distribution and vector control on transmission of *Onchocerca volvulus* in the Niger basin, Guinea

P. Guillet,[1] A. Sékétéli,[2] E.S. Alley,[2] H. Agoua,[2] B.A. Boatin,[2] Y. Bissan,[2] L.K.B. Akpoboua,[2] D. Quillévéré,[2] & E.M. Samba[2]

As part of the WHO Onchocerciasis Control Programme in West Africa (OCP), the attack phase of operations in the Niger basin in Guinea began in 1989 with the simultaneous use of ivermectin and vector control. Larvicide applications coupled with annual large-scale ivermectin distribution have greatly reduced blackfly infectivity (by 78.8% for the number of infective larvae per 1000 parous flies). The combination of vector control and ivermectin has permitted excellent control of transmission. In the original OCP area, it took 6–8 years of vector control alone to obtain an equivalent decrease in blackfly infectivity. For the same number of flies caught, transmission was much higher in areas where ivermectin had not been distributed. The combined use of ivermectin and vector control has opened up new prospects for carrying out OCP operations with, notably, the possibility of reducing larviciding operations.

Introduction

Before ivermectin became available, onchocerciasis control was mainly directed against the vectors of the disease. The basic strategy of the WHO Onchocerciasis Control Programme in West Africa (OCP) consisted in interrupting transmission of the disease by continuing to destroy the vector larvae until the parasite reservoir in humans died out. For this to be achieved, 12–15 years of uninterrupted vector control was necessary (*1, 2*).

The characteristics of ivermectin (single dose, prolonged microfilaricidal effect, and absence of harmful side-effects) make it highly suitable for controlling the disease effectively. During the early treatment trials it was noted that ivermectin also reduced transmission of the *Onchocerca volvulus* parasite. This was established, first, by gorging blackflies on treated onchocerciasis patients (*3–6*); subsequently, community trials confirmed the reduction of transmission under field conditions in West (*7, 8*) and Central Africa (*9*) as well as in Central America (*10*). In African savanna areas, this reduction is reflected immediately after treatment by a 70–85% decrease in blackfly infectivity (No. of infective *O. volvulus* larvae per 1000 parous flies) and in natural transmission, without any vector control (*7, 20*).

In holoendemic areas, even though a reduction in the transmission of onchocerciasis of about 80% is considerable, it is not sufficient to lead to the extinction of the parasite in humans within a reasonable time. Ivermectin alone does not therefore seem capable of replacing larvicides for control of onchocerciasis transmission, at least at present. On the other hand, it rapidly improves the well-being of patients and stops almost completely the progression of some ocular lesions. A period of 7–10 years of vector control is required to obtain the same result. However, some beneficial effects of ivermectin have been called into question following a trial in Sierra Leone (*11, 12*).

Ivermectin has been widely distributed in the OCP area as an adjunct to vector control, and even used on its own in some areas (northern part of the western extension). Priority has been accorded to areas where there was a high risk of blindness and where vector control had just started (western and south-eastern extensions).

In the western extension, the first large-scale distribution of ivermectin began in 1988 in the Milo basin in Guinea and continued subsequently at a fre-

[1] Centre ORSTOM, B.P. 5045, 34032 Montpellier, France. Requests for reprints should be sent to Dr Guillet at this address.

[2] World Health Organization, Onchocerciasis Control Programme in West Africa, B.P. 549, Ouagadougou, Burkina Faso.

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quency of one treatment per year, gradually extending the areas under treatment. At first, the distribution was entrusted partly and then completely to the national health personnel of the countries concerned. For 1991 alone, more than 505 000 persons were treated in the OCP western extension area. At the same time, vector control operations were being carried out normally.

The present article evaluates the impact of this type of distribution on the transmission of onchocerciasis under operational conditions. Since there were no data on the large-scale use of ivermectin alone, its impact was evaluated in combination with vector control. For this purpose, results obtained in the Niger basin in Guinea, where ivermectin has been combined with vector control, were compared with those obtained previously in the original OCP area through vector control alone.

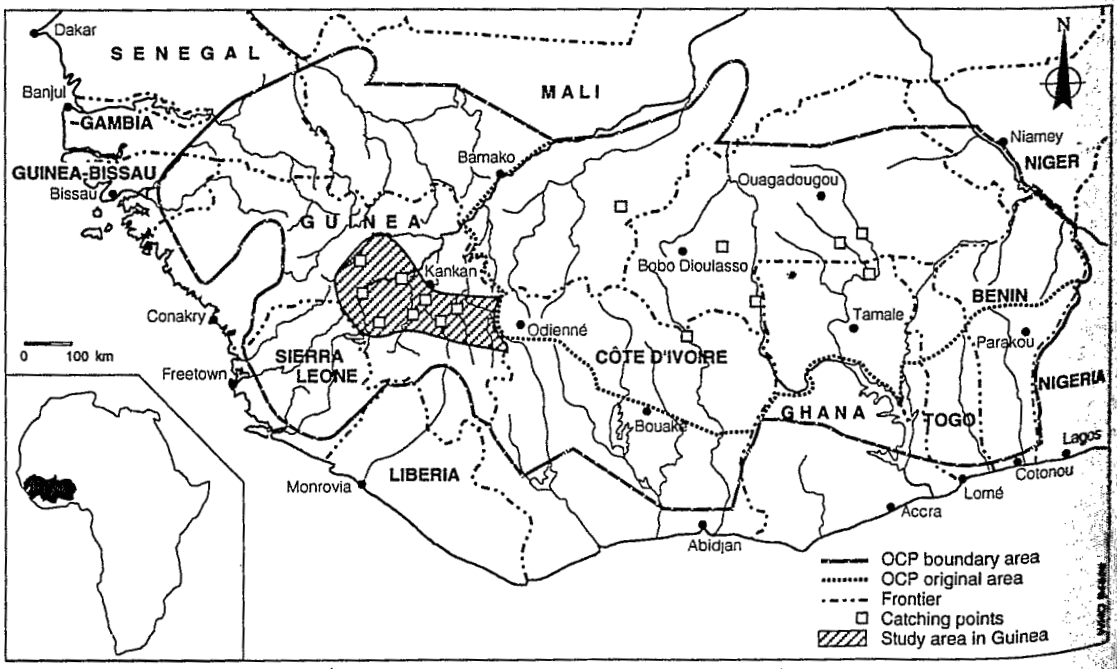
Materials and methods

All the 16 catching points selected for the study lie in savanna areas in holoendemic foci: eight in the Niger basin in Guinea and eight in the original OCP area (Mali, Côte d'Ivoire, Ghana, and Burkina Faso (Fig. 1)). The principal vectors were *Simulium sirbanum* and *S. damnosum* s.s. However, in Guinea, in the southern part of the area considered, other species such as *S. squamosum* or geographical forms of *S. soubrense* (Milo and Menankaya) have played a seasonal role in the transmission. In this area, some of the catching points selected were highly reinvaded up to 1986 (*13*). These reinvasion phenomena were almost brought under control in 1987 and 1988 and completely overcome in 1989 through the extension of larviciding to the west and south-west, notably in Sierra Leone (*23*). On the other hand, all the points located in the original OCP area were outside the classic reinvasion sectors, and the corresponding entomological results therefore reflect fully the impact of vector control alone on transmission, without any skewing caused by reinvasion. Larviciding began on some rivers in the original OCP area in 1975 but was fully operational by 1977.

The catches were made 1–2 days per week, 52 weeks per year, according to the standard procedures defined by OCP (*14, 15*). Of the various entomological criteria normally used for quantifying transmission (*16*), the following were used:

— biting rates (calculated weekly (WBR), monthly (MBR) or annually (ABR));

Fig. 1. **Map showing the locations of the catching points in the OCP original area (larviciding) and in Guinea where larviciding and large-scale ivermectin treatment were combined.**



— transmission potentials calculated from infective larvae in the head (L_3/H) and expressed weekly (WTP), monthly (MTP) or annually (ATP);

— percentages of infective parous flies (with third-stage larvae in the head); and

— number of L_3/H per infective bite.

The MTPs or ATPs can be used to quantify transmission, while the other criteria are used to evaluate the extent of blackfly infection by the larval stages of *O. volvulus*. Of the various developmental stages, only L_3/H were used because they could be counted precisely during routine OCP operations. The entomological results were calculated on a monthly basis from May to April because the attack-phase larviciding started in Guinea in May 1989. Also, May coincided with the usual end of the annual ivermectin distribution campaigns. Seasonal larviciding was carried out in Guinea from March to July in 1987 and 1988 as part of studies of the reinvasion phenomena (*13*).

The epidemiological data were collected and analysed according to the standard procedure developed by OCP (*17, 18*). The criteria adopted were prevalence of microfilariae (mf) in the skin (mfs) and the mean community microfilarial load (CMFL), i.e., the geometric mean mf count per snip (mf/s) among persons aged ≥20 years. Epidemiological surveys conducted beforehand were used to evaluate the endemicity level in the whole western extension before the beginning of the operations, especially in Guinea (*19*); for the eight villages close to the catching points selected, the initial mean prevalence of mfs was 74.4% and the CMFL, 42.2 mf/s. In the original OCP area, close to the selected catching points, the initial mfs was 70.3% and the CMFL, 34.9 mf/s.

Ivermectin was distributed at a dose of 150 µg/kg, respecting the exclusion criteria adopted by the manufacturers. The zone treated in Guinea stretches across the greater part of six river basins, covering almost 80 000 km² (Sankarani to Tinkisso river basins). The Milo river basin has been treated since 1988 (five annual treatments), the Niandan, Mafou and Niger basins since 1989, and the Sankarani and Tinkisso basins since 1990. By 1990 large-scale ivermectin distribution had started in all the basins in the study zone in Guinea.

Results

Ivermectin distribution

Between 1990 and 1992, the number of villages covered by ivermectin treatment increased by a factor of three and the number of people by a factor of six, the latter reflecting a significant increase in treatment compliance. In 1992 a total of 91 840 persons were treated in 550 villages.

The treatment was generally very well received. Most of the frontline villages in the zone, or those having a CMFL >5 mf/s, are currently being treated. Unfortunately, there are very few data on trends in the prevalence of mfs and in microfilarial loads because of the inconvenience of making repeated skin snips. However, there are data for four villages that had two successive treatments. These data were collected 12 months after ivermectin treatment, just before the following treatment. As expected, the prevalences of mfs have not decreased much; however, the CMFLs have decreased by 60–80% relative to the pre-treatment level (Table 1).

Transmission

For the original area, the study covered 10 years during which 34 492 blackflies were caught at the eight selected points, of which 87.8% were parous. Unfortunately, for the original area no baseline entomological data were collected before the start of vector control operations. On the other hand, for Guinea, the data for 1985–86 and 1986–87 were collected before any form of intervention. In Guinea, the intervention covered the period 1987–92, and a total of 206 765 blackflies were caught before the 1989–90

Table 1: **Mean prevalences of microfilariae in the skin (mfs) and CMFLs[a] in the Niger basin, Guinea, calculated 12 months after the first two ivermectin treatments**

	Precontrol:		After 1st treatment:		After 2nd treatment:	
Village	Prevalence (%)	CMFL (mf/s)	Prevalence %	CMFL (mf/s)	Prevalence (%)	CMFL (mf/s)
Bindougou	71.3	35.1	65.2	19.1	63.6	7.5
Faroro	73.2	15.9	39.7	2.6	42.7	5.7
Wassaya	58.6	13.4	27.2	1.3	NA[b]	NA[b]
Keniedougouba	62.7	38.1	59.8	19.3	67.8	10.3

[a] Geometric mean community microfilarial load.
[b] Not available.

season and 33 432 since then, of which 55% and 91%, respectively were dissected; the proportion of parous females was 74.9% before the control operations and 82.1%, subsequently. To facilitate the presentation of the results, we grouped all the entomological data for the original area according to the number of years of vector control. Thus, the data for 1975–76 group together the means observed after a year of control for all eight catching points, although the operations began gradually over the period 1975–77.

A preliminary significant decrease in transmission and even in the infectivity of the blackflies was observed in Guinea after the first two seasonal applications of larvicide in 1987 and 1988 (Fig. 2). These larvicide applications, which were aimed at interrupting reinvasion of the original OCP area, were carried out during the period of highest transmission. Furthermore, the Milo form of *S. soubrense*, which generally had high infectivity, had been virtually eliminated as a result of these larvicide applications.

A marked decrease in transmission was observed in the first year of continuous vector control in 1989–90 in Guinea (Fig. 2). From the second year, transmission was, at all the points, reduced below the tolerable threshold (100 L_3/H per person per year). It is difficult to dissociate the effect of ivermectin from that of vector control; however, in the original area, with vector control alone, it took longer to obtain the same result.

More significant is that the proportion of infective flies decreased rapidly from the first ivermectin treatments. After 2 years of large-scale ivermectin treatment (full coverage), the reduction was 64.6% (Fig. 3). At the same time, the number of L_3/H per 1000 parous flies had fallen by 75.7%. Compared with the 1986–87 data, before treatment began, the decrease was 78.8% for the infective flies and 82.9% for L_3/H. In the original OCP area, it took 6 years of vector control for the blackfly infection to start to fall, and 9 years before it reached the values observed in Guinea after only 3 years of combined use of larvicides and ivermectin.

The mean parasite load of infective flies for each year remained relatively stable for 9 years in the original area and for 6 years in Guinea (Fig. 4). The mean values (1.5–2) are quite representative of the species involved in the transmission (*S. sirbanum* and *S. damnosum* s.s.). However, a decrease in the load occurred in both areas after 9 years of vector control and 3 years of combined use of larvicides and ivermectin. In the latter case, the decrease was perhaps due to ivermectin, but it is too early to draw a conclusion from this.

Impact of ivermectin treatment during a breakdown in vector control in 1992

In February and March 1992, because of the use of a defective larvicide, the entomological situation deteriorated quickly in some river basins under vector control in the original OCP area and in Guinea. Six catching points were chosen in the most affected basins, including three along the western limit of the original area and three in Guinea. The results were for a total of 9390 flies caught over 2 months, 53%

Fig. 2. **Mean annual transmission potential (ATP) for selected catching points in the OCP original area and in Guinea (8 catching points in each zone).** The small arrows indicate that the ivermectin treatment was limited to only a few villages; and the big arrows, the large-scale ivermectin treatment.

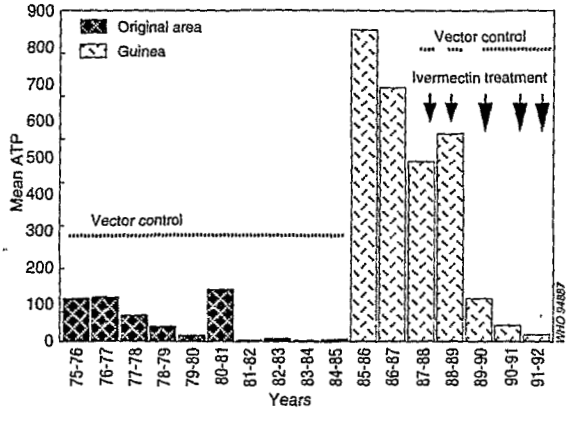


Fig. 3. **Number of infective flies and larvae per 1000 parous flies in the OCP original area and Guinea** (arithmetic mean calculated for 8 catching points in each zone).

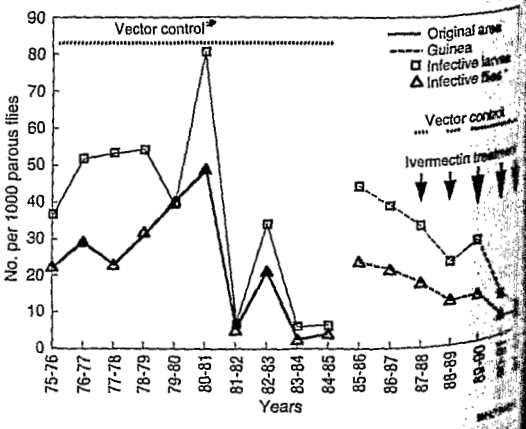
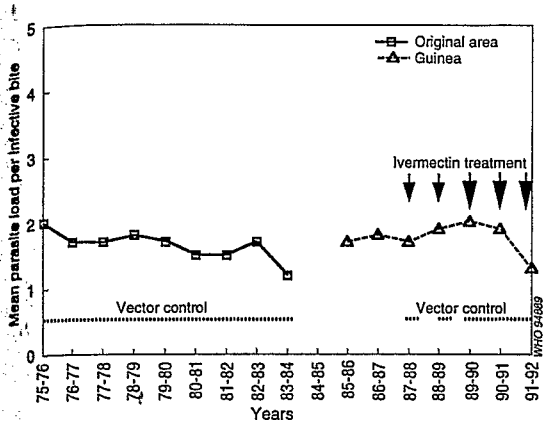


Fig. 4. **Number of infective *Onchocerca volvulus* larvae (L_3/H) per infective bite** (arithmetic mean calculated for 8 catching points in each zone).



of which were dissected. In both cases, the *O. volvulus* strain, the vectors, the larviciding period, and the insecticide used were the same. Also, the parous rates were similar.

The average transmission potential observed during this period in Guinea was 7.3 compared with 93.7 for the original area (Table 2). For the same number of blackflies caught, transmission in the original area was 5.6 times higher; for parous flies alone, the difference was 5.7 times. Consequently, while the breakdown on control had little effect in Guinea, for two of the three selected points in the original area, the acceptable transmission potential for 1 year (100 L_3) had been exceeded in only 2 months. Such a level of transmission in the original OCP area is perhaps surprising since it should have been under control for more than 12 consecutive years. However, the three catching points selected were located in initially highly reinvaded areas. Only after 1987 were the reinvasion problems overcome and transmission interrupted, even though it had been greatly reduced previously.

Discussion

The combined use of vector control and ivermectin has rapidly enabled transmission of onchocerciasis to be interrupted almost completely from the Niger basin in Guinea. The direct effect of ivermectin on transmission is perceptible in the infectivity of the flies. After only 3 years, the proportion of infective flies and their total parasite load (L_3/H) are as low as those obtained after 7–10 years of effective and continuous vector control in the absence of reinvasion. The results that we have described here for the original area are for eight catching points, all of which are located in zones where vector control has fully attained its objectives within the initially planned time limits.

In the original OCP area, the blackfly infestation has followed the same trend as the prevalences of mfs. For the latter, a plateau level is observed for 6–8 years followed by a rapid fall, while the CMFLs decrease more regularly (*1*). Between two annual ivermectin treatments, a considerable proportion of the treated individuals presented very low microfilarial loads for several months. The values calculated 12 months after treatment led to a large underestima-

Table 2: **Impact of ivermectin treatment during breakdown in vector control in 1992**[a]

Treatment	For female blackflies: No. caught	No. infective/1000 P[b]	L_3/1000 P[c]	Transmission potential
Larvicides alone				
Madina Diassa	1192 (87.3)[d]	3.8	6.6	55
Niamotou	1160 (84.5)	5.2	10.4	110
Vialadougou	3717 (85.0)	4.1	4.1	116
Total	6069 (85.6)	4.4	6.3	
Larvicides + ivermectin				
Tere	1704 (84.4)	0	0	0
Morigbedougou	900 (91.3)	1.6	3.2	22
Sansanbaya	717 (92.1)	0	0	0
Total	3321 (88.3)	0.5	1.1	

[a] Shown are the entomological results for February and March 1992 for catching points located in the original OCP area (only larvicides) and in Guinea (larvicides + ivermectin).
[b] No. infective per 1000 parous flies.
[c] No. of L_3 larvae per 1000 parous flies.
[d] Figures in parentheses are the % of flies that were parous.

tion of the impact on the epidemiological indicators and explain why the proportion of infected flies caught throughout the year decreased much more rapidly than the observed prevalences of mfs.

Also, ivermectin may have a cumulative effect. In the Asubende area in Ghana, the microfilarial loads measured 12 months after treatment decreased by 50%, 70%, 75% and 85%, respectively, following the first four treatments (*7, 20*).[a] This cumulative effect could therefore indicate that the entomological results obtained in Guinea will improve if the present therapeutic coverage can be maintained.

The spontaneous participation of the populations in the control activities, which has been excellent, could decrease as the disease regresses, particularly the skin manifestations. Similarly, the distribution teams may become less active with time. With a view to taking these potential risks into account, the following measures have been taken in the OCP area to offer the best guarantees of sustainability: reinforced awareness-raising among villagers; involvement of national health personnel, and adoption of other methods of distributing ivermectin, notably by the village communities themselves.

Will ivermectin therefore replace vector control in OCP? The major benefit of vector control is that it leads to the exhaustion of the parasite reservoir in humans by interrupting transmission; this, however, requires 12–15 years. Subsequently, blackflies can recolonize the freed zones without transmission of onchocerciasis being resumed. Since ivermectin does not completely interrupt transmission and does not kill the adult *Onchocerca* worms, it is not yet possible to forecast for how long it should be distributed and at what coverage level. Simulations made using the epidemiological model ONCHOSIM have shown that ivermectin would have to be distributed for more than 20 years to achieve the same results as vector control (*21*). Whatever the effect of ivermectin on the transmission of onchocerciasis, there is no evidence that the period of vector control should be shortened because of the combined use of ivermectin. For this to be the case, ivermectin would have to affect the lifespan of the adult worms; however, this has not yet been established, even though ivermectin exhibits some toxicity after repeated treatments at short intervals (*22*).

The larviciding problems encountered by OCP in February and March 1992 demonstrate clearly the impact of ivermectin on the success of the operations. For the same level of transmission, many more flies can be tolerated in areas that have been treated with a combination of larvicides and ivermectin. This impact provides an appreciable safety margin in the management of vector control operations, and makes it possible to envisage decreasing larviciding by a greater selectivity: fewer stretches of river treated and fewer larviciding cycles. In this context, distribution of ivermectin has been extended recently to some zones in the original OCP area, notably those that have been reinvaded, not only because of its direct impact on the level of morbidity but also because of its contribution to transmission control.

Larvicides and ivermectin are now two closely complementary tools in OCP activities. Use of this combination has created favourable new prospects that will undoubtedly influence the programme in the coming years.

[a] *Joint Programme Committee, Onchocerciasis Control Programme in West Africa. Thirteenth Session, Geneva, Switzerland, 8–11 December 1992.* Unpublished WHO document.

Résumé

Impact de la distribution à grande échelle d'ivermectine associée à la lutte antivectorielle d'*Onchocerca volvulus* dans le bassin du Niger (Guinée)

Dans le cadre du Programme OMS de lutte contre l'onchocercose en Afrique de l'Ouest, la phase d'attaque des opérations dans le bassin du Niger en Guinée a démarré en 1989 avec l'utilisation simultanée de l'ivermectine et de la lutte antivectorielle. Parmi les seize points retenus pour cette étude, tous situés dans des foyers holoendémiques de savane, la moitié sont répartis dans le bassin du Haut Niger en Guinée et les autres dans l'aire initiale du Programme.

Après trois à quatre années d'opérations avec une distribution annuelle d'ivermectine à grande échelle, on note en Guinée une forte réduction de l'infestation des simulies (78,8% pour la proportion de mouches infestantes et 82,9% pour le nombre de larves infestantes pour 1 000 femelles pares). La prévalence des microfilaires a peu diminué; en revanche, les charges microfilariennes des communautés qui mesurent l'intensité de l'infestation ont chuté de 60 à 80% par rapport aux données de prétraitement. La combinaison de la lutte antivectorielle et de la distribution de masse de l'ivermectine a permis un excellent contrôle de la transmission. Par contre, dans l'aire initiale du programme, il a fallu 6 à 8 ans de lutte antivectorielle seule pour obtenir une réduction équivalente de l'infestation des simulies. A nombre égal de mouches capturées, la transmission est beaucoup plus forte dans les zones où l'ivermectine n'est

pas distribuée, même après plusieurs années de lutte antivectorielle efficace et ininterrompue.

L'utilisation combinée de l'ivermectine et de la lutte antivectorielle ouvre des perspectives nouvelles dans la conduite des opérations avec notamment une possibilité d'allégement de la lutte antivectorielle.

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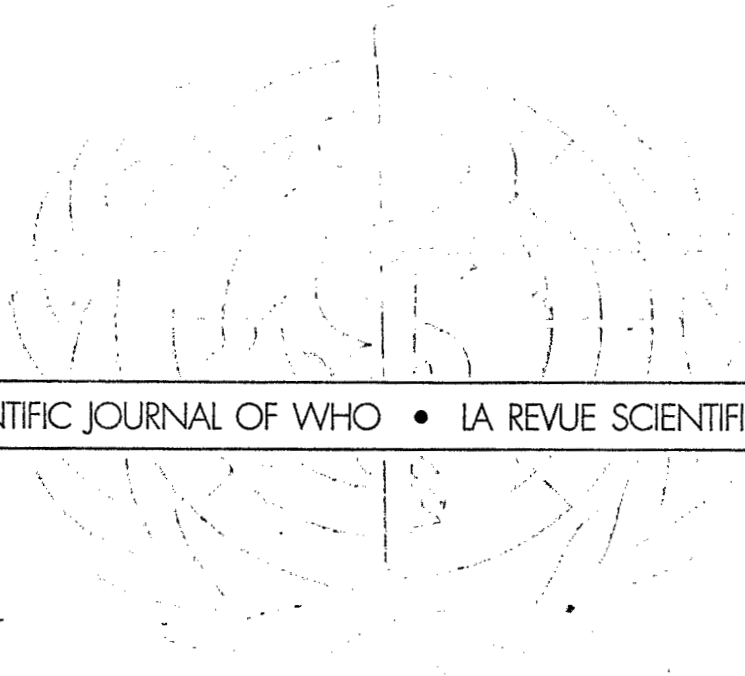

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