

Gender-related family head schooling and *Aedes aegypti* larval breeding risk in Southern Mexico

Rogelio Danis-Lozano, MSc,⁽¹⁾ Mario H Rodríguez, MD, PhD,⁽²⁾
Mauricio Hernández-Avila, MD, PhD.⁽³⁾

Danis-Lozano R, Rodríguez MH, Hernández-Avila M.
Gender-related family head schooling
and *Aedes aegypti* larval breeding risk
in Southern Mexico.
Salud Publica Mex 2002;44:237-242.

The English version of this paper is available too at:
<http://www.insp.mx/salud/index.html>

Danis-Lozano R, Rodríguez MH, Hernández-Avila M.
Escolaridad con relación al género de los jefes de familia
y el riesgo de cría de *Aedes aegypti*
en el sur de México.
Salud Publica Mex 2002;44:237-242.

El texto completo en inglés de este artículo también
está disponible en: <http://www.insp.mx/salud/index.html>

Abstract

Objective. To investigate if family head genre-associated education is related to the risk of domiciliary *Aedes aegypti* larval breeding in a dengue-endemic village of Southern Mexico. **Material and Methods.** A family head was considered to have a low education level if he/she had not completed elementary school. To estimate larval breeding risk within each household, a three-category Maya index was constructed using a weighted estimation of controllable and disposable domestic water containers. A socio-economic index was constructed based on household construction characteristics. **Results.** Low-level education of either family head was associated to higher larval breeding risk. Households with low-educated mothers had more larval breeding containers. These associations persisted after adjusting for household socio-economic level. **Conclusions.** These results indicate that households with female family heads with low education levels accumulate more containers that favor *Ae. aegypti* breeding, and that education campaigns for dengue control should be addressed to this part of the population. The English version of this paper is available too at: <http://www.insp.mx/salud/index.html>

Key words: *Aedes aegypti*; larval breeding; gender; education; Mexico

Resumen

Objetivo. Investigar si la escolaridad asociada con el género de los jefes de familia de una localidad endémica de dengue en el sur de México estaba relacionada con el riesgo de cría intradomiciliar de *Aedes aegypti*. **Material y métodos.** Se consideró que un jefe de familia tenía baja educación si él/ella no había completado la educación primaria. Para estimar el riesgo de cría larvaria en cada domicilio se construyó un Índice Maya de tres categorías a partir de la estimación ponderada de recipientes controlables y desechables. Se construyó un índice socioeconómico basado en los materiales de construcción de la casa. **Resultados.** Niveles bajos de educación de los jefes de familia se asociaron con niveles altos de riesgo de cría de larvas de mosquitos. Pero las casas con jefas de familia con baja educación tuvieron más recipientes en riesgo para la cría de larvas. Estas observaciones no se modificaron después de ajustar por el nivel socioeconómico. **Conclusiones.** Estos resultados indican que las casas con jefas de familia de baja educación acumulan más recipientes que favorecen la cría de larvas *Ae. aegypti*, y que sería conveniente que las campañas de educación para el control del dengue se dirigieran hacia esta parte de la población. El texto completo en inglés de este artículo también está disponible en: <http://www.insp.mx/salud/index.html>

Palabras clave: *Aedes aegypti*; cría de larvas; género; educación; México

This work was financially supported by the Ministry of Health of Mexico.

(1) Centro de Investigación de Paludismo, Instituto Nacional de Salud Pública, Tapachula, Chiapas, México.

(2) Centro de Investigación sobre Enfermedades Infecciosas, Instituto Nacional de Salud Pública, Cuernavaca, Morelos, México.

(3) Centro de Investigación en Salud Poblacional, Instituto Nacional de Salud Pública, Cuernavaca, Morelos, México.

Received on: July 3, 2001 • Accepted on: November 9, 2001

Address requests reprints to: Mario H Rodríguez, Centro de Investigación sobre Enfermedades Infecciosas, Instituto Nacional de Salud Pública, Avenida Universidad 655, Col. Santa María Ahuacatitlán, 62508, Cuernavaca, Morelos, México.

E-mail: mhenry@insp3.insp.mx

Aedes aegypti, the main vector of dengue fever in the Americas, is well adapted to urban environments, where person-made water containers provide suitable habitats for their larvae to breed.¹ In tropical areas, discarded metal drums and concrete-built tanks, used to collect and storage water, are the most frequent habitats for these larvae. Other containers such as flowerpots as well as discarded tires and bottles that accumulate in backyards are also used by this mosquito to lay its eggs, when rainfall provides the necessary water substrate. The use of metal drums and concrete tanks for water storage is used as a remedy to inadequate water supply services, but in places where water is efficiently provided, the use of containers for daily use is determined by culturally-dictated practices.²

Gender has an important effect on the distribution of activities within the household. As family heads are more frequently males, house chores are more frequently carried out by housewives.³ Although it is expected that socio-economic factors may have an important effect on housing conditions, including water storage practices, a gender-related labor distribution within the family suggests that these conditions could be differentially affected by the educational level of its dwellers.³ We present herein the results of a study, conducted in Southern Mexico, to investigate whether the level of schooling of the male and female family heads was associated to the risk for the presence of water containers suitable for *Ae. aegypti* larval breeding within households. These observations may provide useful information to better target future anti-dengue educational programs by health authorities.

Material and Methods

The study was carried out in Huixtla, (92° 97' N; 15° 8' W) a city where dengue fever is endemic, with 45 000 inhabitants located on the Pacific Ocean coastal plain of Chiapas, Southern Mexico. A cross-sectional study was carried out between July and August 1994. The locality was divided into four areas (center, intermediate, peripheral and city edges). In each area 62 households were randomly selected for the study (25% of total). Both male and female family heads were interviewed and a questionnaire to investigate socio-demographic conditions was applied. The questionnaire obtained information on house ownership, both family heads' age, schooling and occupation, as well as the number of persons living in the house. A family head was considered to have a low level education if he or she had not completed six years of formal elementary school.

Following the interview, an entomological survey within the household and its backyard was carried out by the same personnel that conducted the interview. All possible water containers with or without *Ae. aegypti* larvae were registered and classified as controllable and disposable ones. Controllable containers were those in use in the household that could be manipulated by man to avoid mosquito larval breeding. These included: concrete tanks, metal drums, flower pots, aluminum tanks, small buckets, and other plastic containers used to carry or storage water. Disposable containers, abandoned or stored in the backyard, were those not in use in the household but, in the event of rainfall, could become breeding sites; these included: tires, cans, tubs, etc. Bottles were excluded because they contributed with less than 0.01% to the total number of disposable containers.

We used the Maya index (MI) to estimate larval breeding risk.⁴ Briefly, this index was constructed for each household using two indicators: the Breeding Risk Indicator (BRI) and the Hygiene Risk Indicator (HRI). Both indicators were categorized as high, medium and low according to tertiles distribution. To construct the Maya index, both, BRI and HRI values of each household, were plotted in a 3 x 3 matrix where high *Ae. aegypti* larval breeding risks categories corresponded to: BRI3/HRI3, BRI3/HRI2 and BRI2/HRI3, medium breeding risks were: BRI1/HRI3, BRI2/HRI2, BRI3/HRI1, and low breeding risks were: BRI1/HRI1, BRI2/HRI1 and BRI1/HRI2. The BRI was obtained by dividing the number of controllable containers in the house by the mean number of *Ae. aegypti* larvae-positive controllable containers per house among the surveyed households in the community. The HRI was obtained by dividing the number of disposable containers by the mean number of *Ae. aegypti* larvae-positive disposable containers per house among the surveyed households in the community.

The socio-economic level of each household was estimated from the following characteristics: type of floor, walls and roof, and water supply.⁵ A socio-economic index was constructed, including low, medium and high levels according to the household's percentil distribution. An exploratory analysis was conducted on each variable to obtain simple frequencies and histograms. Due to the non-normal distribution of the two indicators BRI and HRI, Spearman's correlations were calculated for the number of total containers per household and the number of positive containers per household. After documenting significant correlations between the BRI and HRI indicators among the households surveyed, these indicators were used to in-

investigate the probability of the presence of *Ae. aegypti* positive containers per household. This probability was obtained by dividing the proportion of positive households classified as corresponding to high and medium BRI or HRI category by the proportion of BRI or HRI low category households. To assess the relationship between demographic factors and the risk of having positive larval habitats we used a polytomous logistic regression model. This statistical procedure can be used as an extension of the logistic regression model for a response variable with three categories. The covariate coefficients are interpreted as odds ratios, as they estimate the change in the log odds of having a medium or high Maya index value by unit change in the independent variable. All analyses were conducted using the STATA statistical package.

Results

A total of 1 965 containers with potentiality for larval breeding were identified in the 248 houses surveyed, corresponding to a mean of 7.9 containers per household. Of these, 44.6% were controllable (10.1% of these had *Ae. aegypti* larvae), and 55.4% were disposable ones (19.1% of these had *Ae. aegypti* larvae) (Table I). More than 50% of controllable containers were buckets; metal drums, plastic containers and tubs contributed with 5.61% each one. Tires represented 30.7% and cans 21.6% of all disposable containers. Regarding entomological and larval breeding indexes, the proportion of houses with low, medium and high MI category were 0.44 (n=109), 0.24 (n=59) and 0.32 (n=80), respectively. Spearman's correlations against number of total containers and the number of positive containers per household resulted in a positive correlation for controllable and discarded containers ($r=0.40$, $p<0.0001$ for BRI, and $r=0.54$, $p<0.0001$ for HRI).

Houses with high and medium BRI levels were 32 ($p<0.01$) and 8.0 (NS) times more likely to have *Ae. aegypti* positive containers than houses of low BRI level. Similarly, high and medium HRI level houses were 58 and 12 times more likely to have positive containers than those of low HRI level (Table II).

Twenty-three households corresponded to high, 146 to medium and 79 to low socio-economic category levels. Low socio-economic level households were two times more likely to be included in the medium MI and three times more likely to be included in the high MI categories than in the lower MI (OR= 1.95, 95% CI 0.6-6.4 and OR= 3.45, 95% CI 0.9-11.9, respectively). Also, medium socio-economic level households were 1.7 more likely to be included in the high MI categories than in the low MI (OR= 1.7, 95% CI 0.3-5.2). After

Table I
WATER CONTAINERS AND PRESENCE OF *Aedes aegypti* LARVAE IN 248 HOUSEHOLDS IN HUIXTLA, CHIAPAS, MEXICO, 1994

Container type	Total number	Number with larvae	% with larvae	% of total larvae in the survey
Controllable	878	89	10.13	29.96
Bucket	445	49	11.01	16.49
Small bottles	6	6	100	2.02
200-liter metal drums	37	5	13.51	1.68
Plastic containers	90	5	5.55	1.68
Plastic bathtubs	54	5	9.25	1.68
Ceramic pots	24	4	16.6	1.34
Metal can lids	47	4	8.51	1.34
Tanks	102	4	3.92	1.34
Casserole pots	7	3	42.85	1.01
Plant pot bases	43	3	6.97	1.01
Wells	23	1	4.34	0.33
Disposable	1087	208	19.13	70.04
Water storage containers	424	69	16.27	23.23
Tires	111	64	57.65	21.54
Cans	282	45	15.95	15.15
Others	222	21	9.45	7.07
Broken vases	48	9	18.75	3.03
Total	1965	297	100	100

adjusting for the education level of family heads, the multivariate model indicated that low economic level households were 1.5 more likely to be included in the medium MI and 2.2 more likely to be included in high MI categories than in the lower MI (OR= 1.5, 95% CI 0.4-5.2 and OR= 2.2, 95% CI 1.6-7.8, respectively). On the other hand, medium economic level households were 1.1 more likely to be included in the high MI category than in the low MI (OR= 1.11, 95% CI 0.34-3.6). The analysis of education level of household family heads and the frequency and abundance of *Ae. aegypti* larval habitats, showed that in 43 out of 248 households included in the study, both male and female household family heads had completed primary school (17.3%); in 78 both family heads did not complete primary school (31.4%), in 106 the male completed primary school but not the female (42.7%), and in 21 the female completed primary school but not the male (8.4%).

The results of the bivariate analysis are presented in Table III. Households where the mother did not complete primary school were two times more likely to be included in the category of medium MI and three times

Table II
**DISTRIBUTION OF Aedes aegypti POSITIVE HOUSEHOLDS
 AND DISPOSABLE CONTAINERS WITH LARVAE ACCORDING
 TO THEIR BREEDING RISK INDICATOR
 AND HYGIENE RISK INDICATOR IN HUIXTLA,
 CHIAPAS, MEXICO, 1994**

	Total containers per households surveyed	Presence of <i>Ae. aegypti</i>		Prevalence of positive Households (95% CI)*
		Number positive households	Number positive containers	
BRI Category				
Low	1/77	1	1	1.2 ; (0.03-7.2)
Medium	86/56	5	5	8.9 ; (2.9-19.6)
High	791/115	37	66	32.1 ; (23.7-41.5)
HRI Category				
Low	59/87	1	1	1.1 ; (0.02-2.6)
Medium	81/55	7	9	12.7 ; (5.2-24.4)
High	947/106	62	151	58.4 ; (48.5-67.9)
Total	1965/248	113	233	

* 95% CI: 95% confidence interval

BRI: breeding risk indicator

HRI: hygiene risk indicator

times more likely to be included in the high MI than in the lower MI category (OR= 2.7, 95% CI 1.3-6.0 and OR= 3.2, 95% CI 1.6-6.6, respectively). Households were only the male family head completed elementary

school were almost three times more likely to be included in the high MI category (OR= 2.4, 95% CI 0.9-6.1 and OR= 2.8, 95% CI 1.2-6.0, respectively). Although the analysis indicated that households where only the female had completed primary school were 1.6 and 1.7 times more likely to be included in medium and high MI categories, this was not statistically significant. When adjusted for household economic level in the multivariate polytomous regression analysis, these observations remained unchanged (Table III). This analysis indicated that households where only females completed primary school were not more likely to be included within the medium and high MI categories (OR= 0.9, 95% CI 0.3-3.3 and OR= 0.8, 95% CI 0.3-2.6, respectively).

Discussion

Aedes aegypti is well adapted to domestic and peri-domestic environments where larval breeding occurs in almost any exposed recipient containing water.⁶⁻¹⁹ Larval breeding also occurs in containers specifically used for water storage, a condition facilitated by the lack of proper water supply. Accordingly, in this study *Ae. Aegypti* larval breeding in households was represented by both controllable and disposable containers, as documented in other dengue endemic areas.¹⁰⁻¹³ The contribution of controllable containers to larval breeding was high, but larval breeding in disposable con-

Table III
**Aedes aegypti LARVAL BREEDING RISK, ESTIMATED BY POLYTOMOUS LOGISTIC REGRESSION,
 AS A FUNCTION OF EDUCATION AND SOCIO-ECONOMIC LEVELS
 OF FAMILY HEADS IN HUIXTLA, CHIAPAS, MEXICO, 1994**

	Bivariate unadjusted model Family head education				Multivariate adjusted model Family head education			
	Both educated (n=43)*	_ educated _ low educated (n=21)	_ low educated _ educated (n=106)	Both with low education (n=78)	Both educated	_ educated _ low educated	_ low educated _ educated	Both with low education
Medium risk vs. low risk	1.0	1.7 (0.5-5.4)†	2.4 (0.9-6.1)	2.7 (1.3-6.0)	1.0	0.9 (0.3-3.3)§	2.7 (0.8-5.8)§	2.6 (1.2-5.9)§
High risk vs. Low	1.0	1.6 (0.5-5.1)	2.8 (1.2-6.0)	3.2 (1.6-6.6)	1.0	0.8 (0.3-2.6)§	2.3 (1.0-5.6)§	2.8 (1.3-5.8)§
	Socio-economic level			Socio-economic level				
	High (n=23)	Medium (n=146)	Low (n=79)	High	Medium	Low		
Medium risk vs. low risk	1.0	0.8 (0.4-2.6)	1.7 (0.3-5.2)	1.0	0.7 (0.2-2.1)†	1.1 (0.3-3.6)†		
High risk vs. low risk	1.0	1.9 (0.6-6.4)	3.4 (0.9-11.9)	1.0	1.5 (0.4-5.2)†	2.2 (1.6-7.8)†		

* n=number of households in the category

† CI, Confidence intervals

§ Adjusted for economic level

Adjusted for education level

tainers was higher (an estimated 70% of total larval production) similar to that reported elsewhere.¹

As larval breeding sites increase in houses that accumulate refuse, including discarded containers,¹³⁻¹⁵ dengue transmission by *Ae. aegypti* has been associated to poor hygienic conditions, which in turn may be associated to low socioeconomic levels and to low schooling of the house dwellers.¹⁶ The data presented here indicate that the risk of dengue transmission, estimated by MI (an estimation of the larval breeding risk in relation to hygiene levels), is higher in households of low socioeconomic level, similar to the situation reported in other areas.¹³ A correlation between low socioeconomic and schooling levels has also been reported.^{1,13} To our knowledge, this is the first report dealing with the association of low schooling with the presence of dengue breeding sites. Additionally, a more important effect of the education level of the female family head was documented.

Several indexes have been instrumental to estimating dengue transmission risk, including the traditional house, recipient, and Breteau indexes.¹⁷ However, these indexes are indicative of the global transmission risk in the community. Within a community, not all houses have the same potential for larval breeding, and the identification of those houses likely to have high larval production is important to better direct control activities. The Maya index has been successfully used to estimate *Ae. aegypti* larval breeding in dengue endemic areas.⁴ The classification of potential breeding sites in controllable and disposable materials incorporates a domestic hygiene index with the MI. Furthermore, this indicator was a predictive element in the breeding risk matrix constructed (Maya index), and indicated that the likelihood of the presence of *Ae. Aegypti* larvae in high and medium HRI houses was 32 and 8-fold than in houses with low HRI.

The analysis of the effect of schooling in adult house dwellers, represented by male and female family heads, indicated that low education levels are associated to higher MI. But more important, if at least one of the family heads has completed primary school, medium and high MI occur when the housewife is the uneducated partner. Higher MI was also associated to low socioeconomic household levels. As low schooling is common in precarious socioeconomic conditions, an adjustment was necessary to better estimate the effect of schooling. In a multiple polytomous regression analysis, after adjusting for socioeconomic conditions, the association of medium to high MI and

low schooling persisted, for both family heads or the housewife only.

A limited number of epidemiological studies on infectious diseases in relation to gender issues are available.¹⁸ These studies indicate the importance of gender-related activities on women's susceptibility to the infection and their participation on control activities. Thus, in Egypt, low-educated and economically dependent women had little knowledge on malaria and schistosomiasis and less access to information and preventive measures.¹⁸ In Bolivia, although most women are familiar with triatomine bugs inside their houses, low-educated women are less likely to identify these insects as Chagas disease vectors.¹⁹ Similar attitudes were observed in our study; although housewives knew of the presence of *Ae. aegypti* larvae in their houses, they were unaware of their potentiality as biting mosquitoes, and less of their potentiality as dengue vectors. Also, in Kenya, the usage of insecticide-impregnated bednets was significantly related to the mothers' educational level,²⁰ and a comprehensive review of the literature noted that worldwide, for each year of mother schooling a decrement of 7-9% in childhood mortality rate was documented.²¹ These studies highlight the role of women in disease prevention and the need of their education.

Cultural conventions imposing different social roles on men and women are determinant for their different exposure to vector-borne diseases. Thus, in India, the risk of malaria infection in men is determined by their exposure in working settings outside their home, while women, having the responsibility of the house chores, are exposed in or nearby household compounds.^{3,22} This social structure may certainly be responsible for a more important participation of women in disease control activities within their households. Women contribution to the community welfare should be addressed using a holistic approach, in which along with the recognition of the social conventions determining their role in family care, their special needs and direct participation in environmental keeping are fully recognized and properly promoted.

The results of the present study suggest that dengue control in southern Mexico could benefit with the participation of female family heads in eliminating larval breeding. As gender roles are difficult to change by direct outside interventions, they also indicate that the best strategy for this purpose could be educational campaigns especially directed to this sector of the population.

Acknowledgments

We thank technicians René Monzón-Vera, Luis Domínguez-Sibaja, Crecencio Díaz-Espinoza, Amilcar Zúñiga-Ambrocy, José Luis Espinoza, and Francisco Maldonado-Vázquez for their assistance in field work.

References

1. Lloyd L, Winch P, Ortega-Canto J, Kendall C. Results of a community-based *Aedes aegypti* control program in Merida, Yucatan, Mexico. *Am J Trop Med Hyg* 1992;46:635-642.
2. Tidwell MA, Williams DC, Carvalho-Tidwell T, Peña CJ, Gwinn TA, Focks DA *et al*. Baseline data on *Aedes aegypti* populations in Santo Domingo, Dominican Republic. *J Am Mosq Control Assoc* 1990;6:514-522.
3. Rathgeber EH, Vlassoff C. Gender and tropical diseases: A new research focus. *Soc Sci Med* 1993;37:513-520.
4. Miller JE, Martínez-Balazar A, Gazga-Salinas D. Where *Aedes aegypti* live in Guerrero; using the Maya index to measure breeding risk. En: Halstead SB, Gómez-Dantés H. ed. *Dengue: A worldwide problem, a common strategy*. México, D.F.: Ministry of Health, Mexico, and Rockefeller Foundation, 1992:311-317.
5. Bronfman M, Guiscafré H, Castro V, Castro R, Gutiérrez G. Strategies for improving the therapeutic patterns used in acute diarrhea in primary medical care units. II. The measurement of inequality: A methodologic strategy analysis of the socioeconomic features of the sample. *Arch Invest Med* 1988;19:351-360.
6. Moore-Chester G, Cline-Barnett L, Ruiz-Tiben E, Lee D, Romney-Joseph H, Rivera-Correa E. *Aedes aegypti* in Puerto Rico: Environmental determinants of larval abundance and relation to dengue virus transmission. *Am J Trop Med Hyg* 1978 27:1225-1231.
7. Slosek J. *Aedes aegypti* mosquitoes in the Americas: A review of their interaction with the human population. *Soc Sci Med* 1986;23:249-252.
8. Kuno G. Review of the factors modulating dengue transmission. *Epidemiol Rev* 1995;17:321-335.
9. Tun-Lin W, Kay BH, Barnes A. The premise condition index: A tool for streamlining surveys of *Aedes aegypti*. *Am J Trop Med Hyg* 1995;53: 591-594.
10. Focks DA, Sackett SR, Bailey DL, Dame DA. Observations on container-breeding mosquitoes in New Orleans, Louisiana, with an estimate of the populations density of *Aedes aegypti* (L.) *Am J Trop Med Hyg* 1981;30:1329-1335.
11. Samarawickrema WA, Sone F, Kimura E, Self LS, Cummings RF, Paulson GS. The relative importance and distribution of *Aedes polynesiensis* and *Aedes aegypti* larval habitats in Samoa. *Med Vet Entomol* 1993;7:27-36.
12. Nathan MB. Critical review of *Aedes aegypti* control programs in the Caribbean and selected neighboring countries. *J Am Mosq Control Assoc* 1993;9:1-7.
13. Barrera R, Avila J, González-Téllez S. Unreliable supply of potable water and elevated *Aedes aegypti* larval indices; a causal relationship. *J Am Mosq Control Assoc* 1993;9:189-195.
14. Ko YC, Chen MJ, Yeh SM. The predisposing and protective factors against dengue virus transmission by mosquito vector. *Am J Epidemiol* 1992; 136:214-220.
15. Fernández-Salas I, Flores-Leal A. El papel del *Aedes aegypti* en la epidemiología del dengue en México. *Salud Publica Mex (Supl)* 1995;37: 545-552.
16. Rodríguez-Figueroa L, Rigau-Pérez JG, Suárez EL, Reiter P. Risk factors for dengue infection during an outbreak in Yanes, Puerto Rico, in 1991. *Am J Trop Med Hyg* 1995;52:496-502.
17. Breteau H. La fièvre jaune en Afrique Accidentale Française. Un aspect de la médecine preventive massive. *Bull World Health Organ* 1954;11: 453-481.
18. Vlassoff C, Bonilla E. Gender-related differences in the impact of tropical diseases on women: What do we know? *J Biosoc Sci* 1994;26:37-53.
19. Weinke TH, Veberreiter K, Alexander M. Cardiac morbidity due to Chagas disease in a rural community in Bolivia. *Epidemiol Infect* 1988;101:655-660.
20. Marsh VM, Mutemi W, Some ES, Haaland A, Snow RW. Evaluating the community education programme of an insecticide-treated bednet trial on the Kenyan coast. *Health Policy Plann* 1996;11:280.
21. Cleland J, Ven Ginneken JK. Maternal education and child survival in developing countries: The search for pathways of influence. *Soc Sci Med* 1988;27:1357.
22. Reuben R, Panicker KN. A study of human behaviour influencing man-mosquito contact and of biting activity on children in a south Indian village community. *Ind J Med Res* 1979;70:723-729.