Dengue and the risk of urban yellow fever reintroduction in São Paulo State, Brazil

Dengue e risco da reintrodução da febre amarela urbana no Estado de São Paulo

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Keywords
Yellow fever, epidemiology. Dengue, epidemiology. Mathematical models. Disease outbreaks. *Aedes*. Yellow fever vaccine.

Abstract

Objective
To propose a mathematical method for the estimation of the Basic Reproduction Number, R_0, of urban yellow fever in a dengue-infested area.
Methods
The method is based on the assumption that, as the same vector (*Aedes aegypti*) causes both infections, all the quantities related to the mosquito, estimated from the initial phase of dengue epidemic, could be applied to yellow fever dynamics. It is demonstrated that R_0 for yellow fever is, on average, 43% lower than that for dengue. This difference is due to the longer dengue viremia and its shorter extrinsic incubation period.
Results
In this study the analysis was expanded to the epidemiological situation of dengue in São Paulo in the year 2001. The total number of dengue cases increased from 3,582 in 2000 to 51,348 in 2001. It was then calculated R_0 for yellow fever for every city which have shown R_0 of dengue greater than 1. It was also estimated the total number of unprotected people living in highly risky areas for urban yellow fever.
Conclusions
Currently there is a great number of non-vaccinated people living in *Aedes aegypti* infested area in the state of São Paulo.

Descritores
Febre amarela, epidemiologia. Dengue, epidemiologia. Modelos matemáticos. Surtos de doenças. Aedes. *Vacina contra febre amarela.*

Resumo

Objetivo
Propor um modelo matemático para a estimativa da reprodutibilidade basal, R_0, *para a febre amarela urbana em uma área infestada pela dengue.*
Métodos
*O método utilizado considera que, como ambas as doenças são transmitidas pelo mesmo vetor (*Aedes aegypti*), poder-se-ia aplicar todos os parâmetros quantitativos relativos ao mosquito, estimados pela fase inicial da curva de crescimento de casos de dengue, à dinâmica da febre amarela. Demonstra-se que o* R_0 *da febre amarela é em média 43% menor que o da dengue. Esta diferença deve-se à viremia mais prolongada da dengue, bem como ao menor período de incubação extrínseco daquele vírus no mosquito.*

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Supported by grants of LIM01/HCFMUSP, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP - Processo n. 2000/01347-4), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq - Processo n. 304560/90-1) and PRONEX. (Processo n. 41.96.0937).
Received on 12/9/2002. Reviewed on 17/3/2003. Approved on 7/4/2003.

Rev Saúde Pública 2003;37(4):477-84
www.fsp.usp.br/rsp

Resultados

Apresenta-se a aplicação desta análise matemática à situação epidemiológica da dengue no estado de São Paulo, para o ano de 2001, onde o número de casos de dengue aumentou de 3.582, em 2000 para 51.348, em 2001. Calculou-se o valor de R_0 *para a febre amarela para cada cidade do estado que tinha R0 para dengue maior que um. Estimou-se o número total de pessoas desprotegidas, sem vacina, e que vivem em áreas de alto risco para a febre amarela urbana.*

Conclusões

Foi demonstrado que existe, um grande contingente de pessoas não vacinadas contra febre amarela vivendo em áreas infestadas por Aedes aegypti *no Estado de São Paulo, até aquela data (2001).*

INTRODUCTION

In a recent publication (Massad et al,[11] 2001) it was proposed a mathematical method for the estimation of the Basic Reproduction Number, R_0 (Anderson & May,[1] 1991), and hence the threshold for triggering a major epidemic of urban yellow fever in a dengue-infested area. The method is based on the assumption that, as the vector of both infections is the *Aedes aegypti*, all the quantities related to the mosquito, estimated from the initial phase of dengue epidemic (see below), could be applied to yellow fever dynamics. It was demonstrated that R_0 for yellow fever is, on average, 34% lower than that for dengue. This difference is due to the longer dengue viremia and its shorter extrinsic incubation period (Monath,[12] 1990; Halsted,[8] 1990). It was then exemplified the method with dengue epidemic data from the state of São Paulo, Brazil, for the year 2000. At that time, 67 cities (about 10% of the total number of cities in the state) presented dengue cases with 12 of them showing $R_0>1$ for both dengue and yellow fever. As the measures for vector control were inadequate, the dengue epidemic spread throughout the state of São Paulo in the following year (2001), becoming worse in intensity and number of cities affected, and therefore increasing the risk of urban yellow fever being reintroduced.

Early in the 20th century, when it was discovered that the yellow fever virus is transmitted in its urban cycle by *Aedes aegypti*, control measures were introduced leading to its almost disappearance of the Americas and, in particular, of Brazil. However, reinfestation with *Aedes aegypti* vector, which began in the late 1960s (Fraiha,[6] 1968; Franco,[7] 1969; Monath,[13] 1999), is now practically complete, and vector control is substantially more difficult than before.

Dengue, another *Flaviridae* infection transmitted by the same peridomestic *Aedes aegypti* mosquitoes, reappeared as a major urban epidemic in Brazil in the state of Rio de Janeiro in 1986, although there has been a previous outbreak of dengue virus reported in Brazil (Marques et al,[10] 1994; Degallier et al,[3] 1996). Since then, it turned into an endemic infection with annual outbreaks, comprising more than 80,000 cases reported in the state of São Paulo in the last 5 years, of which approximately 52,000 cases occurred in 2001.

There has been no case of urban yellow fever reported in Brazil since 1942 (CVE* 2001). The sylvatic yellow fever, however, is enzootic in an enormous area of central and north-northwestern states. In the period between 1990 and 2001, 380 human cases (with 159 deaths) were reported, of which 191 (82 deaths) were reported in the last three years (CVE 2001). In addition, the epidemic is drifting from its original epicenter in the northern and central regions towards the more populated southeastern states. In 2000, two autochthonous human cases were reported in the state of São Paulo, the first ones in more than 50 years.

It should be mentioned that although *Aedes albopictus* is also present in costal areas of Brazil since the early 1980s (Forattini,[4] 1986), it was not included in the study analysis because its role as an important dengue transmitter in the Americas is still to be confirmed (Forattini,[5] 2002).

In this study the analysis presented in Massad et al,[11] 2001, is expanded and data from the 2001 dengue epidemic updated. In addition it is estimated the number of cities with major risk of urban yellow fever reintroduction and the size of the population at risk.

In the next section it is briefly described the method proposed in Massad et al,[11] 2001, for the estimation of R_0 for yellow fever as a function of R_0 for dengue, estimated from the exponential growing phase of the dengue epidemic. Section 3 is dedicated to the description and analysis of the dengue

*Center for Epidemiologic Surveillance. Data available in 2001. Http://www.cve.sp.gov.br/htm/febre_am1.htm

epidemic in the state of São Paulo in 2001 and its potential repercussion on the risk of urban yellow fever reintroduction in affected areas. It is also estimate the total number of unprotected people living in highly risky areas for exposure to urban yellow fever. Finally, in the discussion section there are some observations on the current (2002) dengue epidemic in São Paulo and possible control strategies for avoiding a major epidemic of urban yellow fever in the dengue infested area are assessed.

Estimating R_0 for yellow fever

For a vector-borne disease, R_0 may be understood as the number of secondary infections spread in a community through the vector population, as direct result of the presence of a single primary case (Macdonald,[9] 1952; Molineaux & Gramiccia,[15] 1980; Burattini et al,[2] 1998).

The expression for R_0 is given by (Massad et al,[11] 2001; Burattini et al,[2] 1998):

$$R_0 = \frac{N_m}{N_H}\frac{a^2 bc \exp(-\mu\tau)}{\gamma\mu} \qquad (1)$$

where N_H is the total number of humans and N_M is the total number of mosquitoes. Each female mosquito bites humans at a rate of a times per unit of time. The duration of viremia (and therefore infectiousness) of a given vector-borne infection is γ^{-1} units of time. Only a fraction of bites in infected humans, c, is considered to be infective to the vectors. The average life expectancy of the mosquitoes is μ^{-1} and t is the extrinsic incubation period of the infection. After τ units of time, only a fraction $e^{-\mu\tau}$ of mosquitoes survive and only a proportion b of their bites is effectively infective to humans.

From equation (1) it can be deduced a relation between R_0 of yellow fever and dengue. The resulting expression of R_0 for yellow fever as a function of R_0 for dengue is given by (Massad et al,[11] 2001):

$$R_{0\,yf} = R_{0_{dengue}}\frac{\gamma_{dengue}}{\gamma_{yf}}\frac{b_{yf}c_{yf}}{b_{dengue}c_{dengue}}\exp\left[-\mu\left(\tau_{yf}-\tau_{dengue}\right)\right] \qquad (2)$$

It is also demonstrated in that previous study that R_0 for yellow fever is, on average, 43% lower than that for dengue. This difference is due to the longer viremia of dengue and its shorter extrinsic incubation period (Massad et al,[11] 2001).

The relation between the critical proportion of any control measure to be applied to a population in order to ensure the non-existence of a disease and the value of its R_0 is given by (Anderson & May,[1] 1991):

$$p_c = 1 - \frac{1}{R_0} \qquad (3)$$

Therefore, if a proportion p of the susceptible population is vaccinated (and considered protected), then the critical proportion, p_c, to vaccinate against yellow fever in order to ensure that a single infective would not trigger an epidemic is (Massad et al,[11] 2001):

$$p_c = 1 - \frac{1}{R_{0_{dengue}}}\frac{\gamma_{dengue}}{\gamma_{yf}}\frac{b_{yf}c_{yf}}{b_{dengue}c_{dengue}}\exp\left[-\mu\left(\tau_{yf}-\tau_{dengue}\right)\right] \qquad (4)$$

Estimating R_0 from the initial exponential phase of the number of cases

As mentioned in Massad et al,[11] 2001, in an epidemic of a vector-borne infection, R_0 can be estimated from the initial exponential growing phase of the number of cases in each affected city, i.

Fitting a exponential

$$I_{H_i} = C_{H_i}\exp(\lambda_i T) \qquad (5)$$

C_{Hi} is a constant to the initial growing phase of the dengue number of human cases I_{Hs}, and it can be estimated the coefficient λ, from which $R_{0\text{dengue}}$ can be calculated for each affected city i, according to:

$$R_{0dengue} = 1 + \frac{\lambda_i^2 + \lambda_i(\mu+\gamma)}{\mu\gamma} \qquad (6)$$

Having $R_{0\text{dengue}}$ it is possible to estimate $R_{0\text{yf}}$ and p_c from equations (2) and (3), respectively.

Table 1 - Evolution of Dengue epidemic in the State of São Paulo, Brazil.

Year	N
1987	46
1988	0
1989	0
1990	3,038
1991	3,662
1992	38
1993	638
1994	681
1995	6,048
1996	7,104
1997	2,040
1998	10,631
1999	15,073
2000	3,582
2001	51,348
2002	3,945*

*First 9 weeks only.

The dengue epidemic in São Paulo in 2001

Dengue reemerged in Brazil in 1986 and since then it has recurred with varying intensity every year. In São Paulo, after the first minor epidemics in the late 1980's, dengue has acquired alarming proportions with yearly epidemics of growing intensity and range of geographical spread.

As mentioned before, the number of affected cities in 2000 (67), 12 showing R_0 greater than one, increased to 191, of which 64 with R_0>1. The total number of dengue cases in the state of São Paulo increased from 3,582 in the year 2000 to 51,348 in the year 2001. In the current year, 3,945 cases were confirmed in the state of São Paulo in the first 9 weeks of the year. Table 1 shows the temporal evo-

Table 2 - The number of dengue cases, the Basic Reproduction Number for dengue and yellow fever and the correspondent proportion to vaccinate against yellow fever to prevent and epidemic. São Paulo State, 2001.

City	Dengue cases	R_0 dengue	R_0 yellow fever	P_c
Andradina	1,414	4.26	2.43	0.59
Araçatuba	450	3.25	1.86	0.28
Araraquara	196	3.8	2.17	0.54
Barra Bonita	160	10.33	5.90	0.83
Barretos	3,045	3.91	2.23	0.55
Barueri	414	4.74	2.71	0.63
Bastos	46	4.62	2.64	0.62
Bauru	94	3.36	1.92	0.48
Bebedouro	478	4.14	2.37	0.58
Birigui	64	2.84	1.62	0.38
Borborema	477	7.75	4.43	0.77
Cajobi	307	6.03	3.45	0.71
Campinas	439	3.36	1.92	0.48
Castilho	254	4.26	2.43	0.59
Catanduva	111	3.47	1.98	0.50
Catigua	69	4.62	2.64	0.62
Colina	444	3.15	1.80	0.44
Colômbia	93	2.74	1.57	0.36
Cubatão	2,504	4.26	2.43	0.59
Dracena	48	3.25	1.86	0.46
Espírito Santo do Pinhal	42	4.74	2.71	0.63
Fernandópolis	542	4.03	2.30	0.57
Fernando Prestes	44	6.59	3.77	0.73
Franca	64	4.14	2.37	0.58
Guaíra	944	5.63	3.22	0.69
Guarujá	2.857	6.59	3.77	0.73
Hortolândia	89	2.84	1.62	0.38
Ibitinga	51	2.84	1.62	0.38
Igarapava	296	4.62	2.64	0.62
Ilha Solteira	386	7.16	4.09	0.76
Indaiatuba	49	3.25	1.86	0.46
Itápolis	55	3.04	1.74	0.42
Ituverava	189	4.26	2.43	0.59
Jaboticabal	109	6.45	3.69	0.73
Jardinópolis	1,874	6.03	3.45	0.71
José Bonifácio	51	3.8	2.17	0.54
Limeira	704	4.03	2.30	0.57
Lins	125	4.38	2.50	0.60
Maracai	191	11.57	6.61	0.85
Miguelópolis	190	5.12	2.93	0.66
Mirassol	1,574	5.37	3.07	0.67
Monte Aprazível	44	3.8	2.17	0.54
Neves Paulista	58	4.03	2.30	0.57
Nova Independência	54	4.03	2.30	0.57
Olímpia	772	3.36	1.92	0.48
Osvaldo Cruz	146	8.06	4.61	0.78
Paulo de Faria	197	4.26	2.43	0.59
Penápolis	138	4.62	2.64	0.62
Piracicaba	355	3.36	1.92	0.48
Pontal	449	3.47	1.98	0.50
Praia Grande	278	3.47	1.98	0.50
Ribeirão Preto	2,703	4.99	2.85	0.65
Rio Claro	105	4.03	2.30	0.57
Riolândia	87	4.03	2.30	0.57
Santa Bárbara	79	4.03	2.30	0.57
Santos	11,282	4.99	2.85	0.65
São José do Rio Preto	6.420	5.77	3.30	0.70
São Joaquim da Barra	139	5.24	2.99	0.67
São Paulo	320	6.59	3.77	0.73
São Sebastião	445	7.16	4.09	0.76
São Vicente	3,017	5.9	3.37	0.70
Sertãozinho	743	4.38	2.50	0.60
Sumaré	154	3.58	2.05	0.51
Valparaíso	163	7.6	4.34	0.77

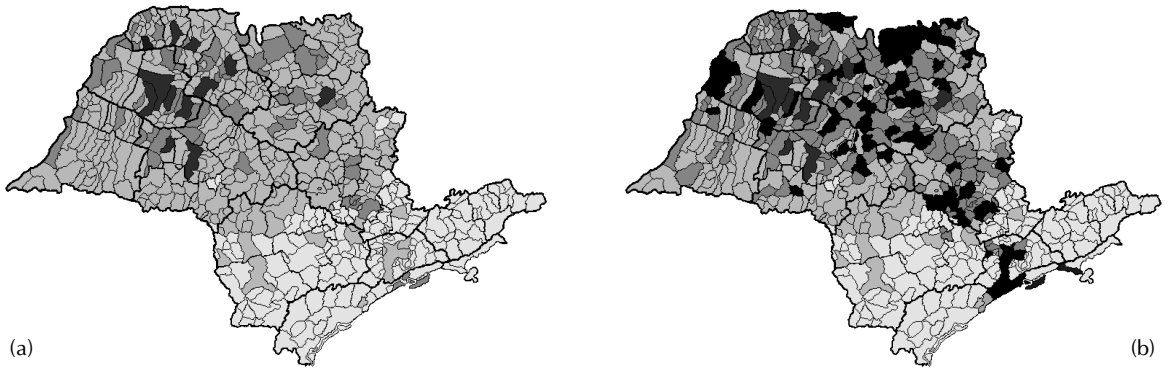

Figure 1 – (a) Dengue distribution in the state of São Paulo in 2000. Shaded areas indicate municipal districts infested with *Aedes aegypti*; light grey areas indicate cities with reported cases of dengue with R_0 below 1; dark grey areas correspond to the 12 municipal districts with R_0 above 1. (b) The same as in Figure 1a for the year 2001. It can be noted that the epidemiological situation deteriorated.

lution of dengue cases in the state of São Paulo since 1987.

In Table 2 the dengue situation is described for the 64 cities with R_0>1 for dengue in the year 2001. The first column shows the name of the city; the second shows the total number of reported cases in those cites; the third column shows the estimated value of $R_{0\,\text{dengue}}$; the fourth column shows the calculated values of R_{0yf}; and the last column shows the estimated proportion of individuals that should be vaccinated against yellow fever in order to prevent an epidemic.

In Figures 1a and 1b, the epidemic evolution is presented for 2000 and 2001. The figures show a map of São Paulo, where light gray areas are those municipalities infested by *Ae. aegypti* but with no cases of dengue reported; dark gray areas are the municipalities with dengue cases reported; and black areas are those municipalities with dengue epidemic and R_0>1.

In Table 3 present the same cities mentioned above with their respective population sizes, actual proportion of individuals vaccinated against yellow fever in the last 10 years, and number of individuals at risk (unprotected by vaccination).

Figure 2a shows the current control strategy against yellow fever in the state of São Paulo. Shaded areas represent municipalities included in what is called a "transition zone," between enzootic and unscathed regions of Brazil, thought to be at risk for yellow fever. Therefore, these are the cities under intense surveillance and where vaccination is recommended, creating a blocking belt.

In contrast, Figure 2b show what it is believed to be a better representation of the actual risk of urban

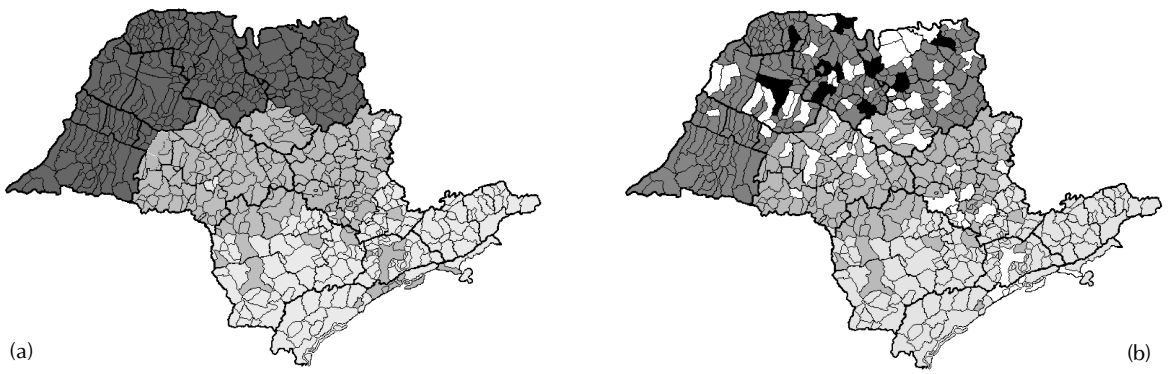

Figure 2 – (a) Current control strategy against yellow fever in the state of São Paulo. Shaded areas indicate municipal districts infested with *Aedes aegypti*; dark shaded areas indicate municipalities included in the so-called "transition zone" between enzootic and unscathed regions of Brazil, subjected to vaccination in order to form a blocking belt zone. (b) Light gray areas (same as in Figure 1) which are infested with *Ae. aegypti*, superimposed by the blocking belt (dark gray area), and those cities with R_0 for yellow fever greater than 1, i.e., at risk urban yellow fever reintroduction. white areas indicate the municipalities with vaccination against yellow fever below the critical proportion required to prevent an epidemic. Black areas correspond to those municipalities with R_0 for yellow fever greater than 1 but with vaccination above that critical proportion.

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yellow fever reintroduction in São Paulo. The figure shows the same light gray areas (as in Figure 1) infested with *Ae. aegypti,* dark gray areas representing the blocking belt as in Figure 2a, and those cities with R_0 for yellow fever greater than 1, i.e., at risk of urban yellow fever reintroduction. Yellow areas indicate municipalities with vaccination against yellow fever below the critical proportion required to prevent an epidemic that could be triggered by a single imported case from the sylvatic yellow fever endemic areas. Green areas represent those municipalities with R_0 for yellow fever greater than 1 but with vaccination above that critical proportion.

DISCUSSION

Since the last three cases of urban yellow fever reported in Brazil in 1942, the disease has been con-

Table 3 - The cities with dengue and yellow fever with R_0 >1, the actual proportion of people vaccinated against yellow fever and the number of individuals at risk of yellow fever. São Paulo State, 2001.

City	Population	P_{real}	Population at risk of yellow fever
Andradina	55,134	0.26	40,535
Araçatuba	169,073	0.279	
Araraquara	181,763	0.2265	140,594
Barra Bonita	35,317	0.2365	26,965
Barretos	103,791	0.4972	52,186
Barueri	207,123	0.0002	207,082
Bastos	20,577	0.0025	20,526
Bauru	315,266	0.262	232,666
Bebedouro	74,725	0.6943	
Birigui	94,123	0.3238	63,646
Borborema	13,165	0.2651	9,675
Cajobi	9,152	0.3788	5,685
Campinas	966,700	0.167	805,261
Castilho	14,943	0.2021	11,923
Catanduva	105,619	0.8311	
Catigua	6,556	0.6048	2,591
Colina	16,647	0.6481	
Colômbia	5,948	0.1477	5,069
Cubatão	107,734	0.2563	80,122
Dracena	40,470	0.2454	30,539
Esp.Santo do Pinhal	40,378	0.0128	39,861
Fernandópolis	61,569	0.8046	
Fernando Prestes	5,423	0.5	2,712
Franca	286,828	0.2231	222,837
Guaíra	34,563	0.4976	17,364
Guarujá	264,575	0.1943	213,168
Hortolândia	150,855	0.0004	150,795
Ibitinga	46,512	0.2294	35,842
Igarapava	25,891	0.0103	25,624
Ilha Solteira	23,966	0.3647	15,226
Indaiatuba	146,312	0.2068	116,055
Itápolis	37,697	0.2635	27,764
Ituverava	36,235	0.8152	
Jaboticabal	67,306	0.0056	66,929
Jardinópolis	30,654	0.0024	30,580
José Bonifácio	28,543	0.7199	
Limeira	248,208	0.2255	192,237
Lins	65,888	0.2689	48,171
Maracai	12,968	0.47	6,873
Miguelópolis	18,990	0.0026	18,941
Mirassol	48,327	1.0303	
Monte Aprazível	18,403	0.6904	
Neves Paulista	8,907	0.8532	
Nova Independência	2,057	0.0732	1,906
Olímpia	46,013	0.5761	
Osvaldo Cruz	29,628	0.0043	29,501
Paulo de Faria	8,469	0.9533	
Penápolis	54,509	0.3181	37,170
Piracicaba	327,805	0.0034	326,690
Pontal	29,583	0.2042	23,542
Praia Grande	191,021	0.2814	137,268
Ribeirão Preto	504,250	0.195	405,921
Rio Claro	167,772	0.2755	121,551
Riolândia	8,553	0.373	5,363
Santa Bárbara	169,479	0.0527	160,547
Santos	417,771	0.2897	296,743
São José do Rio Preto	357,052	0.5065	176,205
São Joaquim da Barra	41,536	0.3109	28,622
São Paulo	10,398,576	0.0122	10,271,713
São Sebastião	57,595	0	
São Vicente	302,335	0.2575	224,484
Sertãozinho	94.,485	0.0054	93,975
Sumaré	195,440	0.2963	137,531
Valparaíso	18,554	0.2156	14,554

fined to enzootics of the sylvatic form (FUNASA,* 2001). This is perpetuated by a cycle involving primates and mosquitoes of the gender *Haemagogus* sp. and *Sabethes* sp. Sporadic human cases of the sylvatic form have been reported since then, with a total of 380 (159 deaths) cases between 1990 and 2001. This relatively low number of cases is due to basically two factors: low migration rates between urban centers and enzootic reservoirs and an effective vaccination program encouraging people to be vaccinated 10 days before visiting enzootic areas. In addition, this control program includes an intense surveillance program of *Ae. aegypti* and vaccination creating a blocking belt of vaccinated individuals living in the transition zone between urbanized areas and enzootic regions.

The state of São Paulo shares borders with enzootic states. In spite of that only two autochthonous cases of sylvatic yellow fever has been reported so far. However, the spread of *Aedes aegypti* towards coastal areas, and the ensuing spread of dengue, is putting at risk cities far away from the blocking belt vaccination areas, as shown in Figure 2b. A global vaccination campaign against yellow fever should be carried out with great care. Although safe the vaccine is not free from adverse effects (Monath,[14] 1999). In Brazil, it has been estimated between 1 and 21 fatality cases per million doses (Struchiner, personal communication). At the moment, considering the worsening of dengue epidemic in São Paulo (more than 10,000 cases reported in the first 8 weeks of the year), and considering the adverse effects of the yellow fever vaccine, the current vaccination strategy should be revised.

The current preventive program of vaccination focuses on areas of the state as shown in Figure 2a, part of the blocking belt. In addition, vaccination of people traveling to enzootic regions is strongly recommended. However, as shown in Figure 2b, this strategy is inconsistent with the current epidemiological scenario of the state of São Paulo. It is worth noting that only 16% of the municipalities in the blocking belt have R_0 for yellow fever greater than 1. Furthermore, only 26% of the cities with R_0 for yellow fever greater than 1 have achieved protective coverage levels. Therefore, it could be that the state of São Paulo is wasting vaccines and resources, and posing a risk of adverse effects to people by routinely vaccinating the remaining 84% of the cities in the blocking area which have R_0 for yellow fever lower than 1 while failing to protect those cities at actual risk.

More serious is the fact that half of the 61 cities with R_0 for yellow fever greater than 1 and inadequate vaccination are outside the blocking belt area, and none of them have achieved the minimum vaccination coverage required.

Therefore vaccination strategy should be urgently revised, as follows: 1) it is important to take into account regional variation in the risk of yellow fever using the new methodology proposed in (1) and applied here for the identification of areas at risk and then periodical calculation of that risk should be undertaken; 2) a *compulsory* vaccination program for people traveling to enzootic areas should be introduced and the education program to warn people of the risk of traveling to those areas without vaccination at least 10 days prior should be improved; 3) routine vaccination should be targeted to the areas at risk in order to avoid unnecessary mass vaccination. This proposed targeted vaccination program would be also more cost effective in the sense that it optimizes allocation of limited resources.

Currently there are more than 15 million non-vaccinated people living in *Aedes* sp. infested area in the state of São Paulo. Although the dramatic dengue epidemic is attracting the attention of public health authorities, these figures are of high concern. The risk of reemergence of urban yellow fever is indeed on one's doorstep.

REFERENCES

1. Anderson RM, May RM. *Infectious diseases of humans: dynamics and control*. Oxford: Oxford University Press; 1991.

2. Burattini MN, Coutinho FAB, Lopez LF, Massad E. Modelling the dynamics of leishmaniasis considering human, animal host and vector populations. *J Biol Syst* 1998;6:337-56.

3. Degallier N, da Rosa AP, Vasconcelos PF, Figueiredo LT, da Rosa JF, Rodrigues SG et al. Dengue fever and its vector in Brazil. *Bull Soc Pathol Exot* 1996;89:128-36.

4 Forattini OP. Identificação de *Aedes (Stegomyia) albopictus* no Brasil. *Rev Saúde Pública* 1986;20:244-5.

*"*Fundação Nacional de Saúde, Ministério da Saúde, Brasil*". Data available in 2001. Http://www.funasa.gov.br

5. Forattini OP. *Culicidologia médica: identificação, biologia, epidemiologia v.2.* São Paulo: EDUSP; 2002. p. 498.

6. Fraiha H. Reinfestação do Brasil pelo *Aedes aegypti*. Considerações sobre o risco da urbanização do vírus da febre amarela na região infestada. *Rev Inst Med Trop São Paulo* 1968;10:289-94.

7. Franco O. Reinfestation of Pará by *Aedes aegypti*. *Rev Bras Malariol Doenças Trop* 1969;21:729-31.

8. Halstead SB. Dengue. In: Warren KS, Mahmoud AAF, editors. *Tropical and geographical medicine*. New York: McGraw-Hill; 1990 p. 675.

9. Macdonald G. The analysis of equilibrium in malaria. *Trop Dis Bull* 1952;49:813-28.

10. Marques CA, Forattini OP, Massad E. The basic reproduction number for dengue fever in São Paulo state Brazil: 1990-1991 epidemic. *Trans R Soc Trop Med Hyg* 1994;88:58-9.

11. Massad E, Coutinho FAB, Burattini MN, Lopez LF. The risk of yellow fever in a dengue infested area. *Trans R Soc Trop Med Hyg* 2001;95:370-4.

12. Monath TP. Yellow fever. In: Warren KS, Mahmoud AAF, editors. *Tropical and geographical medicine*. New York: McGraw-Hill; 1990. p. 661-74.

13. Monath TP. Facing up to re-emergence of urban yellow fever. *Lancet* 1999;353(9164):1541.

14. Monath TP. Yellow fever. In: Plotkin AS, Orenstein WA, editors. *Vaccines*. 3rd ed. Philadelphia: Saunders; 1999. p. 815-80.

15. Molineaux L, Gramiccia G. *The garki project*. Geneva: World Health Organization; 1980.