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Roy H. Turner

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THE PATHOLOGIC PHYSIOLOGY OF PELLAGRA

I. TABULATED CLINICAL AND PHYSIOLOGIC DATA

By ROY H. TURNER

(From the Department of Medicine, Tulane University of Louisiana School of Medicine, and the Medical Services of the Charity Hospital, New Orleans)

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Pellagra is almost unique among major diseases in the scarcity of accurate information concerning it. There is still uncertainty about its etiology; the nature of its pathologic lesion is obscure; the diagnosis in atypical cases is a mere matter of opinion; and there are no adequate criteria for cure or for prognosis. The pellagrin who remains ill for a prolonged period may be suffering from chronic pellagra or may be suffering from some mysterious sequel rather than the disease itself. Prognosis is based chiefly on mass statistics largely unmodified by the clinical features of the individual patient. Even the causes of death are little understood. Pellagrins frequently die unexpectedly when apparently convalescent. The treatment at present is highly unsatisfactory. More than 25 per cent of the pellagrins admitted to the New Orleans Charity Hospital die in the hospital, in spite of treatment along the most approved lines. The treatment is dietary and symptomatic. The dietary is based on inexact knowledge of the dietary fault to be overcome. The symptomatic treatment rests on imperfect knowledge of the disturbed physiology represented by the symptoms. Pellagra takes a variety of clinical forms, so that some writers have suggested that what is called pellagra is a mixture of diseases rather than an entity. If typical skin lesions are accepted as a *sine qua non* there can be little doubt that pellagra is a unique disease for there is hardly any lesion in medicine more distinctive clinically. Even with classic skin lesions the cases fall into sharply contrasting groups. The mechanisms which bring this about are quite mysterious. The studies upon which this and subsequent papers are based were undertaken with the belief that there was no better mode of attack on many of the

TABLE I
Data relative to forty-two pellagrins analyzed in this and succeeding papers
 (For significance of cone designations, see footnote to table)

4	C.	F.	44	-	4	3	2	DU	4	1	0	0	H	0	1	70	41.8	26.7	13.540	2.590	1.040	3.93	3.48	7.31	10.3	3.7	612	44	Syphilis											
5	C.	F.	10	27	8	5	1	D	8	1	0	0	A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	42.2	24.7	13.570	2.670	0.890	3.86	3.07	6.93	13.0	3.5	496	61	Improved
6	C.	M.	26	-	2	2	2	E	3	1	0	0	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	43.1	31.4	3.460	2.340	1.090	3.72	3.74	7.46	9.8	4.1	580	51	139
7	W.	M.	19	-	4	1	1	E	2	1	0	0	A	0	0	-	0	1	61	35.6	37.9	4.380	2.670	1.660	3.93	2.80	6.73	11.2	4.3	616	58	Discharged improved								
8	W.	M.	43	-	2	2	1	E	2	3	0	D	P	-	0	0	75	38.1	42.6	2.97	2.10	5.07	9.3	4.0	508	58	Probable attack 4 months previously													
9	C.	M.	23	-	1	3	2	E	3	1	0	0	A	0	1	65	37.4	43.5	4.830	2.670	2.100	3.72	2.14.5	.86	8.5	4.3	530	64	Third annual attack Improved											
10	C.	M.	26	-	3	1	1	E	50	3	0	0	A	2	1	63	37.2	37.6	4.500	2.790	1.690	3.26	2.45	7.71	11.7	4.1	498	64	Clinically stationary											
11	C.	F.	28	-	4	4	3	U	4	0	0	0	N	0	0	0	0	0	0	0	0	0	0	0	0	0	37.4	36.8	4.980	3.090	1.840	3.18	2.38	5.36	10.9	4.2	500	68	149	
12	W.	F.	37	-	3	5	3	U	3	1	2	0	A	0	1	60	45.9	27.4	3.760	2.900	850	1.88	2.32	4.19	8.8	2.5	444	57	Died 3 days later											
13	W.	F.	27	-	4	2	1	D	50	1	0	0	S	0	1	59	48.1	33.1	3.170	2.100	1.050	2.86	2.32	5.23	9.5	3.1	530	55	Died 1 month later											
14	C.	F.	39	-	5	3	1	D	2	1	0	0	N	0	0	0	61	66.8	32.0	5.370	3.610	1.720	3.34	2.19	5.53	9.8	4.3	528	52	Early carcinoma of cervix										
			11					H	0	0	0	0	N	0	0	0	0	0	0	0	0	0	0	0	0	62.6	32.2	6.720	4.540	2.180	3.48	2.02	5.50	10.6	4.7	540	59	154		
			15					H	0	0	0	0	H	0	0	0	0	0	0	0	0	0	0	0	0	63.5	33.8	6.250	4.120	2.120	3.15	2.22	5.37	10.6	4.2	542	58	162		

TABLE 1—Continued

Case number	Race	Sex	Age	Duration	Severity	Extent	Present state	Diarrhea	Skin lesions		Remarks																				
									Intervall	days	code	code	code	code	code	code	code	code	code	code	code	Total base m.eq. liter	CO ₂ capacity plasma per cent	Chloride as NaCl per cent	Hypochromic phosphorous per cent	Total base m.eq. liter	CO ₂ capacity plasma per cent	Chloride as NaCl per cent	Hypochromic phosphorous per cent	Total base m.eq. liter	CO ₂ capacity plasma per cent
15. C. M.	61	—	1	3	3	B	1	2	1	0	0	A	0	2	72	49.5	34.5	4.260	2,740	1,470	2.87	3.07	5.94	10.7	3.4	492	71	138	Improved		
16. C. F.	60	—	4	3	3	U	4	3	4	1	C	?	A	0	2	64	38.0	31.4	3.060	2,100	930	3.88	2.88	6.76	10.1	4.2	53	53	53	Skin lesions probably re-current	
17. C. M.	46	—	4	3	3	U	4	3	3	1	U	2	0	0	0	0	37.6	31.5	3.100	2,050	980	3.31	2.71	6.02	9.8	5.4	500	41	500	Died 1 day later	
18. C. M.	55	—	3	2	3	U	10	2	1	0	E	0	0	0	0	61	40.8	38.8	3.730	2,260	1,440	3.88	1.89	5.77	9.9	4.1	69	69	69	Skin lesions and diarrhoea developed in the hospital	
19. W. F.	46	—	4	2	1	DE	4	2	0	0	E	1	0	0	0	60	36.4	46.4	4.520	2,370	1,120	4.02	1.99	6.01	10.1	5.1	62	62	62	Died 3 hours later. Autopsy	
20. C. M.	44	—	3	3	2	D	3	1	0	0	E	0	0	0	0	74	57.2	31.4	4.330	3,000	1,350	3.94	3.07	7.01	10.4	3.6	57	57	57	Luetic heart disease	
21. W. F.	29	—	12	3	2	DU	12	2	1	0	O	0	0	0	0	62	57.4	31.5	4.330	2,970	1,400	3.00	2.52	5.52	9.3	3.6	57	57	57	Died suddenly 4 days later	
																	63	57.2	32.9	4.610	3,060	1,520	3.30	2.81	6.11	9.9	2.8	554	49	554	Recurrent skin lesions
																													Unimproved		
																													Syphilis		
																													Discharged improved		
																													Recurrent skin lesions.		
																													Active delirium 1 week later, then died		

22	C.	F.	11	-	12	2	3	D	12	2	1	0	D	0	-	0	0	43	27.2	28.0	-	-	2.22	3.05	27	8.5	5.2	432	53	118	Died 1 hour later	
23	C.	M.	10	-	16	3	3	D	4	2	1	0	0	0	0	0	0	35	24.1	30.1	12.570	1.770	770	2.81	2.11	14.92	8.4	5.3	464	51	123	Improved
24	C.	F.	34	-	5	3	1	H	12	3	0	0	D	0	A	0	0	61	48.7	25.2	24.240	3.090	1.120	2.123	2.285	.40	8.5	3.8	568	53	154	Stricture of rectum Discharged unimproved
25	W.	F.	16	-	12	5	1	H	4	1	0	0	0	0	A	0	0	56	36.3	34.5	2.860	1.830	990	4.82	2.20	7.02	11.4	5.7	53	57	57	Ptyalism. Diarrhea had stopped 3 months before admission
26	W.	F.	23	-	6	2	1	H	0	0	0	0	0	0	0	0	0	36.8	30.6	2.640	1.810	810	4.04	2.13	6.17	10.76	6.2	614	50	50	Clinically stationary	
27	C.	F.	39	-	4	2	2	DU	0	0	1	0	0	0	0	0	0	37.2	32.5	1.30	2.110	1.000	4.16	2.17	6.33	11.0	3.4	604	59	59	Third annual attack. Was edematous 5 days ago. Improved	
28	W.	F.	26	-	5	2	1	H	0	0	0	0	0	0	0	0	0	37.5	33.8	2.600	1.700	880	4.14	2.15	6.29	11.1	4.8	590	60	56	Luetic heart disease Died suddenly 3 days later	
29	W.	M.	36	-	4	2	1	E	0	0	1	0	0	0	A	0	0	67	52.2	36.0	4.940	3.110	1.780	4.03	2.32	6.35	11.8	3.2	620	58	58	Unimproved
30	W.	M.	44	-	6	3	1	E	0	0	1	2	0	0	-	0	0	52.7	35.5	4.550	2.890	1.610	3.91	2.37	6.28	11.8	3.4	540	55	52	Unimproved	
31	C.	M.	53	-	1	1	1	E	0	0	0	0	0	0	A	0	0	70	59.0	43.4	5.580	3.150	2.420	3.60	3.016	6.61	9.8	3.4	492	53	47	Luetic heart disease Died suddenly 3 days later

TABLE 1—Concluded

Patient Data												Treatment and Response																
Initial Assessment												Follow-up																
Demographics						Clinical Findings						Laboratory Findings						Treatment										
Case number						Present state						Weight						Total base										
C.	F.	Age	Race	Sex	Interval	Duration	Severity	Grosses	Vomiting	Psychoses	Neuritis	Edema	Ideal	Present	Red cell volume	Plasma volume	VOLUME blood packed cells	Albumin	Serum proteins	Chloride as NaCl	CO ₂ capacity plasma	Total base	Remarks					
32	C.	25	-	4	1	DE	0	0	0	0	0	A	0	1	59	38.1	35.0	2.790	1.780	980	3.24	2.06	5.30	10.9	4.1	552	46	
33	C.	39	-	4	1	D	0	1	0	0	0	A	0	0	70	62.5	51.8	4.240	2.860	1.350	2.97	4.60	5.57	11.8	3.2	538	51	
34	W.	29	-	4	2	E	0	0	0	0	0	A	0	0	0	59.9	51.0	5.150	3.520	1.600	2.83	4.85	7.68	10.8	4.4	562	54	
35	C.	30	-	12	3	DU	0	0	0	0	0	A	0	0	0	59.4	32.2	4.630	3.100	1.490	2.73	5.11	7.84	6.0	3.9	570	60	
36	C.	23	-	10	3	DU	3	1	0	0	0	A	0	1	53	46.3	50.4	4.3470	1.720	1.680	5.46	2.14	7.50	11.3	4.9	51	51	
32	C.	4	12	4	1	HD	0	0	2	0	0	A	0	0	59	38.1	34.7	3.390	2.190	1.30	2.83	4.85	7.68	10.8	4.4	562	54	
33	C.	14	13	11	13	H	0	0	0	0	0	A	0	0	0	59.9	31.0	5.150	3.520	1.600	2.83	4.85	7.68	10.8	4.4	562	54	
34	W.	29	60	14	14	HD	0	0	0	0	0	A	0	0	0	60.3	39.6	5.200	3.620	1.540	2.63	4.18	6.80	11.1	4.7	552	60	
35	C.	14	14	12	14	H	0	0	0	0	0	A	0	0	0	39.3	47.9	3.770	1.930	1.860	4.01	1.62	5.64	11.1	4.7	536	54	
36	C.	14	14	13	14	H	0	0	0	0	0	A	0	0	0	38.5	46.9	2.690	1.400	1.260	3.51	1.83	5.34	14.3	4.3	530	55	
32	C.	4	12	3	3	DU	0	0	0	0	0	A	0	0	0	37.6	42.2	—	—	—	3.28	1.46	4.17	11.1	4.5	574	54	
33	C.	14	14	12	12	H	0	0	0	0	0	A	0	0	0	37.6	44.2	—	—	—	3.94	1.63	5.54	10.9	5.2	564	56	
34	W.	29	60	14	14	H	0	0	0	0	0	A	0	0	0	60	52.0	22.3	3.630	2.820	810	3.37	2.26	5.63	11.9	4.2	530	56
35	C.	14	14	13	14	H	0	0	0	0	0	A	0	0	0	50.9	22.5	3.570	2.740	810	3.38	2.50	5.88	10.1	4.4	588	57	
36	C.	14	14	13	14	H	0	0	0	0	0	A	0	0	0	55.1	22.7	4.100	3.160	930	3.22	2.50	5.72	9.2	3.8	600	49	
32	C.	4	12	3	3	DU	3	1	0	0	0	A	0	2	56	44.5	19.6	3.810	3.060	750	1.71	3.80	5.57	7.4	2.6	356	57	
33	C.	14	14	13	14	H	0	0	0	0	0	A	0	2	56	44.5	19.6	3.810	3.060	750	1.71	3.80	5.57	7.4	2.6	356	57	
34	W.	29	60	14	14	H	0	0	0	0	0	A	0	2	56	44.5	19.6	3.810	3.060	750	1.71	3.80	5.57	7.4	2.6	356	57	
35	C.	14	14	13	14	H	0	0	0	0	0	A	0	2	56	44.5	19.6	3.810	3.060	750	1.71	3.80	5.57	7.4	2.6	356	57	
36	C.	14	14	13	14	H	0	0	0	0	0	A	0	2	56	44.5	19.6	3.810	3.060	750	1.71	3.80	5.57	7.4	2.6	356	57	

37	W.	F.	50	-	8	3	1	H	1	2	0	0	0	A	0	0	63	52.2	34.0	3.440	2,110	1,320	4.22	2.41	6.63	10.1	3.2	540	58	142		
38	C.	F.	32	-	12	3	1	HE	0	0	0	0	0	-	0	0	62	66	740	85.090	2,970	1,980	3.152.09	5.24	11.1	4.0	560	55	137			
								HD	0	0	0	0	0	-	0	0	68	62.239	65.180	3.110	2.050	3.834	2.45	6.27	10.9	3.8	582	60				
								H	0	0	0	0	0	-	0	0	69	9.38	85.100	3.010	2.050	3.21	1.90	5.11	10.3	4.3	522	55	142			
								H	0	0	0	0	0	-	0	0	70	4.38	15.15	3.270	2.020	3.43	2.27	5.70	11.0	4.4	530	59	162			
								H	0	0	0	0	0	-	0	0																
39	C.	F.	22	-	4	3	2	D	1	1	0	0	0	A	0	0	57	62	2.35	74.740	3.050	1,690	3.066	2.97	6.63	10.4	3.3	490	64	139		
								H	0	0	0	0	0	-	0	0	62	4.435	74.100	2.620	1.460	3.142	2.70	5.84	11.0	3.8	570	55				
								H	0	0	0	0	0	-	0	0	64	4.34	54.160	2.710	1,430	3.40	2.63	6.03	10.7	4.4	534	57	154			
								H	0	0	0	0	0	-	0	0																
40	C.	F.	28	-	4	5	2	DB	0	0	1	0	0	A	0	0	58	53.3	32.84	4.430	2,930	1,450	3.68	2.14	6.42	11.1	5.2	564	49	141		
								U	2	0	0	0	0	-	0	2	53	1.28	74.970	3.520	1,420	3.163	2.07	6.23	9.9	3.4	592	53				
								U	2	0	0	0	0	-	0	3	51.5	30.64	6.640	3.220	1,420	3.23	2.72	5.95	10.0	3.2	506	39	135			
								D	0	0	0	0	0	-	0	0																
41	C.	F.	32	-	2	2	1	E	3	0	1	0	0	A	0	0	60	45.7	35.83	1.140	1,980	1,120	3.71	2.42	6.13	10.0	4.5	530	59			
								DU	0	0	0	0	0	-	0	0	45.7	34.33	2.200	2,080	1,100	3.64	2.19	5.83	11.3	4.6	580	59				
								D	0	0	0	0	0	-	0	0	46	8.32	7.3.370	2	2,00	1,100	3.60	2.40	6.00	11.1	5.0	540	58	150		
								ED	0	0	0	0	0	-	0	0																
67	42	W.	F.	30	-	2	4	2	ED	0	0	1	0	0	?	0	0	56	38.7	34.13	1.740	2	450	1,270	3.40	2.09	5.49	10.3	4.9	480	55	149

Skin lesions: Duration: Time in weeks since appearance of skin lesions of present attack. In a number of cases before skin lesions were healed fresh ones appeared. These are referred to as recurrent skin lesions. They are considered as being a part of the same attack of pellagra as the unhealed lesions. Figures in this column do not refer to the time of appearance of recurrent lesions.

Extent: Figures in this column indicate roughly the surface area involved. The areas referred to are those most commonly involved, their equivalents in extent elsewhere is occasionally substituted. 1 = parts of hands only. 2 = entire surface of hands exclusive of palms. 3 = hands and forearms or elbows. 4 = hands and feet plus other extensive areas.

Severity: Terminology that of burns: 1 = first degree. 2 = second degree. 3 = third degree. Third degree pellagra lesions on healing do not cause contracture but the skin is far from normal.

State: Condition of lesions at the time of study. B = bullous. U = ulceration. E = erythema. D = desquamation. H = healed.

Severity: 1 = 3 to 6 times a day. 2 = 7 to 10 times. 3 = 11 or more times a day.

Glossitis: 1 = mild diffuse redness. 2 = marked diffuse injection with pain. 3 = marked injection plus areas of ulceration. 4 = bald tongue due to atrophy of papillae.

Vomiting: 0 = absent. 1 = occasional. 2 = 3 to 5 times daily.

Psychosis: D = delirium. C = coma. S = suicidal depression.

Neuritis: Symptoms of peripheral neuritis in legs but with exaggerated knee jerks. 1 = mild, chiefly subjective. 2 = moderate. 3 = severe bedridden. — = information not available.

Gastric acidity: A = absence of free hydrochloric acid. N = normal acidity. H = hypacidity. — = information not available.

Edema: Pitting edema: 1 = just demonstrable. 2 = moderate in degree and distribution. 3 = anasarca.

Fever: 1 = temperatures up to 101.5°F. 2 = more than 103°F. 3 = temperatures higher than 103°F.

Blood volume: The figures in italics are estimated values obtained by comparing the hematocrit at that particular time with the hematocrit of the preceding or following study. The calculation is based on the assumption that the volume of circulating blood cells is unchanged from one occasion to the next.

Weight: Given in kilograms. Ideal weights are those given by the tables of the Medico-Actuary Mortality Investigations (5) for sex, age, and height.

problems of pellagra than the accumulation of more exact knowledge of the disturbed physiology.

All patients studied were in-patients of Charity Hospital, and all had typical skin lesions of pellagra together with other evidences of the disease.

Detailed methods will be presented as indicated in subsequent papers of this series.

The first study was usually made one or two days after admission to the hospital, and with few exceptions the blood volume was determined each time blood was taken for chemical study. The studies were repeated, provided the patients remained sufficiently long under observation, at intervals of from 5 to 15 days. All patients were given during their stay in the hospital a special "pellagra diet." This diet has a daily caloric value of 2500 to 3500 calories, contains more than 100 grams of protein, a part of which is liver or sweetbread, and contains an abundance of green leafy vegetables and 500 cc. buttermilk. It is given to patients with diarrhea in bland form, and, when necessary, a liquid diet of similar caloric value was given by gavage. Routinely there was included for the vitamin content 30 cc. of fresh brewer's yeast three times a day, 150 cc. of orange or lemon juice daily and in addition some of the patients received 4 cc. of cod liver oil three times a day. The nurses usually took especial interest in their pellagrins and in their nutrition and fluid intake.

No particular effort was made to influence by treatment the derangements of physiology revealed in these studies. Therapeutic studies are to be made later. In the present studies pellagra was observed under what has been considered an excellent regimen.

The detailed clinical information, the blood volumes, and the results of chemical studies are shown for 42 cases in table 1.

The pellagrins which we have studied made a fairly representative group. The proportion of severe cases of pellagra is much greater in hospital than in general practice, but mild forms of the disease are also present.

In subsequent articles (1, 2, 3, 4) detailed procedures will be presented and the results of the physiologic investigations analyzed and discussed.

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SUMMARY OF CLINICAL DATA

Detailed clinical data obtained from a study of 42 pellagrins are recorded in one table which also includes the results of determinations of circulating blood volume, serum albumin and globulin, serum calcium and inorganic phosphorus, of plasma chlorides, of carbon dioxide combining power, and of serum total base.

The group of patients consisted of 6 white men, 9 white women, 9 negro men, 16 negro women, and 2 negro children. Twenty were less than 30 years old and 36 were less than 50.

Thirteen patients, 31 per cent, died in the hospital.

Thirty-nine had had no previous attacks of pellagra; 3 had had attacks 1 to 7 years previously.

Eleven patients of the group had other diseases: Syphilis, 5, two with heart disease; stricture of the rectum, 4; active gonorrhea, 1; intestinal tuberculosis, 1.

Fifty-nine per cent of the patients were more than 20 per cent underweight and 35 per cent more than 30 per cent underweight, and 10 per cent were overweight.

Eight patients showed edema.

The skin lesions at the time of the first study showed erythema in 26, 62 per cent; 9 of the 26 showed recurrent lesions in the presence of older unhealed lesions.

Vomiting was a serious problem in 2 patients.

Glossitis was present in 26, 62 per cent; diarrhea in 25, 60 per cent.

Gastric analysis was done in 34 and achylia found in 29, 60 per cent, of the entire group; hypoacidity in 3, and a normal acidity in 2 patients.

Seven patients were delirious, 2 were comatose and 1 suicidal; a total of 10, 24 per cent, with psychoses.

Six patients showed evidences of peripheral neuritis.

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