The Laucet, vol. 344, nº 8931, Sat. 29 Oct. 1934

ISSN: 0140-6736



Figure: Survival curves for boys (from age 10 months) who had received EZ-HT at 5 months, SW-HT at 5 months, or SW-STD measles vaccine at 10 months

Children born between February, 1987, and January, 1989, and followed until February, 1994. Comparison made with 10 months of age when children in control group received SW-STD measles vaccine.

From data in the thesis and using a different cut-off of -2 z-scores Garenne concludes that EZ-HT measles vaccine is deleterious for boys, the difference being especially striking for wasting (weight-for-height). It should be noted that with a prevalence of 6-3% and 2.0% for EZ-HT and SW-STD boys, respectively (table), wasting was uncommon in both groups, being actually lower than expected (2.5%) in the SW-STD groups.

The most relevant criteria for malnutrition may be debatable. However, mortality is the critical issue. We have followed the trial cohort until the annual census in February, 1994. As shown in the figure, there was no difference in mortality between boys who had received EZ-HT, SW-HT, or SW-STD. In the subgroup of children participating in the nutritional survey, there was significantly lower survival for EZ-HT girls than in recipients of standard vaccine (mortality ratio [MR] 2:55 [95% CI 1:13-5:71]). Although

High-titre measles vaccines for boys

X

SIR—Garenne (July 25, p 261) analyses data from a trial of high-titre measles vaccines in Niakhar, Senegal. The findings of the trial were reported^{1,2} and in detail more recently.³ Briefly, 1579 children born between February, 1987, and January, 1989, were randomised to receive Edmonston-Zagreb high-titre (EZ-HT), Schwarz high-titre (SW-HT), or placebo at 5 months of age. Recipients of placebo were offered Schwarz standard (SW-STD) measles vaccine at 10 months.

In autumn, 1990, when we suspected that EZ-HT measles vaccine could be associated with reduced survival,²⁴ we conducted a follow-up study and a nutritional survey of all participants still residing in the study area. Weight, height, and arm-circumference were measured in 1261 of 1323 eligible children who were seen at home. At the time, the children were aged 22–45 months. As is being reported elsewhere' there were significantly more EZ-HT girls than females in the standard group who had z-scores of -3 or lower for weight-for-age (14/249 vs 6/269; p=0.045) and height-for-age (34/251 vs 21/269; p=0.033), but no inference for the boys.

1226 PD18

2 7 MARS 1995

	Deaths/number of children				
	Female		Maie		
1	EZ-HT	SW-STD	ez-ht	SW-STD	_: · ·
Number MR (EZ/SW)	19/251 2·55 (1·13-5	8/269 71)	10/238 0·88 (0·39–2	12/251 2·00)	
Weight-for-age <=-3 z-score -3 to -2 z-score > -2 z-score MR (EZ/SW)	3/14 6/54 10/181 2·46 (1·06-5	0/6 1/50 7/213 -72)	1/13 3/63 6/162 0·82 (0·37-1	3/15 4/42 5/194 L·84)	24 - 1
Height-for-age <=-3 z-score -3 to -2 z-score > -2 z-score MR (EZ/SW)	6/34 3/55 10/162 2·40 (1·01-5	0/21 5/70 3/178 69)	2/27 2/65 5/146 0·82 (0·35-1	5/35 4/61 3/156 L-91)	nentaire
Weight-for-height <=-3 z-score -3 to -2 z-score > -2 z-score MR (EZ/SW)	0/1 1/8 18/240 2:57 (1:14-5	0/4 8/265 -81)	0/2 2/13 8/223 0·77 (0·34-1	2/5 10/246 -70)	Onds Docum
Arm-circumferencs <=-11-0 11-1-12-5 >12-5 MR (EZ/SW)	1/3 1/6 17/240 2·54 (1·12-5	1/11 7/258 •75)	0/2 3/12 7/222 0.84 (0-38-1	3/10 9/241 .•87)	S.1.0.M. F

Table: Mortality (1990–94) in relation to nutritional status (z-scores) in November–December, 1990 for recipients of EZ-HT and SW-STD measles vaccing EZ-HT girls were more malnourished, the difference in mortality was not explained by differences in nutritional status, and the MR remained unchanged when adjustment was made for nutritional status (table). For boys, there was no indication of increased risk for recipients of EZ-HT compared with standard vaccine (MR 0.88 [0.39-2.00]).

Hence, in contrast to Garenne and colleagues' earlier conclusion,' there is no indication that high-titre vaccine was deleterious for boys from (a) the complete set of nutritional data (table),' (b) the currently available follow-up data on mortality from the trial (figure), (c) routine use of EZ-HT in Senegal following the trial (unpublished data), or (d) other trials.¹⁵

Although unexplained, the conclusion remains that EZ-HT and Schwarz-HT vaccines are only associated with reduced survival among female recipients compared with girls receiving standard vaccine, and this difference is not explained by nutritional status. Most importantly, there is no increase in mortality for female recipients of EZ-HT compared with unvaccinated girls.³⁴ We caution readers to withhold judgment about the findings in these studies until complete data sets are available for scrutiny.

We thank the Expanded Programme on Immunization, World Health Organization, the Task Force for Child Survival and Development, Atlanta, USA; and Science and Technology for Development Programme of the European Community, Bruxelles (TS3*-CT91-0002) for financial support.

Peter Aaby. Kim Knudsen, Francois Simondon, Badara Samb, Hilton Whittle, Awa Marie Coll Seck, John Bennett

Danish Epidemiology Science Centre, Statens Seruminstitut, 2300 Copenhagen S, Denmark: UR Maiadies Infectieuses et Parasitaries, ORSTOM, Dakar, Senegal: NRC Laboratories, Banjul, the Gambia; Univerité Cheikh Anta Diop, Dakar, Senegal; and Task Force for Child Survival and Development, Atlanta, USA

 Garenne M, Leroy O, Beau JP, Sene I. Child mortality after high-titre measles vaccines: prospective study in Senegal. *Lancet* 1991; 338: 903-07.

2 Aaby P. Samb B, Simondon F, et al. Child mortality after high-titre measles vaccines in Senegal: the complete data set. *Lancet* 1991; 338: 1518.

3 Aaby P, Samb B, Simondon F, et al. Sex specific mortality after high titre measles vaccines in rural Senegal. *Bull World Health Organ* (in press).

Aaby P, Knudsen K, Whittle H, et al. Long-term survival after Edmonston-Zagreb measles vaccination: increased female mortality. *J Pediatr* 1993; 122: 904–08.

5 Holt EA, Moulton LH, Siberry GK, Halsey NA. Differential mortality by measles vaccine titre and sex. *J Infect Dis* 1993; 168: 1087–96.

1227