The Last Fifteen Years of Schistosomiasis in Venezuela: Features and Evolution

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Control of schistosomiasis in Venezuela has been a topic of major interest and controversy among the metaxenic parasitosis. A small area of transmission of approximately 15,000 km^2 was thought to be eradicated some years ago. However, some epidemiological characteristics of our transmission area have limited the success on the way toward eradication. Since 1945, when the Schistosomiasis Control Program started, the prevalence in the endemic area has decreased from 14% in 1943 to 1.4% in 1996. Until 1982, the surveillance of active cases was based on massive stool examination. Since then, the Schistosomiasis Research Group (SRG) recommended the additional use of serologic tests in the Control Program and the selective or massive chemotherapy depending on serological and parasitological prevalence of each community. At present, the real prevalence is underestimated due to the fact that approximately 80% of the individuals eliminate less than 100 eggs/g of feces. Those persons could be responsible for the maintenance of the foci going on and therefore limiting the impact of the control measures.

Efforts of the SRG are being oriented toward improvement of immunodiagnostic tests by using defined antigens (enzymes) and chemically synthesized peptides, derived from relevant molecules of the parasite, either for antibodies or antigens search. On the other hand, introduction of snail competitors has been a biological weapon in the control of the intermediate host in certain areas. However, the recent reinfestation of water courses by Biomphalaria glabrata, *the increased prevalence in some areas, together with important administrative changes at the Control Program of the Minister of Health, have arisen new questions and doubts, challenging the eradication strategy proposed during the last decade.*

Key words: schistosomiasis - Venezuela - epidemiology and control

BRIEF HISTORICAL NOTE

The history of schistosomiasis in Venezuela starts in 1905, when Soto described the first human case. Later on, in 1917, Iturbe described the intermediate host as *Planorbis guadeloupensis* (Iturbe 1955). The first control measures were initiated in 1922 in spite of the fact that the snail distribution was not known in the country. But only in 1943 the Schistosomiasis Control Program (SCP) initiated its activities as a formal structure in the Minister of Health (Incani 1987). Forty years later, in 1984, a group of investigators and people related to the Control Program, agreed to create the Schistosomiasis Research Group (SRG).

Reviews on the epidemiology of schistosomiasis in Venezuela have been reported by Luttermoser (1946), Jove and Marsewski (1955), Gabaldón (1964), Incani (1987), Balzán (1988), Noya et al. (1991) and Rey (1992) among others.

OVERALL SITUATION UNTIL 1982

In 1946, the endemic area was estimated in 7,000 km^2 with 70,000 human cases (Gabaldón 1985) in the northern central region of the country, formed by the states Vargas, Miranda, Aragua, Carabobo and north of Guárico. This area was later estimated in 15,000 km^2 of the territory, which corresponds to 40% of the Venezuelan population.

Although since 1943 the prevalence in the endemic area had been relatively low (14.7 to 0.6%) (Table I) the schistosomiasis distribution in Venezuela did not follow an homogenous pattern. In fact, high focal transmission was found in some localities such as the Caracas valley with 29.1%,

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Aragua 24.8%, Miranda 10.3% and Carabobo states 9.9% (Incani 1987).

Successful control has relayed mainly on snail killing and environmental measures that avoid infected water contact of communities. In relation to snail control, the activities of the SCP were mostly dedicated to application of molluscicide and sanitary engineering. Additional control measures were based on periodical sanitary education and treatment of infected individuals. These activities reduced the prevalence as can be seen in Table I, but were not able to reduce the size of the endemic area (Fig. 1). Moreover, new breeding places of *Biomphalaria glabrata* appeared in states neighbouring the traditional endemic area such as Portuguesa, Lara and Cojedes (Otero et al. 1986).

TABLE I

Schistosomiasis prevalence based on stool examination in the Venezuelan endemic area (1943-1988)

Periods	Persons examined	Positive cases	Prevalences %
1943-1960	87639	12851	14.7
1961-1965	126948	10424	8.2
1966-1970	173645	6916	4.0
1971-1975	235656	4686	2.0
1976-1980	158519	3064	1.9
1981-1984	82877	774	0.9
1985-1988	119651	768	0.6

Source: Balzan 1988, "División de Parasitosis Intestinales, Dirección de Endemias Rurales, Malariología, MSAS", Venezuela.

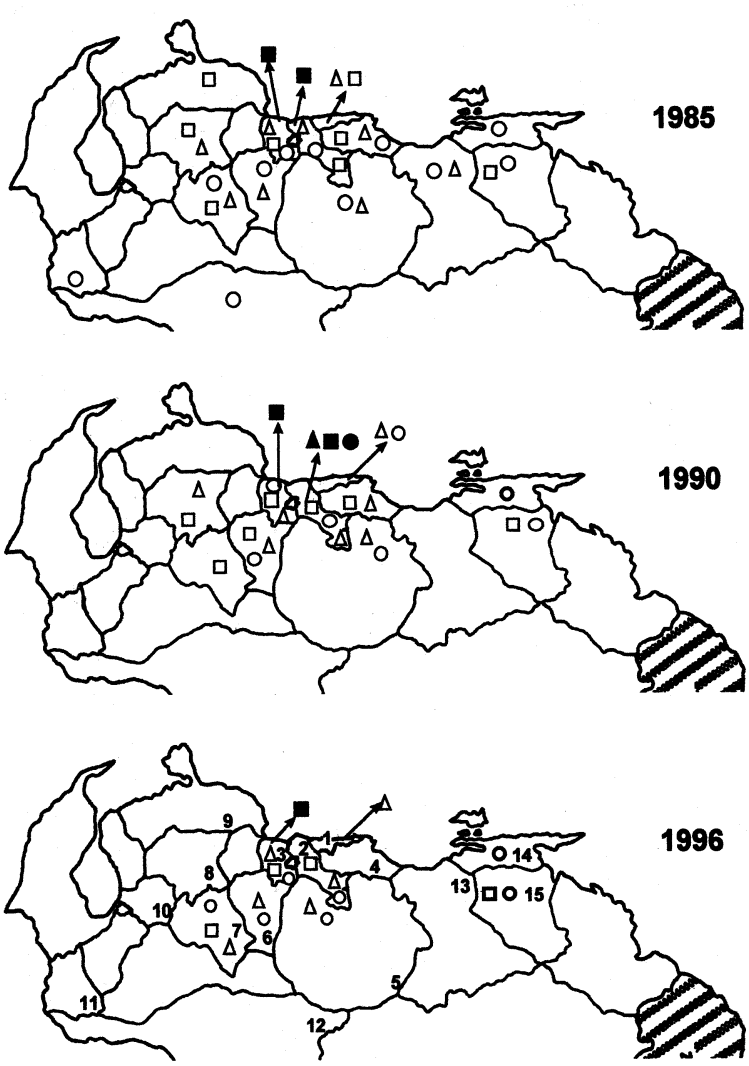

Fig. 1: *Biomphalaria* sp. Distribution and infected snails in Venezuela from 1985 to 1996, □ *B. glabrata*, △ *B. straminea*, ○ *B. prona*; □ ▲ ○ infected snails. 1. Vargas 2. Aragua 3. Carabobo 4. Miranda 5. Guárico 6. Cojedes 7. Portuguesa 8. Lara. 9. Falcón 10. Trujillo 11. Táchira 12. Apure. 13. Anzoátegui 14. Sucre 15. Monagas ///Claimed zone.

Transmission of *Schistosoma mansoni* was reported on the western states of Lara and Portuguesa, from the Chabasquén river basin, with 70 human cases ("Memoria y Cuenta del MSAS" 1979 -1981, unpublished results).

Diagnosis was based in one Kato smear of feces per person and no quantification of intensity of infection was recorded. Chemotherapy was restricted to infected persons. As in the rest of the world, attention was oriented toward snail elimination, and passive search of schistosomiasis was the rule. However at national level, large surveys within the Intestinal Parasites Program in which *S. mansoni* was included, were performed (Benarroch 1966).

SCHISTOSOMIASIS IN VENEZUELA (1982-1997)

Snail surveillance and control - In Venezuela, three species of *Biomphalaria* are commonly found, *B. glabrata, B. straminea,* and *B. prona. B. glabrata* is the intermediate host responsible for the schistosomiasis transmission in the endemic area, which has been traditionally located at the northern central region of the country. However, *B. glabrata* has been found out of this area. In order to illustrate it and to give an idea of its evolution, we selected three cross sectional studies on the distribution of the three more important species of snails (Fig. 1). Between 1982 and 1987 *B. glabrata* was detected in five states out of the classical endemic region. A similar situation was found with *B. straminea,* the second important intermediate host of *S. mansoni* in Venezuela, since it was reported in all states of the endemic area plus four additional states. But, infected *B. glabrata* was only found from Aragua and Carabobo states. In 1990 (period 1987-1992) the *Biomphalaria* sp. fauna was restricted to the central region and infected snails were found again in Aragua and Carabobo states. In this period (1987-1992) in the locality of Turmero (Aragua state) *B. straminea* and *B. prona* were also found naturally infected with *S. mansoni*.

For the period 1992-1997 (year 1996 in Fig. 1) the reports on malacological fauna were scarce. Several infected *B. glabrata* lots were reported from Carabobo state only, with frequencies of infections over 6.25% of the captured snails, in the localities of Güigüe, Manuare and Valencia. The reduced reports of this period were partially due to the efforts of the SCP in reducing the snail population with chemical molluscicides, together with administrative changes that brought budget restrictions and consequent decrease of field surveys that have not allowed snail collections.

An important aspect is that stagnant water streams with high level of organic pollution are highly favorable to *B. glabrata* (Mott et al. 1990). New human settlements have occurred in the endemic area and *B. glabrata* has colonized periurban streams which receive sewer waters from these marginal villages (Caraballeda in Vargas state and quarters at the south of Valencia city and Valencia lake).

The invasion by thiarid snails of the rivers of the seashore of Carabobo, Aragua and Vargas states is an important phenomenon. Prior to 1975, seven of these rivers harbored *B. glabrata* and one of them used to be the only active transmission site of the Distrito Federal (Alarcón de Noya et al. 1987). Several surveys until 1990 revealed that *Thiara granifera* and *Melanoides tuberculata* had displaced *B. glabrata* from this littoral (Pointier et al. 1994). Introduction of thiarid snails to Valencia lake region resulted in the elimination of *Biomphalaria* sp. from artificial ponds but this was not the case in streams and rivers (Pointier et al. 1991).

Outside the endemic region there are two areas with *B. glabrata* in Caripe (Monagas state) and in the confluence of Lara, Portuguesa and Trujillo states. In Caripe, *B. glabrata* has been considered resistant to *S. mansoni* infection (Romero-Morrel & Marta 1978), nevertheless recent studies have revealed that they are susceptible to infection (Moreno-Alvarez & Delgado 1992). This region as well as Portuguesa, Cojedes and Lara deserve more attention since the susceptible *B. glabrata* is present in all of them. *B. prona* is widely distributed in the country but does not seem to be a risky specie due to its lower susceptibility.

Active search of infected human cases - Although the SCP has the entire responsability on the disease control, researchers from three different institutions joined to this program in order to configure a multidisciplinary group (SRG).

There has been a progressive diminution in the surveillance activities as reflected by the lower number of individuals evaluated by stool examination in the last 15 years. Serologic samplings have not compensated the decrease in stool examination (Table II).

Since 1985, a strategy was undertaken pointing to look for active cases and to work on the infected populations. The SCP together with the SRG decided to incorporate serological studies as additional technique of diagnosis in the Control Program. This new strategy was based on the initial screening by ELISA with soluble egg antigen (ELISA-SEA) and confirmation of seropositives by circumoval precipitin-test (COPT) and Kato-Katz (Alarcón de Noya et al. 1992c). A summary of cross sectional studies carried out in the endemic area by different workers is shown in Table III. Although not all of them followed the same protocol, the results reveal that active cases have been

TABLE II

Schistosomiasis prevalence in Venezuela, based on stool examination and ELISA-SEA from 1982 to 1996

Periods	Stool examination			ELISA-SEA		
	Persons examined	Positive cases	%	Persons examined	Positive cases	%
1982-1986	131777	933	0.71	nd	nd	nd
1987-1991	113746	675	0.59	6953	1839	26.4
1992-1996	17945	249	1.39	11679	2405	20.6

nd: not determined.

TABLE III

Cross-sectional studies on schistosomiasis in Venezuela 1985-1997

Localities	Year	Persons examined	ELISA-SEA prevalence (%)	PPCO (%)	Kato- Katz prevalence (%)	References
Caraballeda	1985	896	nd	nd	12.2	Alarcón de Noya 1987
El 25	1986	348	nd	nd	24.9	Lara et al. 1987
Bicentenario	1989	2500	35.6	nd	nd	*a*
Belen	1990	436	30.5	10.5	nd	*a*
Los Naranjos	1991	418	37.0	13.4	20.8	Alarcón de Noya 1992a
Chuao	1992	543	23.0	24.7	0.2	Alarcón de Noya 1992b
Seitifero	1992	328	nd	77.0	30.0	Delgado et al. 1992
Guatire-Araira	1992	446	8.5	nd	nd	*a*
Santa Rosa	1992	562	nd	47.0	14.0	Delgado et al. 1992
Manuare	1993	520	nd	34.0	3.2	Delgado et al. 1992
Los Magallanes	1993	687	22.0	nd	nd	*a*
Anzoátegui	1993	90	15.5	16.6	nd	*a*
Manuare	1996	133	nd	33.0	6.8	García el al. 1997
Los Naranjos	1996	177	nd	59.8	46.0	Sanchez et al. 1997
Caraballeda	1997	188	38.0	10.6	1.0	*a*
Los Mangos	1997	126	22.2	7.9	0.0	*a*
Bicentenario	1997	331	15.1	nd	nd	*a*
S. Juan Morros	1997	126	nd	14.0	nd	*b*

a: Alarcón de Noya et al.; *b:* Arteaga et al. pers. comm.; nd: not determined.

present in high percentages throughout the last fifteen years. We consider as active cases, those persons with eggs of *S. mansoni* in the stools or positive by COPT. In all stool examination-based studies, the intensity of infection was low since 70-80% of cases excreted less than 100 eggs/g of feces. However, the parasitologic prevalence has been high in certain localities: 24.9% in "El 25" in 1986, 13.4% in "Los Naranjos" in 1991, 30% in "Manuare" 1992 and 46% in "Los Naranjos" 1996. This clustering distribution resembles the data presented by Tsang et al. (1997) in Puerto Rico, a country of low intensity of infection.

An age dependent Kato diagnosis has been demonstrated, suggesting that the number of Kato slides seems to be critical in the evaluation of true prevalence. In areas with infections greater than 100 eggs/g of feces, six Kato smears from three stool samples per person can better approximate to the real prevalence in people older than 20 years of age (Gryseels 1996). To infer "true" prevalences from simple count fecal surveys, De Vlas et al. (1993) have proposed a practical chart to avoid underestimation. In Venezuela, six Kato-Katz smears from two stool samples are performed, which is probably insufficient based on the very low intensities of infection. The ideal number is unrealistic, under our socioepidemiological and administrative condition.

Transmission of *S. mansoni* is still active based on the presence of young infected individuals. From studies of Table III, "Belen" and "Los Naranjos", 1990 and 1991 and "Los Naranjos" 1996 (Salas et al. 1997), 85.5% of the egg-excreting people was between 5 to 19 years old.

ELISA-SEA as a first screening search clearly overestimates the prevalence (Table III). Some of us have worked with a locally developed test, the alkaline phosphatase immunoassay (APIA) compar-

ing it with ELISA-SEA and COPT (Alarcón de Noya et al. 1997). We also work in a SEA treated with sodium metaperiodate (SMP), which improves specificity of ELISA-SEA (Colmenares et al. 1998). A field survey is under way to evaluate if APIA or ELISA-SMP could be selected as first screening methods instead of ELISA-SEA. APIA has shown to be highly sensitive, 93%, and 100% specific (Pujol et al. 1989). One of the strongest arguments favoring the switch from ELISA to APIA or ELISA-SMP is their higher specificity, since it is well known that people infected with intestinal nematodes cross react with *S. mansoni* antigens (Correa-Oliveira et al. 1988) and give false positives in ELISA-SEA (Alarcón de Noya et al. 1996).

Recent efforts of the SRG are oriented toward development of antigen detection techniques, using polyclonal antibodies from animals immunized with synthetic peptides or monoclonal antibodies to known molecules of *S. mansoni*.

COPT continues to be our gold standard technique due to its high sensitivity, specificity and correlation with active cases (Alarcón de Noya et al. 1992d). The COPT prevalence in cross-sectional studies is shown in Table III. A range of 8 to 77% has been found, being always these values higher than stool examination, suggesting that there are more persons infected than those excreting eggs in the feces.

The integrated analysis of the central endemic area is the key for the control of schistosomiasis in Venezuela. In Fig. 2, we have marked the outer limits of the main basins where schistosomiasis transmission takes place and the prevalence of active cases (stool examination and COPT). Few studies have been done in the two largest basins of Valencia lake and Guárico river in which three big cities are located. Instead, Manuare and Los Naranjos river basins have been subjected to chemical molluscicides and massive praziquantel treatment and, although prevalence has decreased, they still remain active.

An unknow number of individuals with low parasite loads has been probably responsible for the maintenance of ongoing foci in the endemic area. This reflects the difficulties in the eradication of this disease, since selective treatment of the positive cases is the main control measure, leaving aside an important percentage undetectable by the current diagnostic methods.

Morbidity - Few epidemiological studies have concerned morbidity. Results from four cross sec-

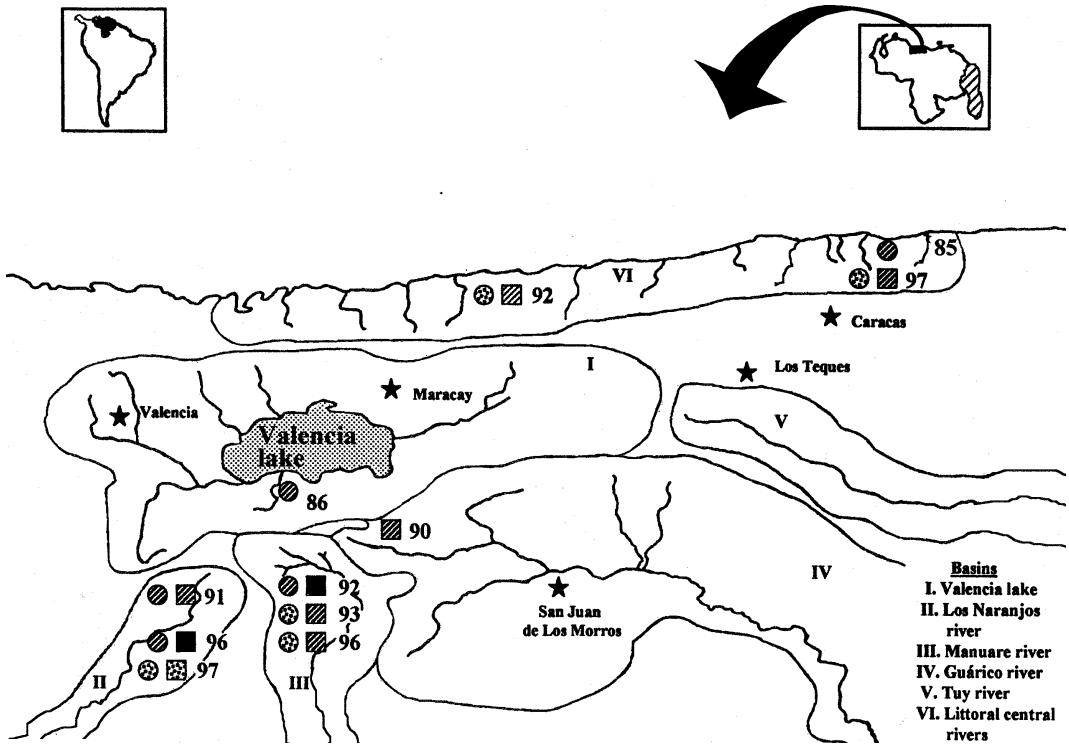

Fig. 2: focal transmission in Venezuela endemic basins. Stool examination prevalences 0-10% 10-50% >50%. Circumoval precipitation test prevalences 0-10% 10-50% > 50%.

tional studies in Table III have revealed that intestinal form predominates ranging from 60 to 85%, while hepatointestinal forms represent 15 to 38%. Hepatosplenic clinical form is rare, one or two cases were reported from these studies (Lara et al. 1987, Alarcón de Noya et al. 1992b, García et al. 1997, Sánchez et al. 1997).

Cases from hospitals and private physicians are usually not recorded, mainly because this is not an obligatory denounced disease. From 290 out patient consultation at Tropical Medicine Institute, we have diagnosed in the last five years 56 individuals being 10.7% intestinal, 39.2% hepatointestinal and 50% hepatosplenic forms. A case of mielitis for *S. mansoni* was reported in a 15 years old girl from the Distrito Federal focus (Caraballeda) in 1985 (González & Céspedes, pers. comm.).

Chemotherapy - Based on the World Healt Organization recommendations (WHO 1985), the SCP adopted in 1987 the new strategy of control based on chemotherapy and two algorithms were accepted, one for diagnosis and one for chemotherapy. Selective treatment was restricted to detected cases when COPT or Kato Katz prevalence were less then 20% and massive treatment when prevalence was higher than 20% (Alarcón de Noya et al. 1992c). However, pressure for eradicate the disease plus political changes made massive treatments to be administrated twice or without previous evaluation of prevalence. At the present time, chemotherapy guidelines and follow-up studies to measure impact of chemotherapy must be achieved specially in view of increasing problems of drug resistance (Redman et al. 1996)

Administrative and political changes - A political and administrative decentralization process has been undertaken in Venezuela since 1992. Each state is autonomous in its health policies and the surveillance of endemic infection disease depends more and more on the administration of each state. Decentralization has been a progressive process in which the Aragua and Carabobo states were the ones first involved. Other temporary endemic problems such as dengue or cholera have occupied much of the attention and resources, leaving aside the surveillance and control of traditionally endemic diseases as intestinal parasitosis and schistosomiasis.

The new administrative tendency is to eliminate the vertical programs of "malariologia", reinforcing the role of rural clinics and hospitals in the diagnosis and control of these endemies. However, as a consequence of low intensity of infection and low morbidity, the patients with schistosomiasis are rarely diagnosed and reported. In this sense, management of *S. mansoni* infected human populations and search for active cases can not be dependent on hospital workers. For this reason, SRG has proposed that in certain endemies as schistosomiasis it should be evaluated the maintenance of a vertical program directed by the SCP on the main water basins, based on sanitary education, active surveillance of cases, chemotherapy and snail control. A cost-effective evaluation should be carried out also.

It is early to evaluate the impact of this political decision on the course of endemic, chronic diseases as schistosomiasis. New strategies in this sense must be implemented jointly to the regional authorities to avoid more dispersion of the susceptible snail and infection of human populations at risk.

FINAL COMMENTS

The review of the epidemiological situation of schistosomiasis in Venezuela in the last 15 years is critically analyzed. First of all, the surveillance does not seem to be as effective as used to be in the 70th decade, based on the reduced number of persons examined by stool examination and/or by serology. A similar situation has been observed with the malacological inspections, which do not reflect the real situation of the *Biomphalaria* sp. distribution and densities in the country. Probably this is the consequence of political and administrative decisions commented above, in which the geopolitical borders of the states limit the activities of the SCP.

We have outlined the main schistosomiasis transmission basins, which include rivers, lakes, streams, ponds and dams. Five basins and one littoral region can be identified as risky areas. In this way, a small labor group of the SCP together with regional authorities could work in both actions, snail and population surveillance and control. Also, the study of these basins by remote sensing images might give valuable information helping to the detection of possible *Biomphalaria* sp. breeding places. Special attention deserves the localities out of the endemic area where some epidemiologic conditions for the establishment of schistosomiasis transmission exist.

The strategy of control, based mainly on chemotherapy must be revised. At the present time, there are no alternative drugs to praziquantel and oxamniquine and, at world level, few groups are working on the discovery of new drugs. For this reason, control programs must rescue other measures that have been relegated after the arrival of oxamniquine and praziquantel. These measures are sanitary education to the general population with special emphasis in school children, community participation and environmental sanitation.

Reduced morbidity and mortality, low intensity of infection, natural biological control of *B. glabrata* in some areas and introduction of serology in the control program have been the most important achievements in the last 15 years.

Time has demonstrated that in spite of good diagnostic tools for active cases, a wonderful drug against *S. mansoni* and a small area of focal sites of transmission, schistosomiasis has proved to be difficult to eradicate if other control measures that avoid fecal human contamination of water bodies are not implemented.

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