

OUTBREAK OF FILARIASIS (*WUCHERERIA MALAYI*) AMONG FRENCH AND NORTH AFRICAN SERVICEMEN IN NORTH VIETNAM

H. GALLIARD, D^r Méd., D^r ès Sc.

Professor of Parasitology, Faculty of Medicine, University of Paris
Membre de l'Académie Nationale de Médecine, France

SYNOPSIS

In 1951 about 150 servicemen returning to Algeria from Tonking, North Vietnam, were found to show symptoms of filariasis. This article describes the investigation of the outbreak. Since on leaving the filarious area many of the patients recovered spontaneously and others were cured by treatment with arsenic or Hetrazan, the author concludes that severe, permanent and incurable lesions result only when constant reinfestation takes place.

In 1951 the attention of military medical officers in Algiers and Constantine was drawn to a typical syndrome occurring among servicemen repatriated from Tonking, North Vietnam. The three main associated symptoms were blood eosinophilia; enlargement of lymph-glands (adenomegalia); and bronchitis with attacks of asthma.

Biopsies of lymph nodes showed the same histological change in their structure in most of the cases. Blood was free from microfilariae, which were found only once in lymph glands by puncture. Pierrou, however, had the idea of putting the sections in saline water and in many cases the embryos were found in the deposit after a few hours.^{8, 9}

These facts were described by Friess, Pierrou & Segalen,⁸ Friess et al.,⁹ Coirault,⁴ Crosnier et al.,⁵ Faure, Geyer & Gueffier.⁷ Galliard & Mallarmé¹¹ reported a case previously treated for Hodgkin's disease and found a microfilaria in a smear of lymph gland tissue withdrawn by puncture.

Segalen¹³ records observations of 75 cases and Carillon³ of 100.

Some patients were repatriated because of the disease. In 24 cases the first symptoms occurred after their return home (14 months later in one case). Patients were between 20 and 33 years of age; 69 were North Africans and 31 were French. They were admitted to hospitals for the following reasons:

adenopathy (25 times)	eosinophilia (7 times)
asthma (13 times)	oedema and lymphangitis (11 times)
bronchitis (7 times)	other reasons (13 times)
pulmonary radiological examination (routine) (10 times)	

Major Symptoms

Adenopathy

Constant, superficial, never profound. Volume: varied roughly from that of a pea to that of an orange, sometimes that of a grapefruit. In 87 cases adenopathy was axillary; in 30, inguino-crural; in 37, cervical; and in 25, epitrochlear. Generally enlargement was noticed in one single lymphatic area (33 cases, and 20 cases axillary); in one case the four groups were involved.

Eosinophilia

Also constant; rates between the extremes of 5% and 92%. Leucocytosis is important (rates between 5900 and 77 400). Segalen records the following observations:

<i>Eosinophilia</i>		<i>Leucocytosis</i>	
<i>percentage</i>	<i>number of cases</i>	<i>rate</i>	<i>number of cases</i>
5-9	6	Below 10 000	24
10-19	29	10 000-14 999	31
20-29	20	15 000-19 999	24
30-49	23	Above 19 999	18
50 +	22		

The eosinophilia rate is independent of the volume of the glands and the intensity of the bronchitis. It falls rapidly after treatment with Hetrazanotezine or arsenic.

Broncho-pulmonary symptoms

These are not as common as the other two. They are encountered in 75% of cases. There is at first cough, with nocturnal asthmatic paroxysms which may be mistaken for typical asthma; mucous or muco-purulent expectoration containing numerous eosinophils occurs. Radioscopical examination revealed transitory opacities in 9 cases. These parenchymatous, heterogeneous condensations disappear in 10 days.

Minor Symptoms

Fever

Fever attacks last two or three days. They seem to correspond to symptomatic "waves" which characterize the disease.

Lymphangitis

The arms and forearms, thighs, and legs are generally involved; less frequently, the scrotum and spermatic cord, with hydrocele. In acute cases inflammation of the lymphatic vessels is apparent, but the oedema is

not inflammatory, and the local temperature is normal. The attacks are transient, occurring without apparent reason. Sometimes the four limbs are involved successively.

Out of 100 observations Segalen reports 8 cases of upper-limb involvement, 2 of lower-limb involvement, and 6 with involvement of the upper limbs followed by that of the lower limbs (in one of these cases the genital lymphatics were involved).

Pruritus

This seldom occurs. It may be either localized at the gland area or generalized. It is sometimes intensely painful (one patient attempted to commit suicide).

Splenomegalia

In one case this occurred during a "wave".

Histopathology

Smears from lymph-node puncture showed an increase of lymphocytes, numerous lymphoblasts, 6% polymorphonuclears, 2% eosinophils, 2% plasmocytes, and some basophilic cells. No Sternberg cell was found.

On biopsy and gross examination of sections of glands, fairly large yellowish-brown areas were noted: microscopically, the general architecture of the gland is not modified, but there is hyperplasia of germ cells and lymphoid crown. Sinuses are congested and vessels have a thickened wall; plasmocytes are very numerous in the capsule and the fibrous septum; mastocytes are numerous in lymphoid infiltration around the vessels.

The reticular and macrophagic system is stimulated. The germinative centres are hyperactive, and contain large reticular cells. Vascular phenomena of inflammation are prevalent. Lymphatic follicles are infiltrated with eosinophilic cells arising from connective tissues and are true histiocytes. They cover large surfaces (pure culture of Friess and all eosinophilic abscesses of Hartz) and give the typical reddish coloration to fresh sections observed macroscopically. Numerous eosinophils are also present in the local blood vessels.

In inflammatory nodules with giant cells the radiate formations of Hartz and Van der Sar were seen in glands which were positive for microfilariae. Degenerated embryos may be noted in these granuloma.

There is no correlation between the importance of the eosinophilic infiltration and the rate of eosinophils in the blood-stream. For example, in one case with considerable infiltration of the glands there were only 5% of eosinophils in the blood.

Clinical Forms

Forms with adenopathy

Some patients¹¹ had been treated for Hodgkin's disease after their return to France. Nevertheless, the rate of eosinophilia was much too high, and moreover, puncture of the enlarged gland did not reveal malignant cells.

Eosinophilic forms

Adenomegalia and bronchial symptoms were not noted. The diagnosis of so-called "tropical eosinophilia" is discussed below.

Forms with bronchitis

If eosinophilia is prevalent a diagnosis may be made of tropical pulmonary eosinophilia or Löffler's syndrome.

Forms with lymphangitis

These forms represent the evolution towards classical forms of advanced filariasis. It should be mentioned that in one case a focal spot of O'Connor was observed and an adult filaria was recovered *in situ*.

Diagnosis

In Constantine no clinical diagnosis was made until microfilariae were discovered. On account of the high rate of eosinophilia, the disease was called asthma, or tropical eosinophilia. Pulmonary transitory condensations may be caused by other parasites (*Ascaris*, liver fluke, etc.) The histological structure of the glands is typical. The results of the test-treatment with Hetrazan-notezine could lead to the diagnosis, but it should be borne in mind that complete cure was obtained with arsenobenzol, and that arsenic is the specific treatment for tropical eosinophilia.

Microfilariae

These were never found in blood, and were withdrawn with a needle only twice (Friess et al.,⁹ Galliard & Mallarmé¹¹). In most cases they were found by gland biopsy. Sections of glands at least as large as an almond were immersed in saline for a few hours and the embryos sought in the sediment.

Adult filariae

Destombes⁶ at Saigon in 1953, when carrying out 20 lymph-gland biopsies, found on two occasions an adult worm at the surface of the gland besides microfilariae. In another instance Carillon³ reported the case of

a North African patient who suffered from bronchitis, adenomegalia, and eosinophilia (25%)—the typical syndrome. In the course of treatment oedema appeared on the dorsum of the forearm. It was neither hot, red, nor painful, but its centre had a nodule as large as a cherry. In a few days the oedema disappeared, but the nodule persisted. Histological section showed a granuloma with giant cells surrounded by an infiltration of plasmocytes and eosinophils. In the centre was the section of a female worm.

Treatment

Friess and co-workers^{8,9} found that novarsenobenzol (neoarsphenamine) gave very satisfactory results: the bronchitis symptoms receded, the enlarged glands subsided and the rates of leucocytosis and eosinophilia were drastically reduced. Various antihelminthic treatments used to free the intestine from parasites had no reducing effect on eosinophilia.

Hetrazan-notezine was the drug of choice and had the most striking effects. The dosage employed was 0.10 g four times a day for a period of 10 days. In one instance dead microfilariae were found in glands after treatment.

The drug had no effect on polymicro-adenopathy, but medium-sized and large-sized glands were rapidly reduced.

The respiratory symptoms—cough, expectoration, and dyspnoea—improved immediately. Sometimes a second course of treatment was necessary; in other cases the symptoms receded without treatment.

The eosinophilia-rate falls during the first course of treatment, and return to normal is achieved in 10 days. The fall of the curve is more rapid and striking than in *Loa loa* as there is no preliminary increase; nevertheless the curve rises again soon and a second course of treatment is required. In some cases a fever attack occurred during treatment, but no intolerance reactions were observed.

In the course of an attack of acute lymphangitis the effect on eosinophilia was not so evident. In some cases a reduction could not be obtained and it was thought that the presence of hookworms was the cause. In one instance the patient also harboured hookworms—*Ascaris* and *Trichuris*. The rate of eosinophils fell from 57% to 2% after treatment lasting 10 days.

Evolution of Disease

The symptoms are not continuous; the disease seems to proceed in short waves, lasting a few days, interrupted by intervals of several days or several months. Bronchial symptoms, however, may persist indefinitely if no treatment is given.

In some cases the patients were repatriated after having lived between six months and two years in Tonking. In others, the symptoms appeared from six to eight months (14 months in one case) after their return home.

In some instances the symptoms (adenomegalia, bronchitis) receded without treatment. In one case the enlarged glands subsided twice, before and after a relapse, after the patient's return to France.

Sometimes adenomegalia persisted for months, as did the pulmonary shadows (one year), and the prevalent symptoms of bronchitis with attacks of asthma.

The eosinophilia rate may be maintained at a high level for a long time (in one case 61 % of eosinophils and 20,200 leucocytes were found six months after return home; in another case 15 % were observed after one year).

Finally, it may be assumed that prognosis was generally good; after two years all patients were cured without sequelae.

Conclusions

The discovery of a prevalent infestation with *W. malayi* in French and North-African servicemen is of great interest. It is the first time that such a high number of cases has been observed in this area of the Indochinese peninsula; they were a result of war conditions which kept servicemen operating in the bush in contact with *Mansonioides*. This is a proof of the contrast between urban filariasis caused by *W. bancrofti* and rural filariasis caused by *W. malayi*, of which not a single case has ever been observed previously among French people living in Tonking.

The symptomatic triad (adenopathy, broncho-pulmonary signs, eosinophilia) is reminiscent of the classical syndrome of tropical eosinophilia and of former reports of Kouwenaar, Hartz & Van der Sar, and others. Nevertheless the number of cases (more than 150) is particularly striking.

The evolution of the disease and the cases of spontaneous cure are proof that the symptoms which appear at the onset of the disease have a purely allergic origin. Another proof lies in the fact that those symptoms, even if they were prevalent, receded dramatically when arsenic and Hetrazan were given.

This syndrome has never been observed by the writer among people living in Tonking, although *W. malayi* is twice as common as *W. bancrofti*; nor has it been reported by other authors in other countries where filariasis caused by *W. malayi* is endemic (for example, China, India, Indonesia, Malaya). Brumpt & Ho Thi Sang,¹ however, have described a case of nodular filariasis with broncho-pulmonary symptoms caused by *W. malayi* in Hanoi.

It is true that in the French and North African servicemen only early symptoms were observed, whereas in autochthonous peoples only advanced

cases were seen. Infection is acquired at a young age, and it is exceptional to see the disease at its onset; attention is evidently never drawn to commonplace pulmonary symptoms of bronchitis. Eosinophilia is commoner still, although its level is never very high. However, it is remarkable that no doctor has ever reported having seen a case of the huge gland enlargements, which are sometimes transitory and spontaneously curable.

On the other hand, according to recent data (Lagarde¹²), the transient and clinically silent pulmonary condensations were observed on routine X-ray examination in Tonking in 7.86% of cases. The mean rate of eosinophils was 8%; 236 cases (70%) harboured *Ascaris*. These different symptoms are generally overlooked and have no great value unless they are associated to give a conspicuous acute syndrome. Nevertheless it seems that this typical syndrome was, until now, observed only in French nationals and North Africans. It is also noticeable that the premonitory symptoms were different from those observed in the South Pacific area, among the USA marines. However, embryos were never found in the blood in the two areas, and evolution of the disease was the same: spontaneous and definitive recovery after a few months. This fact proves, once more, that a long stay in filarial areas, and consequently a constant reinfestation, is necessary to increase the number of worms to a sufficient level to provoke severe, permanent, and incurable lesions.

To conclude, it is obvious that filariasis in Vietnam assumes various forms. In Tonking we see genito-urinary accidents (chyluria, orchitis, epididymitis, hydrocele) caused by *W. bancrofti*, or oedema and elephantiasis of the lower limbs caused by *W. malayi*. These cases may be mingled, but as reported in 1936,¹⁰ *W. malayi* and elephantiasis seem to be prevalent in some well-defined areas. In South Vietnam (Cochin-China area), *W. bancrofti* alone is not very common, but classical symptoms are encountered now and then.

Nevertheless, among the aboriginal populations (Moi-stieng) living in the north of the area formerly known as Cochin-China, along the Annamese Cordillera, Canet² found that the microfilarial index was amazingly high—up to 38% in some villages. Moreover, periodicity was hardly noticeable, the rate of microfilaraemia being 30.92 at 17 hours and only 40.86 at midnight. These data were strikingly different from those observed in Tonkinese coolies working in the same area, in whom the rate of microfilaraemia was almost nil in the daytime. Moreover, 10% of these men had suffered, before their arrival in the area, from various filarial accidents (chyluria and hydrocele especially) while no clinical case was ever seen among the Moi-stieng.

It may therefore be assumed that, in addition to *W. malayi*, there exist in Vietnam at least two biological races of *W. bancrofti*, which are more or less pathogenic for man.

RÉSUMÉ

En 1951, un syndrome apparu chez des soldats venant du Tonkin retenait l'attention des médecins d'Alger et de Constantine. Il s'agissait d'éosinophilie, d'adénomégalie et de bronchite avec crise d'asthme. Plus de 150 cas ont été suivis. Le sang ne contenait pas de microfilaries, mais les embryons trouvés dans les dépôts de coupes de ganglions plongées dans le soluté physiologique indiquaient une filariose à *Wuchereria malayi*.

Après avoir précisé la symptomatologie, l'auteur aborde la question du traitement et celle de l'évolution de la maladie. La néoarsphénamine a donné, dans certains cas, de bons résultats en agissant sur les trois symptômes principaux. L'Hetrazan (Notezine), médicament de choix, a été employé avec plein succès, à raison de 0,10 g quatre fois par jour, pendant 10 jours.

Les symptômes ne se manifestent pas de façon continue. La maladie semble procéder par courtes vagues de quelques jours, séparées par des intervalles de plusieurs jours ou plusieurs mois. La bronchite, pourtant, peut persister indéfiniment si elle est négligée. Dans certains cas, la guérison est spontanée. Le pronostic est en général bon. Au bout de deux ans, tous les malades suivis étaient guéris, sans séquelles.

C'était la première fois que l'on observait un si grand nombre de cas dans cette région de l'Indochine. Il faut les attribuer aux conditions créées par la guerre, qui mettaient les soldats vivant dans la brousse au contact du vecteur de la filariose rurale à *W. malayi*, dont aucun cas n'avait été signalé jusqu'alors chez les Français du Tonkin.

L'évolution de la maladie et les cas de guérison spontanée indiquent que les symptômes initiaux sont d'origine allergique. Ces symptômes n'ont pas été signalés dans les autres pays où la filariose à *W. malayi* est endémique (Chine, Inde, Indonésie, Malaisie). Il est vrai que les débuts de la maladie passent le plus souvent inaperçus chez les autochtones et que ce sont généralement des cas invétérés que l'on rencontre. Toutefois, il semble que ce syndrome initial n'ait été signalé que chez des Français et des Nord-Africains. Il diffère de celui que l'on a observé parmi les troupes américaines dans le Pacifique sud. Dans l'un et l'autre de ces cas, aucun embryon n'a été trouvé dans le sang, et la maladie a évolué vers la guérison. On peut voir là une preuve nouvelle du fait que les lésions permanentes et incurables de la filariose n'apparaissent qu'après un long séjour dans une région infestée, où une réinfestation constante provoque l'accumulation d'un grand nombre de vers.

REFERENCES

1. Brumpt, L. C. & Ho Thi Sang (1954) *Bull. Soc. vietnamo-française Sci. biol.* (avril)
2. Canet, P. (1950) *Bull. Soc. Path. exot.* **43**, 216
3. Carillon, P. (1955) *Les opacités pulmonaires labiles, éosinophiliques d'origine parasitaire (syndrome de Löffler, éosinophilie tropicale) d'après l'étude des 100 premières observations du syndrome adénopathies, éosinophilie, bronchite, observée dans la filariose lymphatique (W. malayi)* (Thesis, Paris)
4. Coirault, R. (1954) *J. Méd. Chir. prat.* **125**, 399
5. Crosnier, R. et al. (1954) *Bull. Soc. Path. exot.* **47**, 87
6. Destombes, P. (1953) *Rapport de l'Institut Pasteur de Saïgon, 1953*, Saïgon
7. Faure, L., Geyer, A. & Gueffier, G. (1954) *Bull. Soc. Méd. Chir. Bordeaux* (juillet)
8. Friess, J., Pierrou, M. & Segalen, J. (1953) *Bull. Soc. Path. exot.* **46**, 1037
9. Friess, J. et al. (1953) *Algérie méd.* p. 436
10. Galliard, H. (1936) *Bull. Soc. Méd. Chir. Indochine*, **14**, 1094
11. Galliard, H. & Mallarmé, J. (1955) *Le Sang*, **26**, 520
12. Lagarde, C. (1955) *Méd. trop.* p. 928
13. Segalen, J. (1953) *De la filariose lymphatique (W. malayi) et de ses rapports avec l'éosinophilie tropicale* (Thesis, Algiers)