The filariases, a group of infections with round worms (nematodes) of the superfamily Filarioidea, constitute a major global health problem. Bancroftian filariasis is spread widely throughout the tropical world, as is the less common tropical pulmonary eosinophilia. Onchocerciasis is seen in Africa and in Central and South America. Malayan filariasis occurs only in southern and Southeast Asia, and loiasis is restricted to western Africa. None of these infections is endemic in the United States at present, but imported cases may be encountered.

The filariases are transmitted to man by the bite of infected insect vectors; mosquitoes transmit bancroftian and malayan filariasis, blackflies spread onchocerciasis, and tabanid flies are the vectors of loiasis. The injected larvae mature into adult worms that may be found (according to the species) in the lymphatic system, the connective tissues, the serous cavities, the chambers of the heart, or the pulmonary arteries. After mating, the adult worms release first-stage larvae (microfilariae) that may be found either in the tissues or in the blood.

The pathogenicity of the adults and the microfilariae varies according to the species of infecting worm. In bancroftian and malayan filariasis, the presence of adult worms in the lymph nodes and vessels is associated with inflammation and obstruction of the lymphatic system resulting in lymphadenitis, lymphedema, and elephantiasis, while the microfilariae, which circulate in the bloodstream, do not appear to be pathogenic. In contrast, microfilariae in the lungs cause tropical pulmonary eosinophilia with cough, wheezing, and dyspnea. In onchocerciasis, the adult worms produce unsightly subcutaneous nodules, but the clinically important dermatitis and eye lesions are produced by the tissue-dwelling microfilariae. In loiasis, skin swellings are thought to be associated with adult worms migrating through the connective tissues. In addition to the major filariases described above, there are a number of other human filarial parasites that are either of doubtful pathogenicity (e.g., Dipetalonema perstans and Mansonella ozzardi) or uncommon (e.g., Dipetalonema streptocerca). Dirofilaria species principally infect animals but have occasionally been found in man.

Definitive diagnosis requires the isolation and identification of the parasite, but it is often difficult to find either the adult worms or the microfilariae. Immunological diagnosis is unsatisfactory because serological tests and skin tests do not distinguish among the various filariases and because there is considerable cross-reactivity with other nematode infections. In some situations a drug-induced exacerbation or alleviation of signs and symptoms provides the only significant evidence of a filarial infection.

Treatment of the filariases is often unsatisfactory. The drug diethylcarbamazine destroys microfilariae, but its administration may be associated with severe allergic reactions. Moreover, this drug is of uncertain value in the therapy of bancroftian and malayan filariasis since microfilariae do not play a major role in the pathogenesis of these infections; neither is such therapy effective in onchocerciasis or loiasis,
which adult worms survive to produce more larvae. Drugs such as suramin will destroy the adult worms of some species but may have severe toxic side effects. Finally, death of the worms may also bring about an exacerbation of symptoms.

**Bancroftian and Malayan Filariasis**

Bancroftian and malayan filariasis (often simply known as filariasis) results from mosquito-transmitted infection with the nematodes *Wuchereria bancrofti* or *Brugia malayi*. The larvae introduced by the insects mature into adults in the lymphatics; thus the clinical features are due to inflammation and obstruction of the lymphatic system. The fertilized females release large numbers of microfilariae, which circulate in the bloodstream for long periods or until they are ingested by a mosquito.

It is estimated that more than 200 million people are infected with these parasites. Bancroftian filariasis is spread widely throughout the tropical and subtropical regions of South America, Africa, southern and Southeast Asia, and the Pacific. Malayan filariasis is more restricted in distribution, being found only in southern and Southeast Asia. Bancroftian filariasis used to be endemic in the United States. In South Carolina in 1915, microfilariae were found in 20% of 400 hospitalized patients, and one in four of these persons had a history suggestive of filarial disease. The last autochthonous case reported in the United States was in 1930. During World War II thousands of American troops serving in the Pacific were infected with *W. bancrofti* [1]. Fear of developing hydroceles and elephantiasis was intense, but chronic sequelae occurred in only a very small proportion of patients. Imported filariasis is occasionally seen in immigrants, especially from the Caribbean and Pacific Islands.

**Life Cycle**

Man is inoculated with the parasite when bitten by an infective mosquito. The larvae pass into the lymphatics and lymph nodes, where they develop to maturity during a period of six months to several years. The white, thread-like adults of both sexes lie tightly intertwined in the lymphatics. The males of *W. bancrofti* are approximately 40 × 0.1 mm and the females 100 × 0.25 mm in size, whereas *B. malayi* are slightly smaller. The fertilized females discharge microfilariae, which pass via the lymphatics into the bloodstream; *W. bancrofti* microfilariae measure 260 × 8 μm, whereas those of *B. malayi* are 230 × 6 μm in size. In addition to size, there are also differences between the caudal nuclear pattern of the microfilariae of *W. bancrofti* and that of *B. malayi*. When microfilariae are ingested in the mosquito's blood meal, they penetrate the thoracic muscles of the insect, where they undergo two molts and then migrate to the proboscis; the entire process takes from one to three weeks.

**Epidemiology**

In many patients with filariasis there is a surge of microfilariae into the peripheral blood around midnight. The mechanism of this phenomenon, which is known as nocturnal periodicity, is not completely understood. While most patients infected with *W. bancrofti* exhibit this periodicity, those infected in the South Pacific show a much less pronounced peak, which is maximal during the day. *B. malayi* infections show nocturnal peaks of various intensities.

Man is the only known host of *W. bancrofti*, but *B. malayi* has also been found in primates and felines. A large number of rural and urban species of mosquito have been shown to transmit the parasite. The biting times of the mosquitoes usually coincide with the periodic microfilaremia of the parasite. Transmission in a given area depends upon the presence of suitable vectors in large enough numbers and an adequate reservoir of circulating microfilariae. In a study in Rangoon, Burma, each person was exposed to approximately 80,000 bites per year of which 300 (0.4%) were by infective mosquitoes. It was calculated that an average of 15,500 bites from infective mosquitoes were necessary to produce one case of microfilaremia [2]. A study undertaken in Calcutta, India showed a similar total number of bites per year but approximately four times as many infective bites and four times as high an incidence of microfilaremia [3]. It seems
likely that patent infections are produced only when a susceptible individual receives a large number of infective larvae during a short period.

**Disease Syndromes**

Many patients in endemic areas have asymptomatic infections. A study in Calcutta showed that only 0.7% of the adult male population had severe lymphedema and 2.2% had large hydroceles, despite a microfilaraemia rate of 20%–25% [3]. Similarly, a survey of 178 Samoan immigrants to the United States showed that 14% had microfilaraemia, but only a small proportion had clinical features of filariasis. Conversely, clinical disease may be found in the absence of microfilaraemia. Thousands of American army and navy personnel stationed in the South Pacific during World War II developed early filariasis with epididymitis, orchitis, lymphangitis, and lymphadenitis; microfilariae were rarely present in the blood, although worms were found in specimens from 22% of 364 reported biopsies [1]. Furthermore, microfilariae are not usually found in the blood of patients with advanced filariasis.

1. **Acute inflammatory reactions.** In bancroftian filariasis, patients may present with an acute lymphangitis or lymphadenitis, usually of the lower limbs. Funiculitis, epididymitis, and orchitis are also common and may be associated with the rapid development of a hydrocele. In malayan filariasis, the upper limbs are more frequently affected, and involvement of the genitalia is less common. Headache, backache, and nausea are often symptoms in both forms, but fever is uncommon. The acute episodes usually subside after a few days to a few weeks but frequently recur. Persistent generalized lymphadenopathy is often seen.

2. **Chronic obstructive lesions.** Continued residence in an endemic area, with recurrent inflammatory episodes and subsequent fibrosis, may lead to the development of lymphatic obstruction. If enough vessels are involved, lymphedema will develop, and lymphatic varices may arise, especially in the femoral, inguinal, and testicular regions. The skin and subcutaneous tissues of the scrotum may become swollen, and effusion of fluid in the tunica vaginalis may lead to a chronic hydrocele. Obstruction of deeply sited lymphatics may result in chylous ascites and in pleural or joint effusions. Chyluria develops when swollen lymphatics burst into the urinary tract. Persistent edema of skin and hypodermis leads to elephantiasis characterized by thickening of the subcutaneous tissue, hypertrophy of the epithelium, development of warty excrescenses, irregular foldings, and secondary infections.

**Diagnosis**

An algorithm illustrating the sequence of steps necessary for the diagnosis of filariasis is presented in figure 1. The presence of microfilariae in the blood does not necessarily denote filarial disease but may simply indicate an asymptomatic carrier. The algorithm is constructed from the point of view of patients with either acute symptomatology (such as lymphangitis, lymphadenopathy, funiculitis, and epididymitis) or signs of chronic lymphatic obstruction (such as hydrocele, chyluria, or elephantiasis). In either case, a geographic history must be taken. If the patient has never been to or has resided only transiently in an endemic area, the diagnosis is unlikely. If the geographic history is positive, microfilariae should be sought in the blood although they are rarely found in either the early or the advanced stages of the disease.

A blood sample taken at midnight will detect all forms of the parasites, whether or not there is nocturnal periodicity. A concentration technique is most effective. Blood (1 ml) is diluted in 10 ml of 4% formalin in water, shaken for hemolysis of the red cells, and centrifuged for 5 min at 1,000 rpm (400 g). The deposit is spread on a glass slide, dried, fixed in methanol for 3 min, dried again, and stained for 30 min with 10% Giemsa in phosphate buffer (Giemsa stain, Fisher Scientific, Fairlawn, N.J.). New, highly sensitive techniques have been developed for the detection of microfilariae, but these methods are of most value for epidemiological studies. For routine diagnosis of individual infection in hospital laboratories, the established techniques are simpler, allow species identification, and provide a permanent record. Microfilariae may occasionally be seen in chylous urine or hydrocele fluid.
Although the differentiation of *W. bancrofti* from *B. malayi* is not critical to the diagnosis, these two types of microfilariae must be distinguished from those of other filariae whose larvae circulate in the blood. The microfilariae of *Loa loa* are also found in the peripheral blood. *D. perstans* is widely distributed throughout Africa and South America, and *M. ozzardi* is found in South America. The adult worms are found in the serous cavities and produce microfilariaemia; the larvae are transmitted by biting midges (*Culicoides*). The vast majority of infections are asymptomatic, although eosinophilia is common. Treatment is unnecessary. Microfilariae are distinguished on the basis of the presence or absence of a sheath, the shape of the tail, and the pattern of nuclei within the tail. A key for species identification is available [4]. Failure to find microfilariae may necessitate lymph node or vessel biopsy, but adult worms are found in only about 25% of specimens.

In the absence of a parasitological diagnosis, serological tests may be considered. These tests are performed by the Mycology and Parasitology Section, Center for Disease Control, Atlanta, Ga. Immunological tests for filariasis, however, are not highly specific in that they do not differentiate among the various filariases and other nematode infections. Eosinophilia is not a reliable indicator of infection and is of little help in making the diagnosis. If the filariae cannot be identified, the
diagnosis must be made on clinical grounds by the exclusion of other causes.

**Management**

Treatment with diethylcarbamazine citrate (Hetrazan, Lederle, Pearl River, N.Y.) rapidly reduces the number of microfilariae in the peripheral blood. This response may be permanent, a fact suggesting that the drug may kill or sterilize the adult worms. Further episodes of lymphangitis are sometimes prevented, but established elephantiasis or hydrocele will not regress. The drug is given initially in small doses because of reactions to dying microfilariae, as manifested by fever, malaise, headache, backache, nausea, and vomiting. After several days of treatment, some patients develop an inflammatory reaction in a lymph node or vessel, presumably around a dead or dying worm. Diethylcarbamazine is administered orally after meals in a three-week course as follows: day 1, 50 mg; day 2, 50 mg three times; day 3, 100 mg three times; days 4–21, 3 mg/kg three times daily. Treatment of symptoms includes rest and administration of anti-inflammatory and analgesic drugs. Mild lymphedema and elephantiasis may be controlled with elastic stockings. Advanced hydrocele requires surgery.

Patients with early filariasis or asymptomatic microfilaraemia should be strongly reassured that the likelihood of developing long-term sequelae is remote. Patients who are returning to an endemic area should institute measures of vector control such as screens, mosquito nets, and insect repellents.

**Tropical Pulmonary Eosinophilia**

Tropical pulmonary eosinophilia (TPE, tropical eosinophilia with eosinophilic lung) is a syndrome that consists of a chronic paroxysmal cough, eosinophilia, abnormal chest X-ray, and a positive therapeutic response to treatment with diethylcarbamazine. TPE is due to microfilariae of uncertain origin in the tissues, especially in the lungs, but diagnosis is difficult since there are no circulating microfilariae. TPE has a distribution similar to that of bancroftian and malayan filariasis and is most commonly seen in southern Asia; it has also been recorded in Africa and South America.

**Life Cycle**

The worms responsible for TPE have not been definitely identified, and thus the complete life cycle of the organism is unknown. Microfilariae have been found in the lungs, lymph nodes, and liver [5], but the adult worms have so far remained elusive. It is uncertain whether the illness represents an unusual reaction to larvae of Wuchereria or Brugia species or a reaction to a worm such as Dirofilaria, which is usually a parasite of animals.

**Epidemiology**

TPE has most frequently been described in areas endemic for bancroftian and malayan filariases. TPE also is presumably transmitted by mosquitoes. Nevertheless, patients with pulmonary infiltrates and eosinophilia are found in the United States, where dirofilaria infections of dogs are common. It is possible, therefore, that the condition occurs in the United States but has hitherto been unrecognized.

**Disease Syndromes**

The onset is usually insidious, with a dry cough that becomes paroxysmal and worse at night. The cough may become productive, and some patients have small hemoptyses. Wheezing and dyspnea may occur. Frequently, there are nonspecific features such as malaise, fatigue, anorexia, and weight loss. Physical examination may yield negative results but often reveals scattered rhonchi and crepitations. Some patients have mild hepatomegaly or lymphadenopathy. These features usually persist for many months, although severity may fluctuate. A variant of the syndrome occurs in which there is persistent eosinophilia with unidentified microfilariae in the lymph nodes and spleen, but microfilariae are again absent from the blood.

**Diagnosis**

An algorithm for diagnosis and management of TPE is outlined in figure 2. The patient may present because of pulmonary symptoms or eosinophilia. If the patient has not been to an endemic area, the diagnosis is unlikely. Eosinophilia occurs in all cases, usually with > 2,000 cells/μL. Chest X-ray is abnormal in 98%
TROPICAL PULMONARY EOSINOPHILIA
- Cough
- Shortness of breath
- Eosinophilia

Geographic history negative Diagnosis unlikely
  positive

Eosinophilia negative Diagnosis unlikely
  positive

Chest x-ray negative Diagnosis unlikely
  positive

Immunodiagnostic tests negative
  positive

Therapeutic trial
Diethylcarbamazine p.o. negative Diagnosis unlikely
  positive

Diagnosis likely

Figure 2. The progression to a diagnosis of tropical pulmonary eosinophilia; po = perorally.
of patients [6]. Translucency of the mid-zonal lung fields is reduced, often with reticulonodular opacities or hilar prominence with perihilar stration and a peripheral net-like pattern. Serological tests for filariasis are performed by the Center for Disease Control, Atlanta, Ga. Although nonspecific, the tests usually yield positive results for TPE. In many cases the final arbiter is a therapeutic trial with diethylcarbamazine; failure of response renders the diagnosis unlikely. Although many patients have been diagnosed by a lung biopsy that shows an eosinophilic granulomatous reaction with or without microfilariae, a presumptive clinical diagnosis can be made and then established by a satisfactory response to diethylcarbamazine.

Pulmonary infiltrates with eosinophilia occur in several other helminthic infections. *Ascaris lumbricoides*, *Strongyloides stercoralis*, and hookworm larvae may produce such a picture as they migrate through the lungs. In these infections symptoms usually last for only a few days; in contrast, TPE tends to be a chronic, recurrent disease.

**Management**

Administration of diethylcarbamazine orally in a dose of 3 mg/kg three times daily for two weeks is an effective form of treatment. There may be fever and exacerbation of symptoms during the first few days of therapy. The eosinophil level falls and the chest X ray clears over a few weeks. Relapses may occur but usually respond to a second course of therapy.

**Onchocerciasis**

Onchocerciasis is caused by the filarial worm *Onchocerca volvulus*, which is transmitted by simulid blackflies. In contrast to most other filarioses, both adult worms and microfilariae are found in the tissues rather than in the blood. The presence of adults is manifested by cutaneous nodules, and the microfilariae by an itchy dermatitis and eye lesions that may eventuate in blindness [7].

In Africa, 30 million people living in rain forest and savannah regions stretching from Senegal to Ethiopia in the north and from Angola to Tanzania in the south are infected by *O. volvulus*. The infection is also found in Central and South America; nearly one million people are affected in Guatemala, Venezuela, and Colombia. There are some epidemiological and clinical differences between the infections on the two continents. Onchocerciasis is sometimes seen in the United States either in visitors and migrants from endemic areas or in Americans who have resided in such areas.

**Life Cycle**

Man is infected by the bite of female blackflies of the genus *Simulium*. The larvae penetrate the skin and migrate into the connective tissues, where they develop into white, filiform adult worms during a period of 12 months. The males (20–40 × 0.2 mm) and females (350–500 × 0.3 mm) are found together in nodules of fibrous tissue, where they may live as long as 15 years. Each female produces large numbers of microfilariae, which are unsheathed and measure 140–350 × 5–9 µm. They migrate through the tissues where they may live for up to two years. After ingestion by a fly, the larvae pass to the thoracic muscles where two molts occur; by the 10th day the infective third-stage larvae are found at the base of the labrum.

**Epidemiology**

Man is the only known definitive host of *O. volvulus*. Onchocerciasis tends to be focal in distribution within its endemic areas. The pattern of infection is determined by variations in the parasite, vectors, and host response. The strains of *O. volvulus* in America differ from those in Africa, and there is also variation (according to area) within Africa. Moreover, the breeding and biting habits of the vectors considerably influence the prevalence and pattern of disease.

In Africa the flies breed in fast-running streams and rivers and tend to bite low on the body. In the rain forest transmission occurs throughout the year and is associated with gross skin lesions, but in the savannah transmission may be seasonal, and eye lesions are more prevalent.

In America the flies breed in small, even minute, streams. The main vector in Guatemala
tends to bite on the upper parts of the body; this fact may explain the greater frequency of head nodules and eye lesions in this area.

Disease Syndromes

Many of the indigenous inhabitants of regions with a low or moderate prevalence of *O. volvulus* have asymptomatic infections. In areas of high prevalence and intensity of infection, signs and symptoms of disease may be common [8]. Expatriates who contract onchocerciasis often suffer greatly from pruritis, even though the worm burden may be light and microfilariae are difficult to find.

1. *Nodules.* Firm, nontender fibrous nodules with freely moving overlying skin may be found; these nodules vary in size from several millimeters to several centimeters. The number of nodules varies greatly, as does their distribution over the body. In the African form of the disease, the majority of nodules are located over the bony prominences, especially the pelvis, lateral chest wall, spine, and knees. In Central America they tend to occur on the upper part of the body, especially the head.

2. *Dermatitis.* Involvement of the skin often begins with intense itching, and scratching may lead to secondary infection. A papular rash is frequently seen on the buttocks. Mottled depigmentation may occur. More severe disease is characterized by cutaneous lymphedema (especially of the trunk), which may be followed by a leathery thickening of the skin. Finally, atrophy with loss of elasticity gives a prematurely aged appearance. Lymphadenopathy is common, and patients in Africa are prone to develop "hanging groin," pendulous sacs containing inguinal and femoral lymph nodes.

Patients in Central America may develop erythematous lesions of the face or upper trunk, a purplish eruption on the upper part of the body resembling lichen planus, or a leonine facies.

3. *Eye lesions.* Impaired visual acuity or blindness is the most serious complication of onchocerciasis and usually takes many years to develop. Microfilariae can often be seen in the anterior chamber or cornea with a slit lamp and may be the only sign of eye involvement. The earliest and by far the most common lesions are punctate keratitis or snowflake opacities of the cornea, which may be followed by pannus formation and corneal fibrosis. Atrophy of the iris is common, and occasionally an acute iridocyclitis is seen. Posterior synechiae may develop and may be followed by secondary glaucoma or cataract. Choroidoretinitis, which may be extensive, has been reported in some patients, and optic atrophy may be found.

Diagnosis

The diagnosis and management of onchocerciasis is illustrated in the accompanying algorithm (figure 3). The infection may be suspected in a patient who presents with itchy dermatitis or subcutaneous nodules or with eye lesions such as keratitis, iritis, or choroiditis. Onchocerciasis may also be considered in the differential diagnosis of eosinophilia. If the patient has not been in an endemic area, the diagnosis is essentially ruled out. If the geographic history is positive, however, a search should be made for microfilariae in skin snips and in the anterior chamber and cornea by means of a slit lamp.

Skin snips are taken by raising small cones of skin about 3 mm in diameter with the tip of a needle, then cutting them off with a razor blade. They should be taken from the thighs, buttocks, and iliac crests in African patients and from the scapula and buttocks in American patients. The snips are placed in drops of 0.9% NaCl, teased and allowed to stand for half an hour, and then examined under a microscope for microfilariae. The snip should be bloodless; otherwise there may be confusion with microfilariae of *L. loa* or *D. perstans* [4]. Microfilariae found in the skin of patients from tropical rain forest areas of western Africa must be differentiated from those of *D. streptocerca*, which may also cause dermatitis [9]. Microfilariae may also be found in the urine of up to 30% of patients on both continents. Sometimes fluid can be aspirated from a nodule and microfilariae found on microscopy. The diagnosis may also be made by excision of a nodule and identification of the adult worms by histological examination.

Eosinophilia is common and may reach very high levels. Immunological tests are of no help in making the diagnosis since they do not differen-
ONCHOCERCIASIS
- Itchy dermatitis
- Subcutaneous nodules
- Keratitis
- Eosinophilia

Geographic history: negative = Diagnosis unlikely; positive

Microfilariae in skin snips, cornea or anterior chamber: negative = Diagnostic trial with Diethylcarbamazine p.o.

Adult worms in nodules: negative = Diagnosis unlikely; positive = Diagnosis possible

Diagnose confirmed

Assess Disease

Asymptomatic

Skin Disease: Treatment Diethylcarbamazine p.o.

Eye Disease: Treatment Diethylcarbamazine p.o., Suramin i.v.

Treatment Suramin i.v.

Figure 3. The progression to a diagnosis of onchocerciasis; po = perorally; iv = intravenously.
tiate among the various filariases and cross-react with other nematode infections.

If nodules are not present and no microfilariae are found, the response to a single oral 50-mg dose of diethylcarbamazine can be assessed (Mazzotti test). If an acute exacerbation of the rash occurs 1–24 hr later or a rash appears in a patient who was previously without skin symptoms, the diagnosis is likely but unproven. If this and all other tests yield negative results, the diagnosis is unlikely.

Management

(1) Chemotherapy. The treatment of onchocerciasis is unsatisfactory since the available drugs can be toxic. The two drugs most commonly used are diethylcarbamazine, which kills the microfilariae but has little effect on the adult worms, and suramin, which kills the adult worms and some of the microfilariae [10].

It is probably wise to treat all symptomatic expatriates, but the recommended regimen varies according to whether the diagnosis has been parasitologically proven, whether the eyes are involved, and whether there are any contraindications to treatment with suramin.

(a) Asymptomatic infection. Patients with proven onchocerciasis who are asymptomatic need not be treated, but it is wise to review the patient periodically for several years, particularly with reference to the development of eye lesions.

(b) Skin disease. Patients with skin disease only should be treated with diethylcarbamazine. If the symptoms continue to recur after several courses of diethylcarbamazine and the diagnosis has been parasitologically proven, suramin should be administered. Patients who have a positive Mazzotti test but in whom parasites have never been found should be treated only with diethylcarbamazine.

(c) Eye disease. Patients with eye disease should be treated with diethylcarbamazine followed by suramin. In patients with renal disease, diethylcarbamazine alone is given, but repeated courses may be necessary.

In view of the severe reactions that may occur with diethylcarbamazine (such as fever, rash, generalized body pains, conjunctivitis, and iritis), the dose is built up gradually as described in the section on bancroftian filariasis. In the case of suramin (Antrypol, Moranyl, Parasitic Drug Service of the Center for Disease Control, Atlanta, Ga.), a test dose of 100 mg is given initially for detection of the rare patient with an idiosyncratic reaction such as vomiting and collapse. One gram is then given iv each week for six weeks. If proteinuria at a level of > 20 mg/100 ml or abundant casts appear in the urine, the drug should be stopped. An exfoliative dermatitis sometimes develops for which corticosteroid therapy may be necessary.

(2) Nodulectomy. Where practicable, it may be worthwhile to remove all identifiable nodules, particularly in patients with the American form of the disease, since such removal reduces the chances of eye lesions.

(3) Ophthalmic treatment. In addition to antiparasitic therapy, expert ophthalmological advice should be sought for the management of patients with onchocercal eye disease.

Loiasis

Loi~as~is~ is~ an~ in~ fe~ ticu~ lar~ worm~ Loa loa,~ which~ is trans~ mitted by biting tabanid flies. The adult parasites reside in the subcutaneous connective tissues; the major clinical manifestations are transient, so-called calabar swellings. Occasionally, the adult worm migrates through the subconjunctival tissues, where it may be directly visualized. The microfilariae that circulate in the blood have not been associated with any specific signs or symptoms.

Loi~as~is~ is~ irreg~ ularly~ dis~ tributed in~ we~ stern~ and central Africa from the Gulf of Guinea to Lakes Victoria and Tanganyika; the disease is most prevalent in eastern Nigeria, the Cameroon Republic, and Zaire. Imported cases have been reported in the United States.

Life Cycle

Man is infected by the bite of female tabanid flies of the genus Chrysops. The larvae penetrate the skin and migrate into the connective tissues, where they develop during the next 12 months into white, thread-like, cylindrical worms (30–70 × 0.3 mm). After maturation and reproduction,
the larvae, surrounded by a sheath and measuring 300 \times 8 \, \mu m, are found in the blood during the day. After ingestion by the fly, the microfilariae pass into the thoracic muscles, where they undergo three moults; after two weeks they make their way to the base of the proboscis, ready for transmission.

**Epidemiology**

Man is probably the only definitive host of *L. loa*. The vectors are day-biting flies that live in the canopy of the rain forest and lay their eggs in the wet mud swamps and river edges below the forest trees. The infection is therefore much more prevalent among inhabitants of the rain forest than among those of the savannah. The flies have specific biting habits, in that they are attracted by dark skin and clothing, woodsmoke, and movement and do most of their biting in the shade at the edges of the open spaces of the rain forest.

**Disease Syndromes**

Many subjects with loiasis are asymptomatic. Eosinophilia is common and may reach very high levels. Patients with overt clinical manifestations usually present in one of two ways, the first being far more common.

1. *Calabar swellings*. These transient swellings are areas of localized subcutaneous edema. They may occur anywhere but are especially common around medium-sized joints and in areas exposed to trauma, such as the legs, hands, and orbits. The onset of the lesions is often heralded by local pain or itching for 1–2 hr; an edematous, nonerythematous swelling 10–20 cm in diameter then develops, lasts for several days, and slowly subsides. These swellings recur irregularly either at the same site or in various locations.

2. *Worm migration*. The adult worms occasionally migrate under the skin producing a prickly, crawling sensation. When they pass under the ocular or palpebral conjunctiva, where they may be directly visualized, they produce an intense, edematous conjunctivitis that may last for several days.

**Diagnosis**

The diagnosis and management of loiasis is illustrated in the accompanying algorithm (figure 4). The infection should be suspected in a patient who presents with recurrent, localized edematous skin lesions or with a history of prickly, creeping sensations in the skin. Occasionally, the worm may have been seen in the subconjunctiva. Loiasis should also be considered in the differential diagnosis of eosinophilia, which may reach high levels in this helminthic infection. The diagnosis is virtually ruled out if the patient has not been to rural areas of western or central Africa. If the geographic history is positive, a search should be made for microfilariae in a specimen of blood by the method described in the section on bancroftian filariasis. In this case, however, best results are achieved when the sample is taken during the daytime (10 a.m.–2 p.m.). Failure to find microfilariae does not rule out the diagnosis. If the adult worm is seen, an attempt should be made to excise it. Immunological tests are not helpful, since *L. loa* cross-reacts with other nematodes as well as with other filarial worms.

**Treatment**

Although diethylcarbamazine may eliminate microfilariae from the blood, its effect on the adult worms is less certain. The drug is administered orally as described in the section on bancroftian filariasis and is given in small doses because of reactions to dying microfilariae, including fever, malaise, swelling of joints, and headache. In the event of a severe reaction to therapy, the drug should be stopped and corticosteroids given if necessary. Symptoms may recur and require additional courses of treatment with diethylcarbamazine.

**Dirofilaria**

Dirofilariasis is a zoonotic infection. Several *Dirofilaria* species that infect animals may occasionally be found in man; the two most common are *Dirofilaria immitis* and *Dirofilaria tenuis* (*Dirofilaria conjunctivae*). Most cases have been reported from the United States, particularly from
LOIASIS
- Subcutaneous swellings
- Migrating worms
- Eosinophilia

Geographic history

positive

Diagnosis confirmed

Treatment: Diethylcarbamazine p.o.

Microfilariae in blood, Adult worm recovered

negative

Diagnosis unlikely

positive

Diagnosis less likely

Figure 4. The progression to a diagnosis of loiasis; po = perorally.

Florida, but others have been described in Europe, Asia, Africa, and Oceania.

Life Cycle
The adult worms of *D. immitis* are normally found in the right heart and pulmonary arteries of dogs and may be up to 25 cm in length and several millimeters in diameter. Unsheathed microfilariae (320 μm long) are released by fertilized females and pass into the bloodstream, where they may be ingested by various species of mosquito. After incubation for two weeks, third-stage larvae are found at the base of the probos-
cis, ready for transmission. Man is a poor host, and in the rare case in which adult worms develop, microfilariae are not found in the bloodstream.

Epidemiology

It is increasingly evident that *D. immitis* is spread widely throughout many of the temperate and tropical countries of the world and that human infection may occur wherever man, mosquitoes, and infected dogs are closely associated. Canine dirofilariasis is spread throughout much of the eastern half of the United States and in scattered areas of the rest of North America. *D. tenuis* has been found in raccoons.

Disease Syndromes, Diagnosis, and Management

There are two common clinical presentations, both of which may be associated with eosinophilia [11].

(1) Pulmonary lesions. Pulmonary lesions are usually produced by *D. immitis*, the heartworm of dogs. In man, the worm is usually seen in the heart or the lungs. It may be found incidentally at postmortem examination. Clinical manifestations of *D. immitis* infection of the lungs may include cough or chest pain or a solitary coin-type lesion that is noted on chest X-ray. Diagnosis and treatment may occur simultaneously by surgical excision of the lesion.

(2) Subcutaneous lesions. Subcutaneous lesions are usually produced by *D. tenuis*. Most patients present with a subcutaneous nodule that may have been present for several weeks before becoming inflamed. The nodules may be found anywhere, are occasionally migratory, and usually do not recur. Diagnosis and treatment are by excision.

References