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THE CONTROL OF LEISHMANIASIS THROUGH PHLEBOTOMUS CONTROL IN ITALY

Riassunto. — Possiamo riassumere nel modo seguente la situazione che si presenta attualmente in Italia. L'esperimento effettuato negli Abruzzi ha dimostrato che la lotta contro il *Flebotomo* per mezzo del DDT, nelle case e nelle stalle, tronca la trasmissione della leishmaniosi. La lotta contro la malaria fa dovunque sparire la leishmaniosi dalle regioni paludose. In seguito ai nostri esperimenti, l'Alto Commissariato per l'Igiene e la Sanità Pubblica ha intrapreso la lotta contro il *Flebotomo* in diverse provincie degli Abruzzi e delle Marche (regioni non malariche). Le nostre ricerche epidemiologiche ci insegnano che la leishmaniosi esiste attualmente allo stato endemico in nuove località nelle quali verrà logicamente estesa la lotta finchè l'esistenza di questa malattia sarà constatata. Possiamo quindi prevedere che la leishmaniosi sparirà progressivamente in Italia, in un avvenire più o meno lontano, a secondo la rapidità con la quale verranno forniti i mezzi necessari.

E' permesso domandarsi, come per la malaria, se la scomparsa della leishmaniosi sarà definitiva o passeggera o, in altri termini, se il *Flebotomo* sia suscettibile di acquisire una resistenza agli insetticidi. Non abbiamo per ora, da qualsiasi parte del mondo, alcuna indicazione che possa dare una soluzione a questa domanda.

Résumé. — Nous pouvons résumer de la façon suivante la situation qui se présente actuellement en Italie. L'expérience effectuée dans les Abruzzes a montré que le lutte contre le *Phlébotome* au moyen du DDT, dans les maisons et les étables, enraie la transmission de la leishmaniose. La lutte contre le paludisme fait donc disparaître la leishmaniose des régions impaludées. Après nos expériences, le Haut Commissariat à la Santé publique a entrepris la lutte contre le *Phlébotome* dans plusieurs provinces des Abruzzes et des Marches (région non-impaludées). Nos recherches épidémiologiques nous apprennent que la leishmaniose existe

actuellement à l'état endémique dans de nouvelles localités, auxquelles s'étendra logiquement la lutte tant que l'existence de cette maladie y sera constatée. Nous pouvons donc nous attendre que la leishmaniose disparaisse progressivement d'Italie, dans un avenir plus ou moins éloigné, selon la rapidité avec laquelle seront fournis les moyens nécessaires.

Il est permis de se demander, comme pour le paludisme, si la disparition de la leishmaniose sera définitive ou passagère ou, en d'autres termes, si le *Phlébotome* est susceptible d'acquérir une résistance aux insecticides. Nous n'avons à l'heure actuelle, de quelque région du monde que ce soit, aucune indication qu'il en soit ainsi.

Summary. — It is possible to summarize in the following manner the present situation in Italy. Experiments conducted in the Abruzzi have shown that the campaign against *Phlebotomus* by means of DDT in houses and stables, checks transmission of leishmaniasis. Therefore the campaign against malaria causes leishmaniasis to disappear from malarial areas. After our experiments, the Commissioners for Public Health took over the campaign against *Phlebotomus* in several provinces of the Abruzzi and the Marches (non-malarial areas). From our epidemiological researches we know that leishmaniasis now exists in an endemic state in fresh localities, whither the campaign will naturally be extended as soon as existence of this disease is confirmed. We may therefore expect that leishmaniasis will progressively disappear in Italy, in the near or distant future, depending on the rapidity with which the necessary means are made available.

We may ask, as in the case of malaria, whether disappearance of leishmaniasis will be final or transient, or, in other words, whether *Phlebotomus* is capable of acquiring a resistance to insecticides. At the present time we have no indication, from any territory in the world, that this will be the case.

Zusammenfassung. — Die Lage, wie man sie jetzt in Italien beobachten kann, kann wie folgt zusammengefasst werden. Die Erfahrungen, die man mit DDT gegen *Phlebotomus* in den Häusern und Ställen von Abruzzi unternommen hat, zeigen dass diese Massnahmen die Uebertragung der Leishmaniose verhindert haben. Daher wird durch die Malariabekämpfung auch die Leishmaniose aus den sümpfigen Gegenden ausgetrieben. Auf Grund unserer Erfahrungen hat das Hohe Gesundheits-

Kommissariat die Bekämpfung gegen *Phlebotomus* in verschiedenen Provinzen von Abruzzi und Marche (nicht sümpfigen Gegenden) unternommen. Unsere epidemiologische Nachforschungen belehren uns dass die Leishmaniose tatsächlich in endemischen Zustand existiert und zwar kommt sie in neu-behafteten Gegenden vor, wo offenbar die Bekämpfung weiter geführt wird, solange die Krankheit dort besteht.

Man könnte demnach voraussehen dass, die Leishmaniose allmählich aus Italien nach einer mehr oder weniger nahen Zukunft, je nach der Eile wie die nötige Mittel geliefert werden, ausgetilgt wird.

Es stellt sich nun die Frage, gerade wie bei Malaria, ob das Verschwinden der Leishmaniose endgültig oder nur vorübergehend sein wird, mit anderen Worten, ob *Phlebotomus* leicht eine Resistenz gegen Insekticiden erwerben kann. Zur Zeit gibt es nirgends im ganzen Weltteil eine Andeutung dass es so sei.

During the years 1948 to 1950 we carried out in Abruzzo (Italy) an experimental control project intended to determine whether the transmission of oriental sore could be prevented solely by the application of residual DDT to the interior of houses and stables.

For this purpose a district located between the two rivers Tordino and Vomano, about 10 kilometres wide and extending 20 kilometres inland from the Adriatic Sea was chosen. This district covers the entire territory of the following four towns of the Province of Teramo: Roseto degli Abruzzi, Moro d'Oro, Notaresco and Castellalto (see graph 1), and lies in the centre of a region in which oriental sore has been known to be endemic. The presence of cutaneous leishmaniasis in the Adriatic region was first reported by Monacelli (1934). He and other workers showed that cases of the disease could be observed in a large zone along the Adriatic, covering the Abruzzo and Marche regions.

Most of the early studies on leishmaniasis in this region were made by dermatologists or physicians and were more concerned with peculiar clinical and pathological forms than with giving an idea of the real incidence of the disease. On the other hand, the reports of public health officers have always indicated that the incidence is rather low. According to Bevere and Tobia (1947) a total of only 115 cases of leishmaniasis had been officially reported in Abruzzo and Marche together during the eighteen years from 1927 to 1945.

EPIDEMIOLOGICAL INVESTIGATIONS IN THE EXPERIMENTAL REGION.

Three different species of Phlebotomus are present in the region: *P. papatasi*, *P. perniciosus* and *P. perfiliewi*. The last is the most abundant and has been considered to be the vector.

Our study started with an epidemiological investigation to determine the real incidence of oriental sore in the area to be treated with DDT (population two-thirds rural, one third urban), and in two entirely rural test zones, portions of Giulianova and Atri, located on either side of the experimental zone, as shown in the map. This investigation was carried out by the examination of the entire population in their own houses, in the towns and villages as well as on the farms. Each individual was examined to determine whether or not he showed lesions or scars of oriental sore. The doubtful lesions were examined microscopically.

A total of 28,599 persons were examined by this method, with the following results:

In the centres of Roseto (including the smaller centres of Montepagano, Cologna, Cologna Spiaggia), Moro d'Oro, Notaresco and Castellalto (including the smaller centre of Castelbasso), 9,410 persons were examined. Of these, 191 (2 per cent) were found with active lesions of cutaneous leishmaniasis, 1,327 (14.1 per cent) showed the scars and 7,892 were negative.

On the farms of Roseto, Moro d'Oro, Notaresco, Castellalto, Giulianova and Atri, a total of 19,189 persons were examined. Of these, 656 (3.4 per cent) had active lesions, 4,616 (24 per cent) showed the scars, and 13,917 were negative. The percentage of active lesions in the rural portion of the zone to be treated (Roseto, Moro d'Oro, Notaresco, Castellalto) was 3.3 per cent, in the rural test zone (Giulianova, Atri) 3.5 per cent.

It may be noted from these results, that the incidence is apparently higher in the rural areas than in the towns or populated centres.

Combining the totals for the urban and rural populations, out of 28,599 persons, 847 (2.9 per cent) had active lesions, and 5,943 (20.8 per cent) had scars. Thus a total of 6,790 persons, or 23.7 per cent of the entire population, were suffering from, or had had, cutaneous leishmaniasis. These results are summarized in Table 1.

EXPERIMENTAL PROPHYLAXS.

The first treatment with DDT was started in the summer 1948. The DDT spraying began on 6 June and was finished on 18 August when

the sandfly season was more than half over. Every house and stable within the territory of the four towns noted above was sprayed once during that summer with two grams of DDT per square metre, applied to walls and ceilings (an emulsion of the xyloltriton solution, containing five per cent DDT, was used).

During the spring (from March to May) of 1949 a second examination of the entire population was made in the treated as well as in the untreated districts. A second application of DDT was made during the summer (10 June-31 July) of 1949: it was not possible to do it earlier, although a pre-season application would theoretically have been desirable. A third examination of the entire population followed during the spring (from March to June) of 1950.

No definite catching stations for *Phlebotomus* were established. During the sandfly season the writer made almost continuous personal surveys of a great number of stables and houses all over both the treated and untreated districts.

After the first application of DDT an immediate and outstanding result was, with one observed exception, the complete disappearance of *Phlebotomus* inside houses and stables, while, on the contrary they were found in great numbers inside the human and animal habitations in the untreated test zones. As described in a previous paper (Corradetti, 1949), on one occasion, two-and-a-half months after the first application of DDT, it was possible to find *Phlebotomus* biting man outside as well as inside a certain house in the treated zone, but after the second treatment in 1949 no *Phlebotomus* was observed in the treated zone either indoors or outside. These results support the hypothesis advanced in the above-noted paper that sandflies found in the treated zone in 1948 represented a newly emerged brood from eggs laid before the first spraying of DDT.

Special attention was paid to the transmission of oriental sore, as revealed by the second and third examination of the population, following respectively the first and second treatment with DDT (see Table 2 and graph 2).

In the spring of 1949 22,709 persons were examined in the treated zone. Of these individuals, 161 (7 per thousand) were new cases of oriental sore, having been negative at the previous examination. In the untreated test zones the new cases numbered 88 out of 2,530 persons examined (34.7 per thousand). This examination showed that in the treated zone, new cases in the spring following the first treatment were proportionately only one-fifth as numerous as in the untreated zones. Moreover, on account of the period of incubation, which may

TABLE 1.

POPULATION	EXAMINED	ACTIVE LESIONS		SCARS	
		Number	Percentage	Number	Percentage
Urban area	9,410	191	2.0	1,327	14.1
Rural area	19,189	656	3.4	4,616	24.0
Total	28,599	847	2.9	5,943	20.8

TABLE 2.

ZONE	ACTIVE LESIONS BEFORE DDT (PER 1,000) (1948)	NEW CASES (PER 1,000) OBSERVED AFTER THE ANNUAL DDT SPRAYS		
		1 year after the 1st spray (1949)	1 year after the 2nd spray (1950)	1 year after the 5th spray (1953)
Experimental	29.0	7.0	1.3	0.4
Test	34.9	34.7	40.4	sprayed since 1950

be very long, there is no evidence that the new cases in the treated area were contracted after the application of DDT.

In the spring of 1950, 25,220 persons were examined in the treated zone; there were 34 new cases of oriental sore (1.3 per thousand). In the untreated zones there were 101 new cases out of 2,449 persons examined (40.4 per thousand).

From the results of the third examination of the entire population, it was concluded that the transmission of oriental sore for all practical purposes had been entirely interrupted in the treated zone. It was considered that the very low proportion of 1.3 new cases per thousand would not be eliminated unless the application of DDT were extended to the entire endemic region. This is because it is obviously impossible to prevent the people living in the treated zone from contracting infection when visiting the nearby untreated zones either to work or for other purposes during the season of transmission. Since 1950 both the test and the treated zones have been annually treated with DDT.

This summer (1953) we made a new survey of the originally treated zone and discovered 11 new cases (0.4 per thousand) covering the three years interval. This figure demonstrates that the annual infection rate was lowered to about a tenth of the 1950 figure, owing probably to the fact that most of the surrounding untreated region was from 1950 onwards treated with DDT.

The cost of this experimental prophylaxis was 160 Italian lire ($ 0,25) per person per year. This figure includes the cost of the DDT, the wages of workmen (three spray crews of seven men each) and transportation, but does not include the salaries of the directing staff.

The following additional notes may be useful to those wishing to undertake an extensive census of the sort described in this paper: (1) one doctor and two assistants constituted the census team; (2) the time required for each examination of the entire population was about two months. This length of time was necessary because of the hilly nature of the country, together with the fact that most of the rural houses are isolated, scattered all over the territory, and could be reached only by walking.

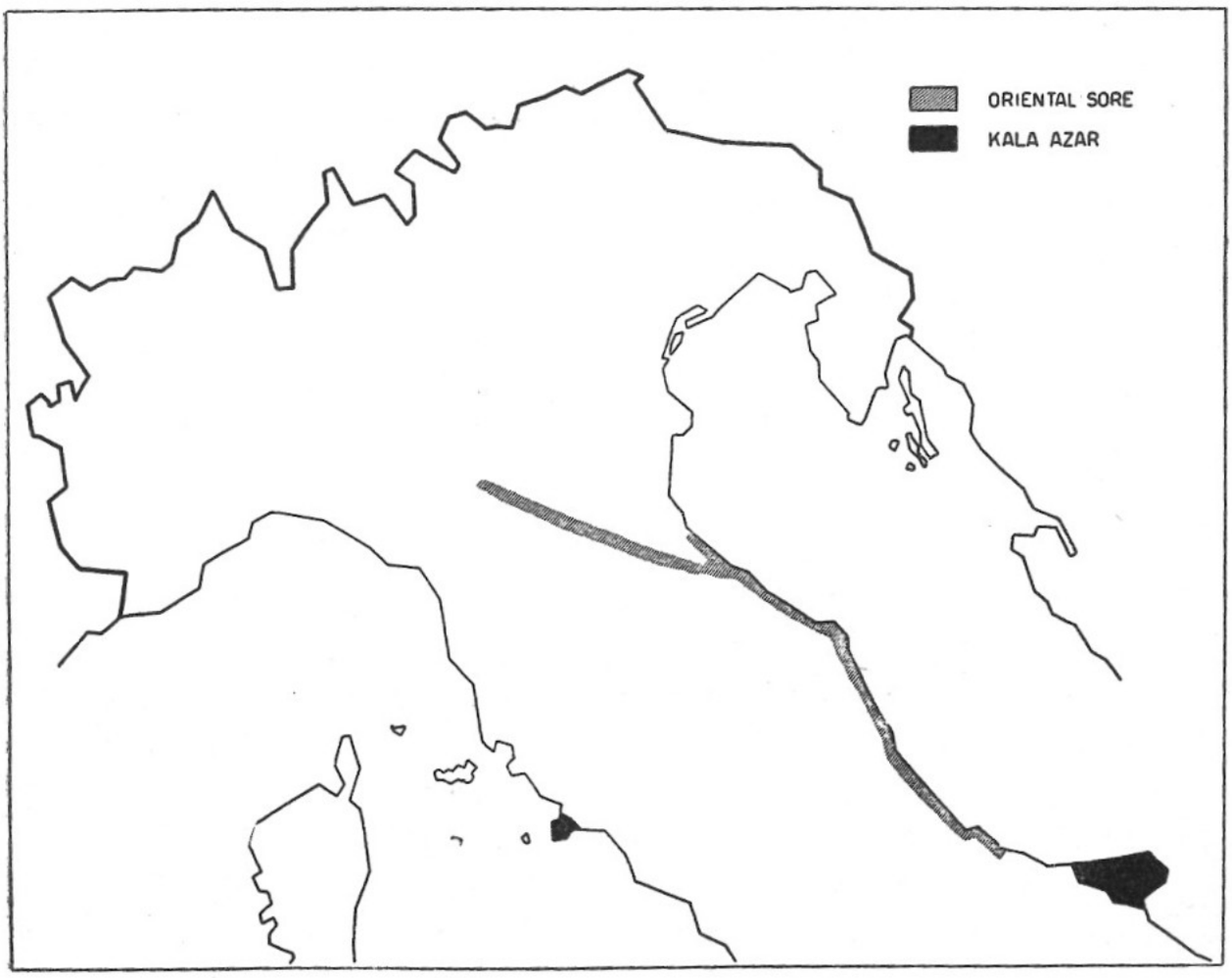
Further epidemiological investigations. Basis for the elimination of leishmaniasis from Italian territory.

After the positive result of the Abruzzo experiment it seemed obvious to extend the control to all the leishmania zones of Italy.

The next step was then to determine in which territories leishmaniasis was autochthonous. The only available data were those of Bevere and Tobia but unfortunately they resulted from the reports sent by the Health Officers of the Provinces to the High Commissariat of Health. These data could not be considered homogeneous from an epidemiological point of view, as the localities in which the leishmania cases were observed often differed from the localities in which the disease was actually contracted. As an example, some cases of oriental sore reported from Pinerolo (Torino) were found by personal investigation to occur only in young soldiers, recently arrived from Abruzzo. It was therefore necessary to carry out the investigation on a different basis.

Theoretically the only scientific method would be to examine the entire population, as done by ourselves in the above noted experiment in the zone of Abruzzo; the real incidence of the disease can be determined only by this method. But it must be recognized that this

method, although very useful and almost necessary for a scientific experiment in a limited zone, cannot be applied to an epidemiological research in large regions with many millions of inhabitants. Moreover, during and after our Abruzzo experiment, the indiscriminate employment



Map showing the extension of the main Italian oriental sore region (on the Adriatic coast and Apennines), together with the situation of the newly discovered kala azar zones.

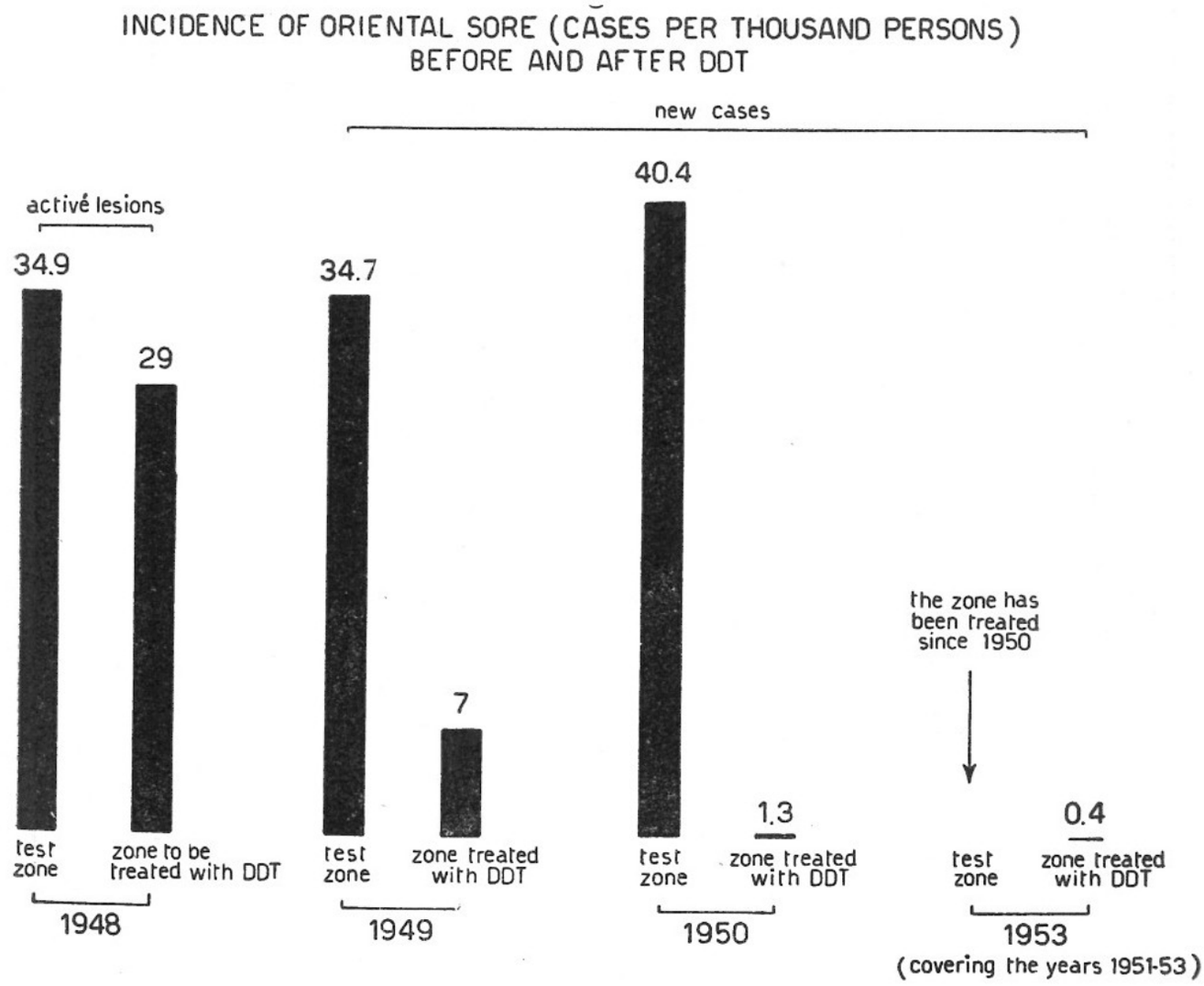
of insecticides by the State, local authorities and private people, in quantities and rhythms differing greatly in different localities, introduced a disturbing element in evaluating the data obtained from an epidemiological inquiry of the type described in our experiment. We shortly had to realize that we were too late to attempt to determine scientifically the real incidence of the infection.

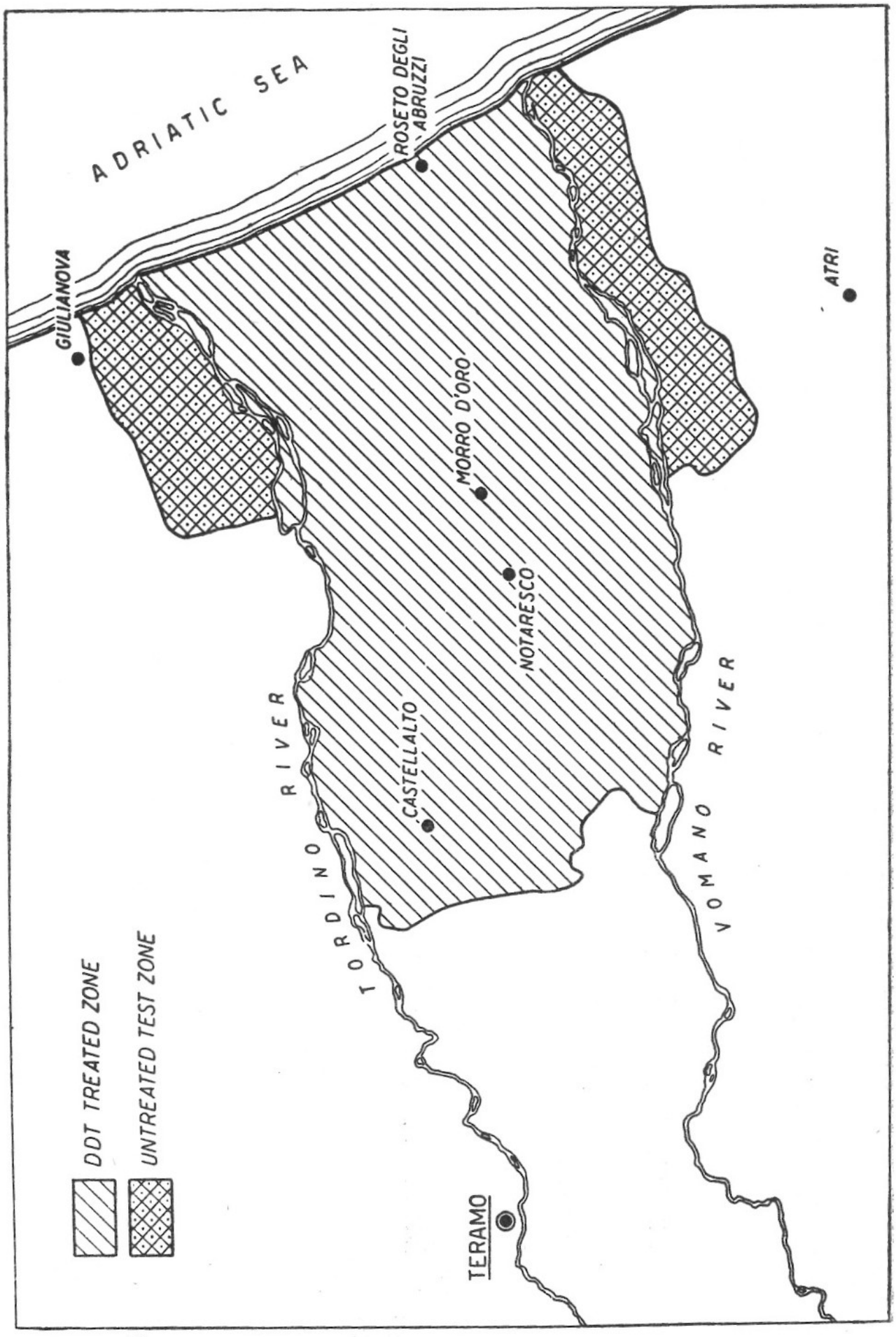
Therefore we were forced to limit our task to the critical determination of the territories in which local transmission of leishmaniasis was actually proved to exist. Such an enquiry seemed to us sufficient

at least to constitute a useful basis for practical control, as it is obvious that the main objective of Public Health Authorities should be the total elimination of the disease wherever it exists.

This year we began a personal survey of many provinces of Marche, Romagna, Emilia, Tuscany, Umbria and Puglie. This survey was carried out with an investigation intended to detect cases proved autochthonous in different localities, and was accomplished with the help of the Provincial Health Officer, the local dermatologists and paediatricians and many local physicians. Captures and classifications of *Phlebotomus* were made systematically in endemic as well as in non-endemic localities. (The entomological study was carried out with the collaboration of Dr. Giuseppe Saccà and Dr. Italia Neri).

This epidemiological investigation is still in progress. The results obtained to date show us that autochthonous leishmaniasis is much more widespread than was previously suspected (see graph 3). Oriental sore extends more or less continuously from Abruzzo to the North through the hilly country of Marche, Romagna and Emilia to reach the border




ADRIATIC SEA
GIULIANOVA
ROSETO DEGLI ABRUZZI
ATRI
MORRO D'ORO
NOTARESCO
CASTELLALTO
TORDINO RIVER
VOMANO RIVER
TERAMO
DDT TREATED ZONE
UNTREATED TEST ZONE

between the Provinces of Modena and Reggio Emilia: oriental sore may penetrate from the hills into the plain confined in a narrow strip (with the observed exceptions of Bagnacavallo and Cervia in the Ravenna province and Mirandola in the province of Modena).

We can also add that two important kala azar zones were revealed in the promontory of Gargano on the Adriatic Sea and Porto S. Stefano in the promontary of Argentario on the Tyrrhenian coast. A yet unknown focus of oriental sore was also detected at Sangemini (Umbria.)

The *Phlebotomus* catches gave abundant *Ph. perfiliewi* in the oriental sore region. In the kala azar zones. *Ph. perfiliewi* was apparently absent: *Ph. perniciosus* was the most abundant type found if not the only one. In the Gargano we found also *Ph. major*, *Ph. minutus* and *Ph. papatasi.*

These epidemiological investigations resulted in notably modifying our previous knowledge according to which leishmaniasis was limited in Italy to Abruzzo, Calabria, Vesuvio zone, Sardinia and Sicily.

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