PN ABU-409
93809

9.271

SCHOOL OF PUBLIC HEALTH

Department of International Health

February 24, 1995

John Daly, PhD
Team Leader
Office of Policy and Programs (Research)
Center for Human Capacity Development
Bureau for Global Programs, Field Support and Research
Agency for International Development
Room 609 SA-18
Washington, D.C. 20523-1814

RE: PSTC Project No. 9.271, "Role of Nutritional Status in the Early Loss of Passive Immunity and Response to Measles."

Dear Dr. Daly,

I am attaching a copy of our final report for the PSTC Project No. 9.271 "Role of Nutritional Status in the Early Loss of Passive Immunity and Response to Measles."

I am sorry that this final report did not reach your office earlier and I apologize for it.

If you have any questions or comments regarding this report, please call me at 205-934-1732 or faxme at 205-975-3329.
Sincerely yours,

Jose' Alvarez

Jose O. Alvarez
Professor and Chairman

REC'D IN R&D/R

FEB 27 1995

CC: BOSTID

The University of Alabama at Birmingham
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PSTC Project 9.271, Role of Nutritional Status in the Early Loss of Passive Immunity and Vaccine Response to Measles.

FINAL REPORT

The study had two objectives; the first was to evaluate the rate of loss of maternally acquired measles antibodies in children from birth to 9 months of age as a function of nutritional status; the second objective was to investigate the rate of seroconversion to measles vaccination in normal and malnourished infants 6-9 months old.

The study was conducted as a collaboration between UAB and UPCH in Lima, Peru. Dr. Abraham Vaisberg, Professor of Microbiology at UPCH was the co-P.I. in charge of the project in Peru. One Hundred forty infants were recruited at birth into the study, that is, a follow up study to evaluate the rate of loss of maternally acquired measles antibody as a function of nutritional status. They were of normal birthweight (>2500g), born at term and recruited at the Universidad Peruana Cayetano Heredia (UPCH)'s newborn unit. Blood samples were obtained from the mother and the newborn within 5 days after birth and the nutritional status of the infant was assessed by anthropometry.

Infants were followed every three months. At each contact, infants were examined, their nutritional status was evaluated and a blood sample was obtained for measuring their measles antibody titers.

At age 9 months, they were not only examined but were also vaccinated with the Edmonton-Zagreb measles vaccine (the same lot number of the vaccine was used to vaccinate all infants participating in the study; samples of this vaccine lot were evaluated in Dr. Vaisberg's laboratory to determine it viability). The final visit of the follow up took place when the children were 12 months old. At this time, a blood sample was obtained to measure measles antibody titers and determine whether seroconversion had occurred.

RESULTS

Table 1 shows the loss of maternally acquired measles antibodies as a function of age in infants followed since birth to age 9 months. None of these infants became malnourished during the follow up period, therefore we could not assess the contribution of nutritional status on the rate of loss of antibodies.

In view of this problem, we recruited infants at age 3-4 months who had come to UPCH's University Hospital because of malnutrition. These infants were incorporated into the study and followed in a similar fashion as the first group of children. Thus, the first group of infants (i.e., recruited at birth) (n = 138) became the well-nourished group and the second group of infants (i.e., recruited at age 3-4 months) became the malnourished group. The comparison of the measles antibodies between these 2 groups is shown in Table 3.

It is clear from Table 3 that there was a significant difference in the level of antibodies between the two groups. At age 3 months and 6 months, the malnourished infants had significantly lower measles antibodies. At age 9 months, this difference no longer existed. Moreover, the malnourished infants had significantly higher antibody titers after vaccination at age 12 months. This observation has been made by other authors in previous vaccination studies.

Thirty-six (26%) of the well nourished infants (n = 138) did not seroconvert after vaccination versus only 4 of 29 (14%) among the malnourished infants. This finding strengthens our observations regarding the impact of malnutrition on the earlier loss of maternal antibodies because the success of vaccination should increase if children had lower maternal titers at the time of vaccination.

Note: The actual measles antibodies titer data for each infant/mother as a function of age for well-nourished infants is included in Appendix I. The same data for malnourished infants is included in Appendix II.

CONCLUSION

This study strongly suggests that malnutrition is associated with earlier loss of maternally acquired measles antibodies in Peruvian infants. Thus, by age 6 months or earlier, the levels of measles antibodies in malnourished infants are no longer protective.

TABLE 1

MEASLES ANTIBODY TITERS IN PERUVIAN INFANTS FROM BIRTH TO 9 MONTHS

	n	At birth	3 mo.	6 mo.	9 mo.
Arithmetic mean	138	2341 ± 984	620 ± 284	309 ± 200	110 ± 38
Geometric mean	138	2170	553	251	86

TABLE 2

MATERNALLY ACQUIRED MEASLES ANTIBODY TITERS IN PERUVIAN INFANTS AND THEIR MOTHERS
(Geometric Means)

n	Mother	At birth	3 mo.	6 mo.	9 mo.	12 mo. (post vacc.)
138	1485	2170	553	251	86	1971

TABLE 3

COMPARISON OF MEASLES ANTIBODY TITERS IN WELL-NOURISHED AND MALNOURISHED INFANTS
(Values in parenthesis are Geometric Means)

	3 mo.	6 mo.	9 mo.	12 mo. (post-vacc)
WELL-NOURISHED	620 ± 284	309 ± 200	110 ± 38	3088 ± 2626
	(553)	(251)	(86)	(1970)
	n = 138	n = 138	n = 138	n = 138
MAL-NOURISHED	197 ± 133	76 ± 37	112 ± 92	4702 ± 2387
	(133)	(68)	(90)	(3529)
	n = 6	n = 17	n = 11	n = 29
	$p < 0.001$	$p < 0.001$	N.S.	$p < 0.02$

APPENDIX 1

MEASLES ANTIBODY TITERS FOR WELL-NOURISHED PERUVIAN INFANTS

- DATA -

SEXO	CODIGO	0 MADRE	1 RN	2 3m	3 6m	4 9m	5 12m
1	402	1910	2560	715	320	212	5028
2	403	2620	3558	993	419	186	1735
1	405	1612	1979	458	276	72	3215
1	406	1876	2332	514	312	199	233
2	407	1002	1238	412	163	52	4018
2	408	956	1205	315	198	93	1367
1	409	1189	1712	498	350	84	696
1	410	1536	2921	814	453	215	5555
2	411	2101	2993	637	232	59	3221
2	413	1122	1815	425	293	39	615
2	414	1880	2511	577	205	88	5901
1	415	1602	2003	525	334	72	6500
1	416	1903	1815	422	567	338	6500
2	417	1781	2012	215	123	80	3459
1	419	1505	4401	499	203	59	3896
1	421	2816	4912	515	332	81	409
2	422	2018	1934	301	115	98	6500
2	426	952	1703	205	190	31	1558
1	428	1038	2947	423	308	115	6389
2	429	992	1306	538	285	193	2786
1	430	1713	2938	415	342	203	5798
1	431	1020	1919	207	98	72	4012
2	432	2725	4202	318	215	72	1499
1	435	1504	3703	472	327	102	2901
2	438	817	1015	720	612	92	6010
2	439	2001	2254	327	152	78	3021
1	441	2018	1555	473	207	102	1118
2	442	1978	2102	389	295	52	504
2	443	915	1842	473	3302	107	2918
1	444	1208	804	302	193	62	1849
2	445	907	1502	409	315	133	3752
2	447	2531	2902	1304	233	98	4215
2	448	1573	2006	572	325	102	355
2	449	893	1002	342	203	132	3814
2	450	607	912	358	193	63	3392
2	451	905	1119	293	151	93	262
1	452	958	1236	316	172	35	3916
1	453	2125	3082	518	326	174	1191
2	454	1703	2705	459	203	97	5528
1	457	1206	1978	327	179	87	3416
1	458	712	994	539	318	133	321
2	459	1845	2513	608	394	1172	4823
1	461	3008	4885	2119	1017	876	3912
1	464	9013	1915	852	438	51	3405
1	466	1584	1895	572	325	187	1276
2	467	2117	2792	426	215	93	2738
1	468	2521	3052	817	349	191	6386
2	470	813	1093	620	301	83	232
1	471	1001	2111	1095	825	512	654
2	472	902	1705	352	193	72	8035
2	473	1522	2083	416	179	55	809
1	474	1305	1999	426	207	80	5232
1	475	1915	1074	576	318	120	6492

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1	476	2841	3916	1014	806	513	1195
1	477	1035	1718	292	148	52	968
1	478	1814	2712	527	372	126	348
2	479	2615	2912	250	196	79	3944
2	481	2520	3115	417	176	48	540
2	483	2123	2789	539	315	126	3319
1	484	1202	1718	572	296	73	432
2	485	2074	1814	326	134	58	231
2	486	2384	2819	538	316	93	756
2	487	2546	3089	715	399	107	3492
1	489	2019	2523	402	198	45	1190
1	490	913	1714	428	215	63	6500
2	491	739	915	279	123	85	3412
1	492	2504	3106	614	379	123	6528
2	494	993	1097	342	138	73	6517
1	495	2162	2439	518	345	90	1543
2	496	2983	4002	536	208	90	3173
2	498	132	1080	310	125	54	332
2	500	3456	3801	1002	750	187	4006
2	506	1992	2911	804	306	93	2923
1	507	945	1512	910	208	52	3001
2	510	1720	2040	1015	318	99	1510
1	512	3218	1813	707	105	81	234
2	513	3225	907	1320	483	64	153
1	514	2739	3116	718	124	51	1527
2	516	2429	2115	919	243	99	654
1	517	1504	1815	498	112	73	5755
2	519	2018	2923	814	326	199	6010
2	521	992	2997	458	215	88	3987
1	524	1058	912	225	98	39	897
2	525	2018	2018	978	425	105	3993
1	526	1781	2511	1031	453	69	1015
2	527	1505	1205	543	293	43	4819
1	528	1602	2720	329	198	52	225
1	531	1122	2914	837	310	87	3814
1	532	2109	2810	995	527	101	2999
2	533	1198	1280	423	118	52	5898
1	534	1670	2513	910	223	88	510
2	537	1216	2710	646	138	31	5383
1	539	2620	3204	512	189	103	3476
2	540	2983	2801	821	217	70	4315
1	543	108	2977	1043	825	35	237
2	544	1934	2525	720	312	92	1097
1	545	4410	2520	538	191	73	2193
1	546	2620	3010	842	312	68	195
2	547	1043	2111	318	93	30	1649
1	548	1917	2914	1193	524	193	4843
1	550	1610	2523	532	183	75	910
1	551	1425	2710	1028	215	96	3200
2	553	1915	2999	928	316	99	1125
2	554	186	3816	713	98	43	3458
2	555	1795	2176	558	217	75	2017
1	556	912	1915	916	118	83	1348
2	557	2739	2998	821	291	58	761
2	559	1416	2340	326	98	31	6500
2	560	2711	3111	813	210	112	254

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1	561	510	1101	302	98	39	262
1	562	1120	1943	721	321	101	4910
2	563	1982	2993	1023	455	90	332
1	564	2150	2513	819	326	97	6500
1	565	824	1025	328	112	83	6010
1	566	1614	2026	431	99	42	5439
2	567	1443	2842	593	104	64	58
2	568	2943	3494	415	98	53	6330
2	569	720	1898	918	343	110	5893
1	570	1494	3510	723	225	93	3415
1	571	1218	2296	324	104	77	210
2	574	1713	2048	1002	814	58	5814
2	575	1001	3093	382	113	32	509
1	577	204	910	710	327	93	5743
1	578	2019	3450	919	298	78	4908
1	579	1005	2210	543	119	53	3819
2	580	1944	2998	318	101	42	5003
2	582	1893	3015	1005	718	83	6500
2	583	993	1996	723	326	98	6500
1	585	2712	3078	984	398	53	3809
2	586	814	1515	103	193	31	6500
2	588	1324	1819	821	427	209	1153
1	590	1818	3421	983	538	128	147
2	591	1910	2316	736	326	98	4310
1	593	1723	2728	542	563	89	5527
1	594	2125	1114	419	123	35	6500
1	598	1062	3093	1991	455	92	893
2	600	623	2721	318	99	64	1725
2	602	1208	1502	723	334	123	5753
N		138	138	138	138	138	138
MEDIA ARITMETICA.		1721.3	2341.2	620.0	308.9	110.4	3088.0
MEDIA GEOMETRICA.		1485.1	2169.7	553.2	250.7	86.0	1970.8

MUJERES

SEXO	CODIGO	0 M	1 0m RN	2 3m	3 6m	4 9m	5 12m
2	602	1208	1502	723	334	123	5753
2	600	623	2721	318	99	64	1725
2	591	1910	2316	736	326	98	4310
2	588	1324	1819	821	427	209	1153
2	586	814	1515	103	193	31	6500
2	583	993	1996	723	326	98	6500
2	582	1893	3015	1005	718	83	6500
2	580	1944	2998	318	101	42	5003
2	575	1001	3093	382	113	32	509
2	574	1713	2048	1002	814	58	5814
2	569	720	1898	918	343	110	5893
2	568	2943	3494	415	98	53	6330
2	567	1443	2842	593	104	64	58
2	563	1982	2993	1023	455	90	332
2	560	2711	3111	813	210	112	254
2	559	1416	2340	326	98	31	6500
2	557	2739	2998	821	291	58	761
2	555	1795	2176	558	217	75	2017
2	554	186	3816	713	98	43	3458
2	553	1915	2999	928	316	99	1125
2	547	1043	2111	318	93	30	1649
2	544	1934	2525	720	312	92	1097
2	540	2983	2801	821	217	70	4315
2	537	1216	2710	646	138	31	5383
2	533	1198	1280	423	118	52	5898
2	527	1505	1205	543	293	43	4819
2	525	2018	2018	978	425	105	3993

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2	521	992	2997	458	215	88	3987
2	519	2018	2923	814	326	199	6010
2	516	2429	2115	919	243	99	654
2	513	3225	907	1320	483	64	153
2	510	1720	2040	1015	318	99	1510
2	506	1992	2911	804	306	93	2923
2	500	3456	3801	1002	750	187	4006
2	498	132	1080	310	125	54	332
2	496	2983	4002	536	208	90	3173
2	494	993	1097	342	138	73	6517
2	491	739	915	279	123	85	3412
2	487	2546	3089	715	399	107	3492
2	486	2384	2819	538	316	93	756
2	485	2074	1814	326	134	58	231
2	483	2123	2789	539	315	126	3319
2	481	2520	3115	417	176	48	540
2	479	2615	2912	250	196	79	3944
2	473	1522	2083	416	179	55	809
2	472	902	1705	352	193	72	6035
2	470	813	1093	620	301	83	232
2	467	2117	2792	426	215	93	2738
2	459	1845	2513	608	394	1172	4823
2	454	1703	2705	459	203	97	5528
2	451	905	1119	293	151	93	262
2	450	607	912	358	193	63	3392
2	449	893	1002	342	203	132	3814
2	448	1573	2006	572	325	102	355
2	447	2531	2902	1304	233	98	4215
2	445	907	1502	409	315	133	3752
2	443	915	1842	473	3302	107	2918
2	442	1978	2102	389	295	52	504
2	439	2001	2254	327	152	78	3021
2	438	817	1015	720	612	92	6010
2	432	2725	4202	318	215	72	1499
2	429	992	1306	538	285	193	2786
2	426	952	1703	205	190	31	1558
2	422	2018	1934	301	115	98	6500
2	417	1781	2012	215	123	80	3459
2	414	1880	2511	577	205	88	5901
2	413	1122	1815	425	293	39	615
2	411	2101	2993	637	232	59	3221
2	408	956	1205	315	198	93	1367
2	407	1002	1238	412	163	52	4018
2	403	2620	3558	993	419	186	1735
N		71	71	71	71	71	71

MUJERES

MEDIA ARITMETICA	1666.0	2277.3	581.4	306.4	100.7	3150.4
MEDIA GEOMETRICA	1456.7	2112.8	519.3	238.0	80.0	2060.9

VARONES

SEXO	CODIGO	0 M	1 0m RN	2 3m	3 6m	4 9m	5 12m
1	598	1062	3093	1991	455	92	893

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1	594	2125	1114	419	123	35	6500
1	593	1723	2728	542	563	89	5527
1	590	1818	3421	983	538	128	147
1	585	2712	3078	984	398	53	3809
1	579	1005	2210	543	119	53	3819
1	578	2019	3450	919	298	78	4908
1	577	204	910	710	327	95	5743
1	571	1218	2296	324	104	77	210
1	570	1494	3510	723	225	93	3415
1	566	1614	2026	431	99	42	5439
1	565	824	1025	328	112	83	6010
1	564	2150	2513	819	326	97	6500
1	562	1120	1943	721	321	101	4910
1	561	510	1101	302	98	39	262
1	556	912	1915	916	118	83	1348
1	551	1425	2710	1028	215	96	3200
1	550	1610	2523	532	183	75	910
1	548	1917	2914	1193	524	193	4843
1	546	2620	3010	842	312	68	195
1	545	4410	2520	538	191	73	2193
1	543	108	2977	1043	825	35	237
1	539	2620	3204	512	189	103	3476
1	534	1670	2513	910	223	88	510
1	532	2109	2810	995	527	101	2999
1	531	1122	2914	837	310	87	3814
1	528	1602	2720	329	198	52	225
1	526	1781	2511	1031	453	69	1015
1	524	1058	912	225	98	39	897
1	517	1504	1815	498	112	73	5755
1	514	2739	3118	718	124	51	1527
1	512	3218	1813	707	105	81	234
1	507	945	1512	910	208	52	3001
1	495	2162	2439	518	345	90	1543
1	492	2504	3106	614	379	123	5528
1	490	913	1714	428	215	63	6500
1	489	2019	2523	402	198	45	1190
1	484	1202	1718	572	296	73	432
1	478	1814	2712	527	372	126	348
1	477	1035	1718	292	148	52	968
1	476	2841	3916	1014	806	513	1195
1	475	1915	1074	576	318	120	6492
1	474	1305	1999	426	207	80	5232
1	471	1001	2111	1095	825	512	654
1	468	2521	3052	817	349	191	6386
1	466	1584	1895	572	325	187	1276
1	464	9013	1915	852	438	51	3405
1	461	3008	4885	2119	1017	876	3912
1	458	712	994	539	318	133	321
1	457	1206	1978	327	179	87	3416
1	453	2125	3082	518	326	174	1191
1	452	958	1236	316	172	35	3916
1	444	1208	804	302	193	62	1849
1	441	2018	1555	473	207	102	1118
1	435	1504	3703	472	327	102	2901
1	431	1020	1919	207	98	72	4012
1	430	1713	2938	415	342	203	5798

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1	428	1038	2947	423	308	115	6389
1	421	2816	4912	515	332	81	409
1	419	1505	4401	499	203	59	3896
1	416	1903	1815	422	567	338	6500
1	415	1602	2003	525	334	72	6500
1	410	1536	2921	814	453	215	5555
1	409	1189	1712	498	350	84	696
1	406	1876	2332	514	312	199	233
1	405	1612	1979	458	276	72	3215
1	402	1910	2560	715	320	212	5028
N		67	67	67	67	67	67

VARONES

MEDIA ARITMETICA	1779.9	2408.9	660.9	311.6	120.8	3022.0
MEDIA GEOMETRICA	1515.8	2231.7	591.7	264.9	92.9	1879.7

RESUMEN

	0 M	1 0m RN	2 3m	3 6m	4 9m	5 12m
MUJERES: N=71						
MEDIA ARITMETICA	1666.0	2277.3	581.4	306.4	100.7	3150.4
MEDIA GEOMETRICA	1456.7	2112.8	519.3	238.0	80.0	2060.9
HOMBRES: N=67						
MEDIA ARITMETICA	1779.9	2408.9	660.9	311.6	120.8	3022.0
MEDIA GEOMETRICA	1515.8	2231.7	591.7	264.9	92.9	1879.7

BEST AVAILABLE COPY

APPENDIX 2

MEASLES ANTIBODY TITERS FOR MALNOURISHED PERUVIAN CHILDREN

- DATA -

ELIMINANDO 1012-1 Y 1022-1 YA QUE DEFINITIVAMENTE HAY UN ERROR EN ELLAS

	COD.	3-4	log	6-7	log	8-9	log	SC	log
1	801	320	2.5051	148	2.1703				
2	803	90	1.9542	74	1.8692			3664	3.5640
1	806			32	1.5051			615	2.7889
nueva	807	557	2.7459	156	2.1931	90	1.9542		
	808			32	1.5051			302	2.4800
1	814	82	1.9138					1172	3.0689
1	834	74	1.8692	49	1.6902				
1	1002					344	2.5366	582	2.7649
1	1003			82	1.9138			2262	3.3545
1	1005					205	2.3118	6500	3.8129
1	1006			65	1.8129			6500	3.8129
1	1007					49	1.6902	4647	3.6672
1	1008					90	1.9542	6500	3.8129
1	1009			49	1.6902			4319	3.6354
1	1010					66	1.8195	6303	3.7995
2	1012							6500	3.8129
1	1013					156	2.1931	6500	3.8129
2	1014			90	1.9542			1131	3.0535
1	1015							6500	3.8129
1	1016					49	1.6902	6500	3.8129
2	1017					90	1.9542	6500	3.8129
1	1018			66	1.8195			6500	3.8129
2	1019					49	1.6902	6024	3.7799
2	1021					49	1.6902	6500	3.8129
1	1022							6500	3.8129
2	1027	57	1.7559					6500	3.8129
1	1028			107	2.0294			402	2.6042
2	1029			49	1.6902			6500	3.8129
2	1030			49	1.6902			6500	3.8129
1	1031			49	1.6902			4402	3.6437
1	1032			115	2.0607			3041	3.4830
1	1033			82	1.9138			6500	3.8129
		1180	12.74	1294	31.20	1237	21.48	138366	102.8812
n		6	6	17	17	11	11	29	29
MED. ARIT.		196.7	2.12403	76.1	1.83519	112.5	1.95314	4702.3	3.5476
			133.05		68.42		89.77		3528.811
S		184.450	0.366378	36.0357	0.200053	87.30	0.273193	2345.74	0.412624
		1.09544	1.095445	1.03077	1.095445	1.048	1.095445	1.01770	1.095445
S ^		202.055	0.401347	37.1447	0.219147	91.57	0.299268	2387.26	0.452007
			2.519690		1.656331		1.991905		2.831442

MEDIA ARIT	196.7	76.1	112.5	4702.3
MEDIA GEOM	133.1	68.42	89.77	3528.8
DES.STD	202.1	37.14	91.57	2387.3
**	P<0.001	P<0.001	P<0.90	P<0.02
To	6.77	8.6	0.22	2.5325

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