

One point to stress is that some subjects develop a significant fear of parasites on their return from the tropics, and the physician must be careful not to encourage such a complex. This is most often seen in individuals who have had amebic dysentery or who have heard of the disease. Years after returning from the tropics they attribute any symptoms, especially those relating to the G-I tract, to a possible amebic infections, and in spite of negative tests they travel from physician to physician in an effort to identify a non-existent parasite.

B. CO-EXISTENT DISEASE.

The physician should be careful not to ascribe all the patient's symptoms to a particular parasite, and care should be taken not to overlook any associated organic disease. Thus one student, in his mid-twenties was seen on account of vague abdominal symptoms. The history revealed that two years previously he have been in South America. The subject mentioned that previous stool examinations had been negative, but these had been preserved samples. Examination of a fresh stool sample showed evidence of a heavy giardia infection. This responded to a course of metronidazole, and the subject had no further abdominal symptoms. However after several months his original symptoms re-appeared. Further review of his case revealed a history suggestive of a duodenal ulcer, and he responded well to a suitable diet and antacids. Further stool samples were negative.

C. MULTIPLE PARASITIC INFECTIONS ARE NOT RARE.

A 25 year old man, originally from Pakistan, but who had been in Canada for over a year, presented with a complaint of severe headache. His friends told him that he had "flu" but increasing doses of analgesics failed to ameliorate his symptoms. Peripheral blood films revealed the presence of P.vivax, and his symptoms soon responded to a course of chloroquine. As he intended to stay in Canada a course of primaquine was then given to eradicate his malaria. His blood picture soon returned to normal. However a routine W.B.C. several weeks later revealed an eosinophilia of over 25%-a finding which had not been present earlier. Examination of his stools revealed the presence of a hookworm infecction which responded to pyrantel pamoate. Thus even when one major parasite is found, one should always be on the lookout for other infections. Patients with amebiasis in association with other intestinal infections are by no means rare.
D. PROLONGED PURSUIT FOR PARASITES.
A young student from West Africa complained of painless hematuria. An obvious parasite to eliminate was *S. hematobium*, but repeated urine tests failed to reveal the eggs of the worm. An I.V.P. and blood work revealed no abnormalities. It was only on cystoscopy that the diagnosis was confirmed and he made a good recovery on niridazole. Another young male gave a history of a lengthy stay in India and Nepal, and on his return to Canada *giardia* had been found in his stools. He had been given a course of metronidazole and appeared well. However one year later he suffered from attacks of vague lower abdominal pain and some diarrhea. Repeated investigations and stool examination revealed no abnormalities. His symptoms persisted for many months and he was admitted to hospital for observation. Again fresh stool tests were negative. Months later fresh stool tests revealed the presence of *giardia*, and he was given a further course of metronidazole. He then remained symptom-free. Sometimes amebic infections and giardiasis are only detected many years after the original exposure, and one negative stool test does not mean too much.

E. "WE STOPPED THE MALARIA PILLS TOO EARLY, DOCTOR".
Many families return from the tropics and readily admit that they took their antimalarials incorrectly or stopped them too early. In most cases it is best to warn them that if they have an unexplained fever or malaise after their return, then the possibility of malaria must always be kept in mind and blood films must be done. Once they have been away from the tropics for several months there is little point in them taking further antimalarials.

F. ANEMIA IN CHILDREN RETURNING FROM THE TROPICS.
A mild degree of iron-deficiency type of anemia seems to be common in young infants returning from the tropics. In all cases it is essential to rule out the presence of any parasites or other causes (blood dyscrasias etc) but when this has been done many of these subjects have an unexplained anemia. Any persistent eosinophilia would lead one to continue to search for a possible parasite. In most of the cases the anemia gradually improves when the child is away from the tropics and presumably dietary causes play a role.

G. UNDE VENIS?-THE RIGHT TIME BUT THE WRONG DRUG.
A young Malaysian student lived in Europe for some 5 years. Following this she returned home for a five-week vacation. No antimalarials were taken. She developed episodes of fever but a search for malaria was negative. Prior to leaving for N. America *malaria* was eventually detected and she was given a course of Quinine.
In N. America she continued to have episodes of fever and *Plasmodium vivax* was seen on blood film examination. A short course of Chloroquine, followed by Primaquine resulted in a cure. Points to remember are that when an indigene from a malarious area spends several years out of the tropics, there is some loss of immunity to malaria and antimalarials may be needed when they eventually return home. Also for *P. vivax* infections, Primaquine is needed in order to effect a radical cure.

**H. PARASITES IN GENERAL PRACTICE?**

Is it worthwhile looking for parasites in a general practice unit? The answer is an emphatic yes, especially for the physician with a good number of peripatetic subjects. Thus in one general practice unit 60 subjects with a history of travel in the tropics were investigated, and 20 of these had positive findings (including *Entamoeba histolytica*, giadiasis, hookworm, ascariasis, schistosomiasis, tapeworm and trichuris). As these parasites constitute a threat to the individual and to the community, the investigation and treatment of parasitic disease is well worthwhile.
**Countries / Pays**

- **Required / Exigée**
- **Recommended / Recommandée**

<table>
<thead>
<tr>
<th>Country / Pays</th>
<th>Required / Exigée</th>
<th>Recommended / Recommandée</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afghanistan</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Albania</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Algeria</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>American Samoa</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Angola</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Argentina</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Australia</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Austria</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Bahrain</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Bangladesh</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Barbados</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Belgium</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Bermuda</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Bolivia</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Botswana</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Brazil</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>British Honduras</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>British Virgin Islands</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Brunei</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Bulgaria</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Burma</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Burundi</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Cameroon</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Cape Verde</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Ceylon (Sri Lanka)</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Country</td>
<td>Yellow Fever</td>
<td>Small Pox - On Return</td>
</tr>
<tr>
<td>------------------</td>
<td>--------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>CHAD</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>CHILE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHINA, PEOPLE'S REPUBLIC OF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHINA (TAINW) - CHINA (TAINW)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHRISTMAS ISLAND - (INDIAN OCEAN - OCEAN INDIA)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COLOMBIA - COLOMBIA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COMORO ARCHIPELAGO - TERRITOIRE DES COMORES</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CONGO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COOK ISLANDS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COSTA RICA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CUBA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CYPRUS - CYPRÉ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CZECHOSLOVAKIA - TCHÉCOSLOVAQUIE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DENMARK</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOMINICA - DOMINIQUE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOMINICAN REPUBLIC - REPUBLIQUE DOMINICAINE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EQUADOR - ÉQUATEUR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EGYPT - EGYPTE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EL SALVADOR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EQUATORIAL GUINEA - GUINÉE ÉQUATORIALE</td>
<td>R</td>
<td></td>
</tr>
<tr>
<td>ETHIOPIA - ÉTHIOPIF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FALKLAND ISLANDS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FAROE ISLANDS - ILES FÉROÉS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FLAT - FIDJI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FINLAND - FINLANDE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRANCE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRENCH POLYNESIA - POLYNÉSIÉ FRANÇAISE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GABON</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAMBIA - GAMBIE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GERMANY, DEMOCRATIC REPUBLIC OF ALLEMAGNE, RÉPUBLIQUE DÉMOCRATIQUE ALLEMANDE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GERMANY, FEDERAL REPUBLIC OF ALLEMAGNE, RÉPUBLIQUE FÉDÉRALE D'ALLEMAGNE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GHANA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* R: REQUIRED
* R: RECOMMENDED
<table>
<thead>
<tr>
<th>Country</th>
<th>Required/Exigé</th>
<th>Recommended/Recommandé</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gibraltar</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gilbert &amp; Ellice Islands</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Greece</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Greenland</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grenada</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guam</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guatemala</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Guernsey, Alderney and Sark</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Guernsey, Alderney et Sark</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Guinea</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Guyana</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Haiti</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Honduras</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Hong Kong</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hungary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iceland</td>
<td></td>
<td></td>
</tr>
<tr>
<td>India</td>
<td>*</td>
<td>R</td>
</tr>
<tr>
<td>Indonesia</td>
<td>*</td>
<td>R</td>
</tr>
<tr>
<td>Iran</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iraq</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Ireland</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isle of Man</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Israel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ivory Coast</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Jamaica</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jersey</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jordan</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Kenya</td>
<td>*</td>
<td>R</td>
</tr>
<tr>
<td>Khmer Republic</td>
<td>*</td>
<td>R</td>
</tr>
<tr>
<td>Kuwait</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laos</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lebanon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lesotho</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liberia</td>
<td>*</td>
<td>R</td>
</tr>
<tr>
<td>Libyan Arab Republic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liechtenstein</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease</td>
<td>Return</td>
<td>Country List</td>
</tr>
<tr>
<td>------------------</td>
<td>---------</td>
<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Yellow Fever</td>
<td></td>
<td>* Australia, Brazil, Cambodia, Egypt, India, Portugal, Thailand, Vietnam</td>
</tr>
<tr>
<td>Cholera</td>
<td></td>
<td>* Bangladesh, Cambodia, Egypt, India, Indonesia, Pakistan, Thailand, Vietnam</td>
</tr>
<tr>
<td>Smallpox</td>
<td>On Return</td>
<td>* Afghanistan, Bangladesh, Cambodia, Egypt, India, Pakistan, Thailand, Vietnam</td>
</tr>
<tr>
<td>Variola</td>
<td>AU Retour</td>
<td>* Burkina Faso, Congo, Cote d'Ivoire, Liberia, Nigeria, Sierra Leone, Sudan</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Country List</th>
<th>Required/Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luxembourg</td>
<td>*</td>
</tr>
<tr>
<td>Madagascar</td>
<td>*</td>
</tr>
<tr>
<td>Malawi</td>
<td>* R</td>
</tr>
<tr>
<td>Malaysia</td>
<td>* R</td>
</tr>
<tr>
<td>Maldives</td>
<td>* R</td>
</tr>
<tr>
<td>Mali</td>
<td>* R</td>
</tr>
<tr>
<td>Malta</td>
<td>* R</td>
</tr>
<tr>
<td>Mauritania</td>
<td>* R</td>
</tr>
<tr>
<td>Mauritius</td>
<td>*</td>
</tr>
<tr>
<td>Mexico</td>
<td>*</td>
</tr>
<tr>
<td>Monaco</td>
<td>*</td>
</tr>
<tr>
<td>Mongolia</td>
<td>*</td>
</tr>
<tr>
<td>Montserrat</td>
<td>*</td>
</tr>
<tr>
<td>Morocco</td>
<td>*</td>
</tr>
<tr>
<td>Mozambique</td>
<td>* R</td>
</tr>
<tr>
<td>Namibia</td>
<td>* R</td>
</tr>
<tr>
<td>Nauru</td>
<td>*</td>
</tr>
<tr>
<td>Nepal</td>
<td>* R</td>
</tr>
<tr>
<td>Netherlands</td>
<td>*</td>
</tr>
<tr>
<td>Netherlands Antilles</td>
<td>*</td>
</tr>
<tr>
<td>New Caledonia</td>
<td>*</td>
</tr>
<tr>
<td>New Caledonia and Dependencies</td>
<td>*</td>
</tr>
<tr>
<td>New Hebrides</td>
<td>*</td>
</tr>
<tr>
<td>New Zealand</td>
<td>*</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>*</td>
</tr>
<tr>
<td>Niger</td>
<td>* R</td>
</tr>
<tr>
<td>Nigeria</td>
<td>* R</td>
</tr>
<tr>
<td>Norway</td>
<td>*</td>
</tr>
<tr>
<td>Oman</td>
<td>*</td>
</tr>
<tr>
<td>Pacific Islands</td>
<td>*</td>
</tr>
<tr>
<td>People's Democratic Republic of Yemen</td>
<td>* R</td>
</tr>
<tr>
<td>People's Republic of Yemen</td>
<td>* R</td>
</tr>
<tr>
<td>COUNTRY - PAYS</td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td></td>
</tr>
<tr>
<td>* REQUIRED/EXIGÉE</td>
<td></td>
</tr>
<tr>
<td>PERU - PÉROU</td>
<td>R</td>
</tr>
<tr>
<td>PHILIPPINES</td>
<td>R</td>
</tr>
<tr>
<td>PITCAIRN ISLAND</td>
<td></td>
</tr>
<tr>
<td>POLAND - POLOGNE</td>
<td></td>
</tr>
<tr>
<td>PORTUGAL</td>
<td></td>
</tr>
<tr>
<td>PORTUGUESE GUINEA - GUINÉE PORTUGAISE</td>
<td></td>
</tr>
<tr>
<td>PORTUGUESE TIMOR - TIMOR PORTUGAIS</td>
<td></td>
</tr>
<tr>
<td>PUERTO RICO - PORTO RICO</td>
<td></td>
</tr>
<tr>
<td>QATAR</td>
<td></td>
</tr>
<tr>
<td>REPUBLIC OF KOREA - RÉPUBLIQUE CORÉE</td>
<td></td>
</tr>
<tr>
<td>ROMANIA - ROUMANIE</td>
<td></td>
</tr>
<tr>
<td>RWANDA</td>
<td></td>
</tr>
<tr>
<td>RYUKYU ISLANDS - ILES RYU-KYU</td>
<td></td>
</tr>
<tr>
<td>SAINT HELENA - SAINTE HELENE</td>
<td></td>
</tr>
<tr>
<td>SAINT KITTS-NEVIS-ANGUILLA</td>
<td></td>
</tr>
<tr>
<td>SAINT CHRISTOPHE ET NIÈVES ET ANGUILLA</td>
<td></td>
</tr>
<tr>
<td>SAINT LUCIA - SAINTE LUCIE</td>
<td></td>
</tr>
<tr>
<td>SAINT PIERRE &amp; MIQUELON</td>
<td></td>
</tr>
<tr>
<td>SAINT VINCENT</td>
<td></td>
</tr>
<tr>
<td>SAO TOME &amp; PRINCIPE</td>
<td></td>
</tr>
<tr>
<td>SAUDI ARABIA - ARABIE SAOUDITE</td>
<td></td>
</tr>
<tr>
<td>SENEGAL - SÉNÉGAL</td>
<td></td>
</tr>
<tr>
<td>SEYCHELLES</td>
<td></td>
</tr>
<tr>
<td>SIERRA LEONE</td>
<td>R</td>
</tr>
<tr>
<td>SINGAPORE - SINGAPOUR</td>
<td>R</td>
</tr>
<tr>
<td>SOMALIA - SOMALIE</td>
<td></td>
</tr>
<tr>
<td>SOUTH AFRICA - AFRIQUE DU SUD</td>
<td></td>
</tr>
<tr>
<td>SOUTHERN RHODESIA - RHODÉSIE DU SUD</td>
<td>R</td>
</tr>
<tr>
<td>SPAIN (EXCEPT CANARY ISLANDS) - ESPAGNE (EXCEPTE LES CANARIES)</td>
<td></td>
</tr>
<tr>
<td>CANARY ISLANDS - ÎLES CANARIES</td>
<td></td>
</tr>
<tr>
<td>SPANISH SAHARA - SAHARA ESPAGNOL</td>
<td></td>
</tr>
<tr>
<td>SUDAN - Soudan</td>
<td>R</td>
</tr>
<tr>
<td>SURINAM</td>
<td>R</td>
</tr>
<tr>
<td>SWAZILAND - SWAZILAND</td>
<td></td>
</tr>
<tr>
<td>SWEDEN - SUÈDE</td>
<td></td>
</tr>
<tr>
<td>SWITZERLAND - SUISSE</td>
<td></td>
</tr>
<tr>
<td>SYRIAN ARAB REPUBLIC - RÉPUBLIQUE ARABE SYRIENNE</td>
<td>R</td>
</tr>
</tbody>
</table>
**COUNTRY—PAYS**

<table>
<thead>
<tr>
<th>Country</th>
<th>Vaccination Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thailand—Thaïlande</td>
<td>R</td>
</tr>
<tr>
<td>Togo</td>
<td>R</td>
</tr>
<tr>
<td>Tonga</td>
<td>R</td>
</tr>
<tr>
<td>Trinidad and Tobago—Trinité-et-Tobago</td>
<td>R</td>
</tr>
<tr>
<td>Trucial Sheikdoms—Cheikhats sous régime de Traité</td>
<td>R</td>
</tr>
<tr>
<td>Tunisia—Tunisie</td>
<td>R</td>
</tr>
<tr>
<td>Turkey—Turquie</td>
<td>R</td>
</tr>
<tr>
<td>Uganda—Uganda</td>
<td>R</td>
</tr>
<tr>
<td>Union of Soviet Socialist Republics—Union des Républiques socialistes soviétiques</td>
<td>R</td>
</tr>
<tr>
<td>United Kingdom—Royaume-Uni</td>
<td>R</td>
</tr>
<tr>
<td>United Republic of Tanzania—République-Unie de Tanzanie</td>
<td>R</td>
</tr>
<tr>
<td>United States of America—États-Unis d'Amérique</td>
<td>R</td>
</tr>
<tr>
<td>Upper Volta—Haute-Volta</td>
<td>R</td>
</tr>
<tr>
<td>Uruguay</td>
<td>R</td>
</tr>
<tr>
<td>Venezuela</td>
<td>R</td>
</tr>
<tr>
<td>Viet-Nam (Republic of)—Vietnam (République Du)</td>
<td>R</td>
</tr>
<tr>
<td>Virgin Islands USA—Isles vierges des États-Unis d'Amérique</td>
<td>R</td>
</tr>
<tr>
<td>Wake Island</td>
<td>R</td>
</tr>
<tr>
<td>Western Samoa—Samoa-Occidental</td>
<td>R</td>
</tr>
<tr>
<td>Yemen—Yémen</td>
<td>R</td>
</tr>
<tr>
<td>Yugoslavia—Yougoslavie</td>
<td>R</td>
</tr>
<tr>
<td>Zambia—Zambie</td>
<td>R</td>
</tr>
<tr>
<td>Zaire—Zaïre</td>
<td>R</td>
</tr>
</tbody>
</table>

Travelers are advised that the vaccination requirements of countries in which they arrive are related to the health conditions in the country of departure and to health conditions in the countries in which travelers disembark during their journey.

Les voyageurs sont avisés que les exigences de vaccination des pays d'arrivée sont soumises aux conditions sanitaires du pays d'origine et aux conditions sanitaires existantes dans les pays de séjour.
RECOMMENDED READING.

2. Preservation of Personal Health in Warm Climates, Ross Institute of Tropical Hygiene, London U.K.
INDEX.

AMEBIASIS 29.
ANTIMALARIALS 17.
ASCARIS 38.
BALANTIDIOSIS 45.
BEPHENIUM 40, 52.
BITHIONOL 52.
CHLOROQUINE 19, 52.
CHOLERA 6, 45.
DAPSONE 53.
DEHYDROEMETINE 54.
DENGUE 45.
DIARRHEA 28.
DIETHYLCARBAMAZINE 54.
DIIDOHYDROXYQUIN 55.
DILOXANIDE 55.
DRACONTIASIS 45.
EMETINE 55.
EOSINOPHILIA 35.
FILARIASIS 45.
GAMMA GLOBULIN 8.
GIARDIASIS 47.
HALAZONE 5.
HOOKWORM 39.
IMMUNIZATIONS 5.
KATAYAMA SYNDROME 42.
LARVA MIGRANS 47.
LASSA FEVER 47.
LEISHMANIASIS 48.
LEPROSY 48.
LIVER ABSCESS 31.
LIVER FLUKE 41.
LOEFFLER'S SYNDROME 38.
LYMPHOGRANULOMA VENEREUM 50.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Page(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria</td>
<td>16</td>
</tr>
<tr>
<td>Mebendazole</td>
<td>55</td>
</tr>
<tr>
<td>Mepacrine</td>
<td>56</td>
</tr>
<tr>
<td>Metroxidazole</td>
<td>31, 56</td>
</tr>
<tr>
<td>Myasis</td>
<td>30</td>
</tr>
<tr>
<td>Niclosamide</td>
<td>42, 57</td>
</tr>
<tr>
<td>Niridazole</td>
<td>42, 57</td>
</tr>
<tr>
<td>Overlander Syndrome</td>
<td>36</td>
</tr>
<tr>
<td>Paludrine</td>
<td>20</td>
</tr>
<tr>
<td>Paragonimus</td>
<td>50</td>
</tr>
<tr>
<td>Pentamidine</td>
<td>57</td>
</tr>
<tr>
<td>Pinworms</td>
<td>43</td>
</tr>
<tr>
<td>Piperazines</td>
<td>39, 43, 58</td>
</tr>
<tr>
<td>Primaquine</td>
<td>21, 23</td>
</tr>
<tr>
<td>Pyrantel Pamoate</td>
<td>39, 58</td>
</tr>
<tr>
<td>Pyrimetamine</td>
<td>21, 23</td>
</tr>
<tr>
<td>Pyrvinium Pamoate</td>
<td>40, 44, 59</td>
</tr>
<tr>
<td>P.U.O.</td>
<td>33</td>
</tr>
<tr>
<td>Quinine</td>
<td>21, 27</td>
</tr>
<tr>
<td>Romana's Sign</td>
<td>51</td>
</tr>
<tr>
<td>Schistosomiasis</td>
<td>41</td>
</tr>
<tr>
<td>Smallpox Vaccine</td>
<td>6</td>
</tr>
<tr>
<td>Strongyloides</td>
<td>40</td>
</tr>
<tr>
<td>Tapeworms</td>
<td>42</td>
</tr>
<tr>
<td>Thiabendazole</td>
<td>40, 59</td>
</tr>
<tr>
<td>Trichuriasis</td>
<td>41</td>
</tr>
<tr>
<td>Trypanosomiasis</td>
<td>51</td>
</tr>
<tr>
<td>Typhoid Vaccine</td>
<td>7</td>
</tr>
<tr>
<td>Typhus Vaccine</td>
<td>8</td>
</tr>
<tr>
<td>Worms</td>
<td>38</td>
</tr>
<tr>
<td>Yaws</td>
<td>51</td>
</tr>
<tr>
<td>Yellow Fever Vaccine</td>
<td>6</td>
</tr>
</tbody>
</table>