In the case of calomel, certain hypersensitive reactions have been described, such as acute exanthemata, with small scarlatiniform or urticarial eruptions on the body, excepting the palms of the hands and the soles of the feet (areas in which the signs of acrodynia are most marked), abdominal pains and diarrhoea, and elevation of the temperature ; or there may be an acute eczematous type of dermatitis. These symptoms usually occur within six to eight days of taking the drug, disappear within a few days, and do not affect the general health. None of these symptoms is associated with acrodynia, nor were any present in these cases, except possibly the pyrexia, which could probably be explained on other grounds. It is quite natural, however, that children will differ considerably in their degree of sensitivity to calomel, or to any other drug, and it would appear that this child, the subject of the second inquest, was certainly more sensitive to calomel than the previous one. Distinction must be made, nevertheless, between normal variations in sensitivity and the state of hypersensitivity or idiosyncrasy, and in view of the absence of any of the usual hypersensitive symptoms, and also the proved very high mercurial content of the organs, it is quite impossible to sustain any suggestion of abnormal hypersensitivity in this case.

Controversy during the first of the two inquests revolved largely around the relatively small number of cases of acrodynia, in the face of truly startling sales of teething powders ; these were stated by counsel representing the manufacturers to be no fewer than 30,000,000 per annum for this one firm alone. The other argument which was brought forward in opposition to the mercurial aetiology of acrodynia was the high incidence of the disease in the North and Midlands as against the South of England, which, according to the information supplied by counsel, is by no means proportionate to the sales of that brand of powder. The *Lancet* (1953) follows a very similar line of reasoning.

It is not denied that other factors, as yet not determined, may well play a part in the aetiology of acrodynia. These unknown factors may simply act by influencing the absorption of mercury from the bowel.

It cannot, however, be denied that evidence has been steadily increasing since 1948, and from a wide diversity of sources, incriminating mercury as an important factor in the causation of acrodynia. This series of cases, culminating in two deaths in which the organs contained very large amounts of mercury, must add considerable weight to that evidence.

Apart from the close association of mercury and acrodynia, the nephrotoxic effects of inorganic salts of mercury have long been recognized, and recent papers by Wilson, Thomson, and Holzel (1952), and by Farquhar (1953) have emphasized this danger.

At the end of the second inquest it was announced by counsel representing the manufacturers of the powders concerned in both inquests that this firm has now discontinued the use of calomel in the preparation of teething powders or soothing powders. This decision to omit the calomel from one of the popular brands of teething powders having a very wide circulation must be regarded as a highly satisfactory statement. Matters should not, however, be allowed to stop there, for there remain other manufacturers who may not take the same action. The only safe solution would appear to be for calomel and other inorganic salts of mercury to be included in Schedule 1 of the Poisons List.

On December 10 last the attention of the Home Secretary was drawn to the first of these cases, and he was asked whether, in view of the evidence, action should not be taken to prohibit the use of these substances. During the course of his reply he stated that inquiries were not yet complete. Thus his reply differed little from that made on behalf of the Minister of Health 20 months earlier.

Summary

The literature is reviewed up to date concerning the association of mercury with acrodynia. Thirteen cases are added to the number so far recorded in which there was found to be a close association ; this series included two deaths which were the subject of coroners' inquests. The factors concerning the aetiology of acrodynia are discussed, with special reference to the steadily increasing evidence incriminating mercury as a major factor. A plea is added for the inclusion of calomel in Schedule 1 of the Poisons List.

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CLINICAL AND CHEMICAL STUDIES IN HUMAN LACTATION*

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IV. TRENDS IN MILK COMPOSITION DURING COURSE OF LACTATION

The change which occurs in the composition of milk during the course of lactation was probably the first variation in milk to be recognized. As far back as the second century A.D., Soranus of Ephesus wrote that "during the first twenty days the mother's milk is, as a rule, unfit for consumption by the child, being thick, cheesy, and difficult to digest" (quoted by Ruhräh, 1928).

The literature of the past half-century is almost unanimous that the yield rises rapidly during the first week and more slowly thereafter, that the lactose content also rises during the first week to a level which is almost constant for the rest of lactation, and that the nitrogen content falls steeply during the first few days and more slowly thereafter. There is little information about the trends of fat content, although what evidence there is suggests a rise during the first few weeks of lactation. Morrison (1952), in his comprehensive review of human milk composition, discusses the evidence for all these changes in detail.

The present data are reported because they amplify current knowledge of these trends, although they were collected with other purposes in view. The following 24-hour samples were studied. (*a*) From lying-in patients at the Aberdeen Maternity Hospital 210 samples were collected during the first two weeks of lactation. Most of those taken during the first six days were primarily intended for the examination of diurnal variation and were therefore selected so that there would be enough milk available at each feeding for a complete analysis. In order to study differences in milk composition between individuals, 150 samples were collected on the seventh day. There was a preponderance of primiparae, but the cases otherwise form an approximately random sample of maternity hospital patients. (*b*) Thirty

*Parts I, II, and III were published last week (*Journal*, January 23, p. 175).

samples of mature milk from the 21st day of lactation or later were collected from a variety of sources; two subjects were still lying-in patients of the Aberdeen Maternity Hospital on account of post-partum complications; nine were resident in the mother and baby unit of the Royal Aberdeen Hospital for Sick Children with babies requiring some medical or surgical treatment; and another nine had been admitted with some feeding difficulty. Ten subjects were unmarried and living in the Aberdeen Mother and Baby Home. From eight of these latter subjects and from three others samples were obtained on the seventh post-partum day and also later in lactation. (*c*) From five women whose infants were premature and unfit to be put to the breast samples were obtained on a number of days during the lying-in period, and, from two of these, further samples were obtained by manual expression.

Method.—The whole contents of both breasts were removed by the "humalactor" at the usual feeding-times of 6 a.m., 10 a.m., 2 p.m., 6 p.m., and 10 p.m. After the last feeding prior to the sampling period the

TABLE I.—*Samples From the First Two Weeks of Lactation, Excluding the Seventh Day*

Case No.	No. of Pregnancy	Day	Volume (ml.)	Fat (g./100 ml.)	Lactose (g./100 ml.)	Total N. (mg./100 ml.)	N.P.N. (mg./100 ml.)	Protein (g./100 ml.)
221	5	1	54	6·80	2·40	1,061	332	4·67
223	1	1	15	2·20	5·00	1,852	654	7·68
224	1	1	28	15·65	5·21	956	437	3·33
229	1	1	12	0·90	7·05	1,791	1,082	4·54
230	1	1	7	—	4·11	—	245	—
233	2	1	12	2·65	3·97	1,292	274	6·53
117	3	2	115	2·50	6·02	449	80	2·37
172	3	2	40	1·90	5·38	925	234	4·43
201	1	2	2	—	—	951	228	4·63
220	1	2	94	3·40	6·37	550	105	2·85
224	1	2	46	6·35	6·26	550	178	2·38
233	2	2	17	3·55	4·11	960	109	5·45
236	1	2	28	0·50	6·57	1,532	563	6·21
28	1	3	461	2·55	6·61	371	70	1·93
29	6	3	121	2·15	—	—	—	—
31	2	3	124	1·85	—	—	—	—
42	2	3	699	2·40	6·17	280	50	1·47
49	2	3	307	3·20	6·02	401	64	2·16
117	3	3	530	3·30	6·41	345	92	1·62
172	3	3	323	3·45	5·65	370	64	1·96
201	1	3	52	1·20	5·27	486	102	2·46
224	1	3	295	3·85	6·37	384	85	1·92
233	2	3	170	2·90	6·37	370	111	1·66
236	1	3	235	1·90	6·09	468	85	2·46
21	2	4	566	2·90	6·17	—	—	—
27	1	4	325	3·85	6·47	409	—	—
43	2	4	459	3·20	6·04	361	68	1·88
48	1	4	500	2·20	6·57	311	87	1·44
56	2	4	810	2·60	5·82	280	73	1·33
117	3	4	550	2·90	6·71	322	88	1·50
172	3	4	416	2·70	6·01	294	63	1·48
224	1	4	425	2·80	6·34	349	88	1·67
233	2	4	190	2·80	6·47	386	109	1·78
236	1	4	340	2·60	6·19	353	83	1·73
23	1	5	342	2·40	—	—	—	—
26	3	5	287	2·30	—	—	—	—
30	1	5	270	2·80	—	—	—	—
34	8	5	304	3·05	4·83	506	62	2·85
117	3	5	745	3·45	6·78	312	70	1·55
172	3	5	431	3·55	6·44	294	63	1·48
224	1	5	450	3·50	6·51	343	83	1·67
233	2	5	180	4·40	6·02	361	87	1·76
236	1	5	305	2·95	6·23	350	87	1·69
22	1	6	681	3·50	—	—	—	—
33	1	6	738	3·65	6·64	252	67	1·19
37	3	6	372	2·70	6·56	297	73	1·44
40	3	6	418	2·10	6·29	302	70	1·49
41	3	6	502	4·80	5·98	395	82	2·01
172	3	6	524	2·90	6·47	283	61	1·42
224	1	6	419	4·60	5·96	340	77	1·69
233	2	6	275	2·40	6·16	302	73	1·47
236	1	6	560	2·80	6·44	342	87	1·63
38	1	8	219	1·45	6·56	255	68	1·20
70	2	8	710	2·00	6·57	260	53	1·33
172	4	8	670	3·05	6·64	270	68	1·29
233	2	8	310	4·20	5·96	246	56	1·22
236	1	8	560	2·80	6·82	311	73	1·53
233	2	9	325	4·00	6·37	263	59	1·31
224	1	13	540	4·20	6·64	294	62	1·49
268	1	13	380	2·90	5·79	210	53	1·01

TABLE II.—*Samples From the Seventh Day of Lactation*

Case No.	No. of Pregnancy	Volume (ml.)	Fat (g./100 ml.)	Lactose (g./100 ml.)	Total N. (mg./100 ml.)	N.P.N. (mg./100 ml.)	Protein (g./100 ml.)
25	2	691	3·80	—	—	—	—
32	1	71	5·25	4·80	456	84	2·39
36	1	514	3·10	6·45	—	—	—
39	1	522	2·70	6·40	323	69	1·63
51	1	258	2·70	5·55	260	76	1·18
52	2	695	1·70	6·23	241	50	1·22
53	1	409	3·70	6·44	286	53	1·49
54	1	356	3·40	6·78	—	64	—
55	1	352	2·40	5·82	312	60	1·62
59	1	410	3·60	6·92	274	67	1·33
60	1	550	2·65	6·50	252	57	1·25
61	1	170	2·70	5·12	405	31	2·08
62	1	240	3·20	6·44	297	62	1·51
63	1	150	1·90	6·57	283	56	1·46
65	2	990	4·50	6·30	269	46	1·42
66	2	220	2·75	6·30	309	76	1·49
67	7	360	3·00	6·44	235	59	1·13
68	1	405	3·70	5·96	274	67	1·33
69	1	380	3·50	6·16	339	70	1·72
71	1	440	4·10	6·37	305	71	1·50
72	1	433	2·10	6·16	302	76	1·45
73	1	220	4·50	5·82	347	59	1·85
74	1	400	2·20	6·16	255	56	1·28
75	1	460	3·20	6·37	297	67	1·47
76	1	330	2·80	6·16	260	62	1·27
77	1	280	3·50	5·48	305	53	1·62
79	1	720	2·80	6·91	258	53	1·31
80	1	235	2·95	5·82	304	57	1·58
81	2	91	3·40	3·91	423	63	2·31
82	1	385	4·10	6·16	308	76	1·49
83	1	170	3·80	4·25	329	48	1·80
84	1	315	2·70	6·16	288	64	1·44
87	1	470	2·90	6·44	249	55	1·24
88	1	855	2·90	7·05	239	62	1·13
89	1	560	2·80	6·51	274	59	1·38
90	1	350	2·90	6·64	294	76	1·40
91	2	426	1·85	6·52	274	66	1·33
92	1	265	2·40	6·44	300	78	1·42
93	3	490	3·00	6·71	280	67	1·37
94	1	590	3·80	6·70	287	71	1·38
95	3	590	2·40	6·51	269	61	1·33
96	8	225	5·90	5·62	316	50	1·71
97	1	470	2·50	6·51	204	28	1·13
98	1	260	2·70	5·89	276	70	1·32
99	1	555	3·00	6·44	286	77	1·34
100	1	680	3·20	6·51	274	50	1·44
103	1	450	2·40	6·71	232	53	1·15
104	2	275	3·30	5·55	263	60	1·30
105	1	480	4·00	6·54	280	66	1·37
106	1	415	3·75	6·09	363	73	1·86
107	1	310	2·60	6·51	246	62	1·18
108	1	450	2·60	6·54	274	86	1·21
109	1	225	3·00	5·89	288	80	1·33
110	1	480	2·70	6·57	298	67	1·48
111	1	350	2·80	6·37	364	90	1·76
112	1	690	3·30	6·64	242	64	1·14
113	1	800	2·20	6·37	294	70	1·44
114	1	690	2·60	6·37	295	67	1·46
116	1	190	2·70	6·67	354	100	1·63
118	1	380	3·00	6·33	342	90	1·63
119	2	298	3·00	6·78	263	70	1·24
120	1	540	4·10	—	287	52	1·51
121	1	250	4·10	5·45	286	48	1·53
122	2	930	3·40	6·37	259	76	1·17
123	1	235	2·50	5·55	315	104	1·35
124	1	430	3·50	6·02	259	65	1·24
125	1	445	1·80	5·78	270	81	1·21
126	2	620	3·70	6·88	262	76	1·19
127	5	730	3·75	6·60	287	75	1·36
128	1	375	3·25	6·67	271	63	1·33
129	1	455	3·05	6·41	293	95	1·27
130	1	630	3·80	6·19	308	77	1·48
131	1	420	2·00	6·30	269	65	1·31
132	1	450	3·20	6·44	302	73	1·47
133	1	275	2·10	5·62	371	76	1·89
134	1	390	3·60	5·96	287	70	1·39
135	2	555	3·50	5·89	290	48	1·55
136	5	270	2·40	6·60	281	76	1·31
137	2	350	2·70	6·60	283	64	1·40
139	1	510	3·60	6·37	292	60	1·49
140	1	570	3·20	6·74	255	60	1·25
141	1	420	3·40	6·85	323	75	1·59
142	3	450	2·85	6·57	301	70	1·48
143	1	270	3·50	6·02	290	68	1·42
144	1	370	3·50	6·30	301	72	1·47
145	1	670	4·00	6·30	277	55	1·42
146	3	265	4·60	6·54	321	78	1·56
147	7	880	4·35	6·54	263	70	1·24
148	1	1,034	3·50	6·00	260	63	1·26
149	1	225	2·20	6·02	318	64	1·63
150	1	260	1·60	6·19	277	70	1·33
152	1	575	2·25	6·37	267	67	1·28
153	1	545	2·30	6·78	253	68	1·19
154	1	310	2·30	6·64	299	81	1·40
155	1	550	5·00	6·64	320	91	1·47
156	1	330	3·50	6·16	335	73	1·68
157	4	560	3·00	6·44	294	70	1·44
160	1	375	1·70	6·33	309	71	1·53
163	1	518	3·65	6·44	290	58	1·49
164	8	610	3·10	6·30	300	72	1·46
165	1	400	2·90	6·57	283	72	1·35
166	1	615	4·40	6·41	346	79	1·71
167	1	690	4·10	6·41	307	58	1·60
168	1	440	2·35	6·30	293	69	1·44

TABLE II.—*(Continued)*

Case No.	No. of Preg-nancy	Volume (ml.)	Fat (g./ 100 ml.)	Lactose (g./ 100 ml.)	Total N. (mg./ 100 ml.)	N.P.N. (mg./ 100 ml.)	Protein (g./ 100 ml.)
169	1	465	3·15	6·57	290	66	1·44
170	1	220	5·00	5·62	365	73	1·87
172	3	583	2·75	6·46	274	64	1·35
173	1	450	4·65	6·02	312	70	1·55
175	1	210	2·35	6·64	239	60	1·15
176	1	124	5·30	5·34	340	59	1·80
178	1	290	3·30	5·89	330	70	1·67
179	1	535	2·70	6·37	251	57	1·24
180	1	360	2·65	6·44	293	53	1·54
181	1	431	3·00	6·60	315	67	1·59
182	5	270	5·00	5·48	303	54	1·60
183	1	390	3·20	6·26	316	76	1·54
184	1	565	3·90	6·30	337	68	1·73
185	1	102	2·15	6·30	347	102	1·57
186	1	482	2·95	6·34	265	75	1·22
187	1	380	2·30	6·78	262	65	1·26
188	1	395	3·30	6·54	282	73	1·34
189	1	76	2·10	5·75	315	62	1·62
192	1	530	3·20	6·64	223	51	1·10
194	1	367	4·60	6·25	372	82	1·86
200	1	356	3·50	7·10	262	69	1·24
204	1	230	4·30	6·85	351	108	1·56
205	1	830	3·10	7·33	270	93	1·13
206	1	325	2·80	—	293	76	1·39
207	1	460	3·10	6·64	272	65	1·33
210	1	480	3·40	6·64	291	79	1·36
211	1	50	3·50	5·96	326	79	1·58
212	1	485	2·80	6·02	274	65	1·34
213	1	360	4·10	6·44	281	65	1·38
214	2	610	2·70	6·71	276	58	1·40
215	1	645	3·00	7·05	270	74	1·26
216	2	335	1·70	6·64	286	83	1·30
217	1	255	3·60	6·71	283	—	—
218	1	390	2·95	6·78	248	77	1·10
219	1	445	2·65	6·44	329	85	1·56
222	1	430	4·00	6·57	357	91	1·71
224	1	215	5·00	6·16	336	71	1·70
226	1	270	3·55	6·23	294	76	1·40
227	3	255	2·75	6·44	287	80	1·33
228	1	680	4·15	6·19	323	85	1·53
231	1	485	2·90	6·26	281	77	1·31
232	1	430	2·60	6·16	286	74	1·36
233	2	300	4·00	5·96	276	50	1·45
235	1	530	4·20	6·51	266	55	1·35
236	1	610	3·05	6·54	322	76	1·57
238	1	535	2·40	7·05	277	95	1·17

TABLE III.—*Samples From Later Than the Second Week of Lactation*

Case No.	No. of Preg-nancy	Day	Volume (ml.)	Fat (g./ 100 ml.)	Lactose (g./ 100 ml.)	Total N. (mg./ 100 ml.)	N.P.N. (mg./ 100 ml.)	Protein (g./ 100 ml.)
236	1	20	510	3·10	7·01	260	53	1·33
35	9	21	954	3·60	6·87	266	67	1·28
234	1	21	419	4·55	6·98	250	87	1·04
159	1	22	299	4·25	6·19	270	67	1·30
224	1	22	540	4·40	7·12	277	90	1·20
158	2	27	541	4·30	6·89	196	43	0·98
183	1	28	534	3·75	7·30	215	62	0 98
224	1	28	500	4·90	—	246	53	1·24
162	1	32	615	3·55	6·78	189	54	0 87
225	1	34	488	3·50	6·98	209	57	0 97
35	9	37	935	3·55	7·01	205	47	1·01
198	1	38	681	3·70	6·92	197	50	0·94
138	2	40	475	3·40	6·50	222	57	1 06
119	2	41	308	3·50	7·08	181	54	0 81
235	1	42	440	4·70	6·16	192	38	0 99
151	1	47	743	4·15	6·96	212	70	0·91
199	3	47	471	3·55	6·71	224	57	1·07
116	1	48	530	2·60	7·05	216	59	1·01
161	2	48	481	2·05	6·78	172	40	0·85
163	1	48	957	4·15	7·02	209	55	0 99
115	1	49	302	1·45	6·92	196	56	0 90
74	1	50	560	2·55	7·18	185	62	0·79
102	2	50	523	3·25	7·01	191	48	0·92
139	1	50	954	3·80	6·87	195	52	0·92
110	1	53	511	2·95	7·12	183	52	0·84
177	3	53	633	3·25	6·57	235	49	1·19
205	1	58	950	4·50	6·85	197	62	0 86
121	1	62	775	4·65	6·71	189	52	0·89
174	1	62	443	3·45	6·75	192	50	0 91
75	1	135	762	4·00	7·07	144	39	0·67

breasts were emptied so that no residual milk from the previous 24 hours would be included in the sample. The methods of analysis have been detailed in Part II of this paper (see *Journal*, January 23, 1954, p. 175). Protein was estimated by multiplying the protein nitrogen by 6.41 (Escudero, 1946).

Results

The values for milk volume and for fat, lactose, total nitrogen, non-protein nitrogen, and protein contents are shown in Tables I, II, and III, arranged in order of the day of lactation they represent.

Volume.—For the first few days the yield is usually very small, but it rises rapidly from the point where, clinically, the milk "comes in." It is obvious from the small numbers of samples and from their range of values that a curve of average values would have little significance in practice, and the construction of such a curve has not been attempted. The volumes from the subjects providing the more mature samples are not likely to provide a representative picture of the volumes secreted at this stage of lactation, since some of these women were emotionally upset, either because their babies were ill or because they were experiencing some feeding difficulty. This effect has been discussed in Part I of this paper.

Nitrogen.—The findings of previous authors are broadly confirmed. There is a rapid drop in total nitrogen during the first three days of lactation, and this can be clearly seen in the Chart, where the total nitrogen contents of the milk on a number of days during the first nine days are shown for four subjects. After the third day the drop is more gradual. The mean value for 150 samples on the seventh day was 296 ± 38 mg. per 100 ml.; for 15 samples obtained between the third and sixth weeks, 225 ± 33 mg. per 100 ml.; and for 15 samples taken later than the sixth week, 196 ± 26 mg. per 100 ml. The non-protein nitrogen constitutes between 20 and 30% of the total nitrogen, the mean proportion being about 25% on the seventh day, and about 27% in the more mature milks. For protein, the mean value on the seventh day was 1.44 ± 0.22 g. per 100 ml.; between three and six weeks, 1.07 ± 0.16 g. per 100 ml.; and after the sixth week, 0.91 ± 0.12 g. per 100 ml. The range of values from the seventh day onwards is almost constant, the coefficient of variation remaining at about 15%.

Lactose.—The lactose content shows a rise during the first week of lactation, but there may be considerable fluctuations from day to day in the same subject, in contrast to the smoothly progressive trend shown by total nitrogen. Table IV shows the lactose content of milks from four subjects

TABLE IV.—*Lactose Content of Milk in g. per 100 ml. During the First Week of Lactation in Four Subjects From Whom Serial Samples Were Obtained*

Case No.	Day of Lactation							
	1	2	3	4	5	6	7	8
172	—	5·38	5·65	6·01	6·44	6·47	6·64	6·46
224	5·21	6·26	6·37	6·34	6·51	5·96	6·16	—
233	3·97	4·11	6 37	6·47	6·02	6·16	5·96	5·96
236	—	6·57	6·09	6·19	6·23	6·44	6·54	6·82

whose milk was examined daily during the first eight days. At seven days the mean value for 150 samples (Table II) was 6.29 ± 0.45 g. per 100 ml. and for mature milk (Table III), 6.87 ± 0.26 g. per 100 ml. There is no significant change in the mean lactose content after about the first month of lactation, and the final mature value is probably reached at about this time. The range of variation diminishes as the milk matures.

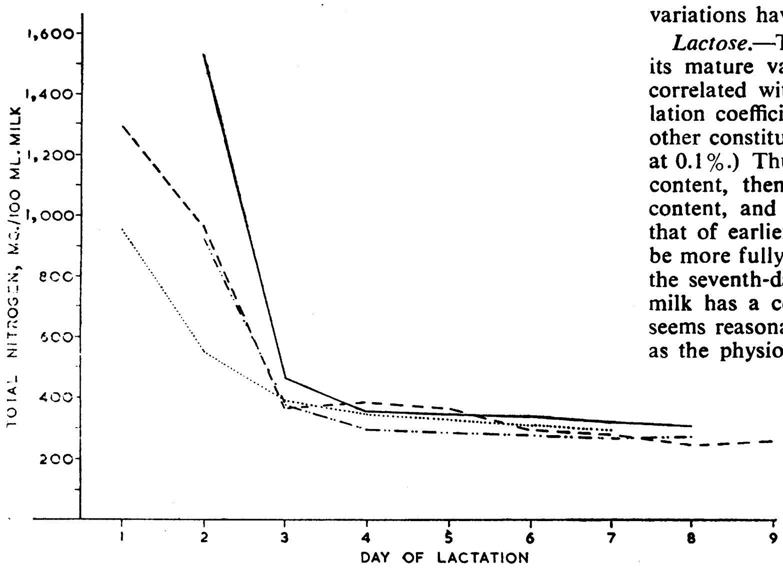
Fat.—It is not surprising that no consistent trend has been found for the fat content of milk, since the differences from one subject to another are so great that a large number would have to be examined to give a mean which would have any statistical validity. For this reason, data from the few subjects from whom samples were obtained at intervals give a clearer indication of the direction of any trend.

Table V shows the fat contents of the milk of the four women from whom serial samples were taken up to and beyond the end of the first week of lactation, those samples obtained after the second week having been expressed manually. On the first day the fat content is usually low, although one of the subjects produced 15.65 g. per 100 ml., the highest percentage of fat recorded in a 24-hour specimen. After the first day the fat content tends to rise, but there are large fluctuations from day to day up to the end of the first week, after which values become more stable. During the first week the absolute quantity of fat produced in 24 hours rises progressively, but the rate of increase is not enough to

TABLE V.—*Trend of Fat Content of Milk (g./100 ml.) in Four Subjects From Whom Serial Samples Were Obtained*

Case No.	Day of Lactation											
	1	2	3	4	5	6	7	8	9	14	21	28
172	—	1·90	3·45	2·70	3·55	2·90	2·75	3·05	—	—	—	—
224	15·65	6·35	3 85	2·80	3·50	4·60	—	—	—	4·20	4·40	4·90
233	2·65	3·55	2·90	2·80	4·40	2·40	4·00	4·20	4·00	—	—	—
236	—	0·50	1·90	2·60	2·95	2·80	3·05	2·80	—	3·10	—	—

maintain a stable fat content in the more rapidly increasing total milk yield. The trend beyond the end of the first week is illustrated by Table VI, in which 11 subjects, from whom samples were collected on the seventh day and again later in lactation, are detailed. The day of lactation on which the second specimen was taken is shown in the last column.



Four cases from whom serial milk samples were taken during the first nine days of lactation, showing the steep drop in total nitrogen content which occurs in the first three days, after which there is a gradual fall and a convergence to a narrow range of values.

It is clear, even from these few samples, that there is a rise in the fat content of milk beyond the seventh day, but, more important, Table VI shows that, unlike nitrogen and lactose, there is no tendency for the range to narrow towards what might be a physiological norm. The difference which occurs between subjects at the seventh day is maintained, and there is a high correlation between the fat contents of the seventh-day milks and the fat contents of more mature milks ($r = +0.88$). There does not appear to be a continuous rise, because mature samples taken two or three months after the seventh day show no greater increment than those taken after an interval of only a month. It is likely, therefore, that the mature fat content of the milk is reached by the beginning of the second month of lactation.

TABLE VI.—*Fat Content of Milk on the Seventh Day and in Mature Milk in Eleven Subjects*

Case No.	7th Day Fat (g./100 ml.)	Mature Milk	
		Fat (g./100 ml.)	Day of Collection
74	2·20	2·55	50
75	3·20	4·00	135
110	2·70	2·95	53
116	2·70	2·60	48
119	3·00	3·50	41
121	4·10	4·65	62
139	3·60	3·80	50
163	3·65	4·15	48
183	3·20	3·75	28
205	3·10	4·50	58
235	4·20	4·70	42

Discussion

Volume.—The few results presented here conform broadly to the accepted picture. The enormous range of milk outputs is well recognized clinically, and has been studied in far greater numbers by the indirect method of test-weighing the baby.

Nitrogen.—The decline in the content of total nitrogen which occurs during the progress of lactation has never been explained. It has been suggested that the initially very high protein content, showing as it does a preponderance of globulin, is due to equilibration with the blood of milk secreted during pregnancy and lying in the acini. But this mechanism cannot explain the further decline which occurs after the milk is being secreted in large volumes. On the seventh day the protein content varies considerably, and in some subjects it is still as high as that found typically on the fourth or fifth day. By the end of the first month these variations have practically all disappeared.

Lactose.—The rate at which the lactose content reaches its mature value also varies, and the values are inversely correlated with total nitrogen content. (The partial correlation coefficient of lactose with total nitrogen, volume and other constituents remaining constant, was -0.49, significant at 0.1%.) Thus, if milk on the seventh day has a low lactose content, then it will almost always have a high protein content, and the milk secretion as a whole will resemble that of earlier lactation. This difference in maturation will be more fully discussed in Part V of this paper, dealing with the seventh-day milk alone. The lactose content of mature milk has a coefficient of variation of less than 4%, and it seems reasonable to consider the value of 6.9 g. per 100 ml. as the physiological norm for the species.

Fat.—There can be little doubt from the figures presented that the fat content of milk increases from the beginning of lactation up to the second month. The fluctuations which occur during the initial stages of lactation appear to be due to an asynchronism between the increasing fat production and the more rapidly increasing total yield of milk, suggesting that there is a separate mechanism for the control of fat secretion. The differences in fat content on the seventh day seem to be the expression of individual characteristics and are not due, like differences in nitrogen and lactose contents, to differences in the speed of maturation of the milk. The fact that these individual differences in fat production are maintained throughout lactation means that the seventh-day sample can be used as a reliable index of the general level of fat production. For example, if the fat content of the milk on the seventh day is low, it will be low at any subsequent point in lactation.

In view of the above findings, it seems worth while to examine the meaning of the word colostrum in relation to human lactation. The colostral period has been defined in the past by a number of authors as varying from three to twenty days, and some have refined the division still further by adding, between the colostral and the mature milk, a period for "transitional milk." It is impossible to fix a time for the colostral period, such as the first seven days, since a number of subjects will be producing milk within this period which is chemically similar to mature milk. It would appear, therefore, that if a term is required which will indicate an immature secretion, then it should be based on the chemical characteristics and not on some arbitrary date-line. Since the term seems to have little practical value in clinical medicine it is not intended to suggest any criterion by which it could be redefined.

Summary

Fat, lactose, total nitrogen, and non-protein nitrogen have been estimated in 240 24-hour samples of milk collected at different stages of lactation from 194 subjects.

During the first week of lactation there is a wide range of values for total milk yield, and for all the constituents examined.

The yield rises rapidly during the first week and more slowly thereafter; the lactose content rises from an initially low level to a stable level of about 6.9 g. per 100 ml. within the first month of lactation; total nitrogen and protein content fall steeply from an initially high level during the first three days and then much more slowly until at least the second month.

The fat content is usually low during the first few days of lactation, but increases slowly to a level which is characteristic of the individual by the second month. The value, however, is stable enough by the seventh day to indicate fairly accurately the fat content of the mature milk in the individual case.

The use of the term "colostrum" is discussed.

I am grateful to Professor Dugald Baird, to the staffs of the Midwifery Department, the Aberdeen Maternity Hospital, the Royal Aberdeen Hospital for Sick Children, and to Miss G. Winship, of the Aberdeen Mother and Baby Home, for invaluable help; to Dr. I. Leitch, of the Commonwealth Bureau of Animal Nutrition, Bucksburn, for criticism and advice; and to Dr. F. H. C. Marriott for statistical assistance.

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V. INDIVIDUAL DIFFERENCES IN COMPOSITION OF MILK

When all the variations in milk composition which may be due to sampling methods have been eliminated so far as is possible by the taking of 24-hour samples under specified standard conditions (see Part III), the composition of the milk yielded by different individuals varies widely. The study of this variation has been confused in the past by the use of unreliable sampling methods or by the selection of such unrepresentative subjects as professional wet-nurses. There is still a widely held belief that the composition of human milk varies very little, and this point of view has been summed up by Bourne and Williams (1953) as follows: "Researches on the quality of milk, that is the percentages of the main constituents, show that there is not much variation, even under harsh nutritional or other conditions or when the quantity is seriously falling." In the lay mind, on the other hand, the quality of milk is often blamed for unsatisfactory breast-feeding; a plentiful milk supply with a baby losing weight seems to be a not uncommon clinical syndrome.

It has been shown in Part IV of this paper that by the seventh day the composition of milk is stable enough in the individual case to indicate the composition of the mature milk. Detailed studies of individual variations in the seventh-day milk are here discussed.

Methods

All the subjects were in the lying-in wards of the Aberdeen Maternity Hospital. It is necessary to limit studies of individual variation to milks obtained at one period of lactation in order to minimize differences of maturity. The seventh day of lactation was chosen for the reason indicated above and because there was a day or two in which to re-establish the infant at the breast after the 24-hour break, before the mother was discharged from hospital. In addition to these considerations, it is desirable to obtain milk as early as possible in lactation, because breast milk of low calorie value is likely to be replaced before long by artificial feeds, and then will not be available for analysis.

Analyses were carried out on seventh-day milk from 121 primiparae and 29 multiparae. For six of the latter, volume and fat content of the seventh-day milk were known for a previous lactation.

The methods of milk collection and chemical analysis have been detailed in Parts I and II of this paper. The calorie value was calculated by using the factors 9.0, 3.75, and 4.0 for fat, lactose, and protein respectively. (The absolute calorie equivalents for human milk are not known, but the above factors are likely to be accurate enough for present purposes.)

Results

The results of the analysis of 150 samples collected on the seventh day have already been given (Part IV, Table II). There was no statistically significant difference in average volume and composition between the 121 primiparae and 29 multiparae.

The fat content and volume of seventh-day samples of milk obtained from six subjects during their first lactation in 1949 and during a subsequent lactation in 1952 are shown in the accompanying Table. No consistent trend can be seen in the Table, but it is curious that in each subject the fat content is different in the two lactations. There is also some clinical evidence of gross differences between lactations of the same woman. Subject 161, for example, had fed her first baby for eight months with great ease (the milk was not analysed), but in the second lactation, although the milk yield was adequate, the baby lost weight and the fat content at seven weeks was found to be only 2.05 g. per 100 ml.

Fat Content and Volume of Milk During Two Lactations

Subject No.	Fat (g./100 ml.)		Volume (ml.)	
	1949	1952	1949	1952
52	2 40	1·70*	765	695*
65	3·60	4 50	880	990
66	2·50	2·75	158	220
70	3·30	2·00	910	710
122	2·75	3·40	1,100	930
227	2·50	2·75*	100	255*

* Third lactation; the remainder from 1952 are second lactations.

It is clear that more data will be needed to understand changes with parity; meanwhile analyses of individual differences will be restricted to the results from the 121 primiparae.

The mean values, together with their coefficients of variation (to illustrate the relative variability), are as follows:

		Coefficient of Variation
Volume	414 $\pm$172 ml.	41 5%
Fat	3 17 $\pm$ 0 78 g./100 ml.	24 6%
Lactose	6 29 $\pm$ 0 45 g./100 ml.	7·2%
Total nitrogen	296 $\pm$ 38 mg. 100 ml.	12 8%
Protein	1·44 $\pm$ 0·22 g./100 ml.	15·3%

The mean calorie value, which is very closely associated with the fat content ($r = +0.97$), was 578 ± 73 calories per litre.

The frequency distributions of values for volume and for fat, lactose, and total nitrogen contents are shown in Figs. 1, 2, 3, and 4. The curves for volume and fat are not significantly different from normal. The distribution of values for lactose is skewed to the left (there is an excess of low values) and significantly so ($P<0.05$), and the distribution of values for total nitrogen is obviously skewed to the right (an excess of high values), although the deviation from normal is not statistically significant. These deviations from a truly normal distribution suggest that there is a physiological upper limit to lactose content and a lower limit to protein content.

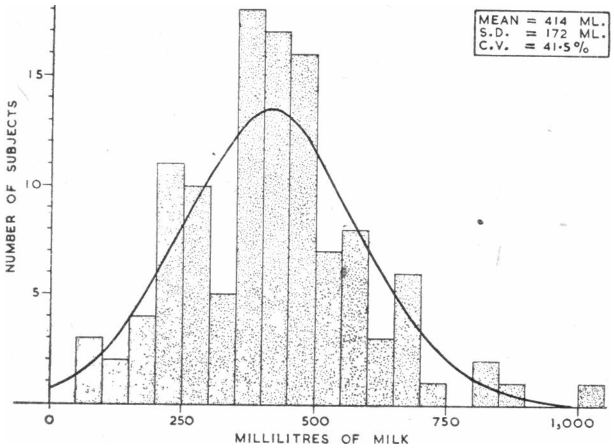

FIG. 1.—The frequency distribution of milk volume secreted on the seventh day. The normal curve is superimposed.

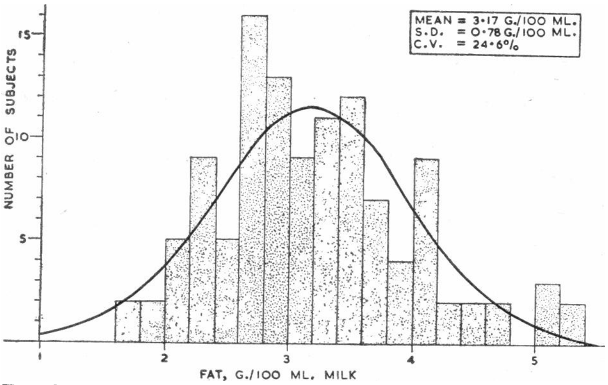

FIG. 2.—The frequency distribution of the fat content of milk secreted on the seventh day. The normal curve is superimposed.

Tests were applied to discover to what extent values for the several constituents were related to each other.* Briefly, it was found that the fat content of a given milk sample is virtually unpredictable without direct analysis. On the other hand, milk produced in large volume is likely to have a high lactose content and a low protein content, and vice versa.

Discussion

It has been pointed out in Part IV of this paper that, when samples from different individuals are considered, the values for the fat contents cover a wide range at all stages of lactation, but that the lactose and protein contents, although they may show a wide range in early milk, converge to within narrow limits as the milk matures. This is confirmed by the present study of the seventh-day milk: the fat content is clearly independent of volume and of lactose and protein, which are equally clearly closely concerned with each other. Simplified, the results indicate that if the volume of a sample is low then the lactose content is likely to be low and the protein content to be high; or that if one of these values is "immature," then the milk as a whole will be "immature." It therefore seems that the differences which are found in lactose and protein content on the seventh day of lactation are due to variation in the maturity of the milk. The skewness of the frequency distributions for the values of lactose and total nitrogen also lends support to this view, the longer tail of the graph comprising those milks which are maturing more slowly (and are therefore relatively immature at the seventh day), and the more abrupt drop at the other end indicating that a physiological norm is being approached.

Since the fat content of milk retains its wide range of values throughout lactation, it is reasonable to suppose that in mature milk there will be a distribution of fat similar to that shown in Fig. 2, shifted by perhaps 0.5 g. per 100 ml. to the right to accommodate the increase in concentration which occurs as the milk matures. On this basis there will be about 20% of women whose mature milk will have a fat content of 3 g. or less per 100 ml., and a calorie value of 570 calories or less per litre. Assuming that these women are capable of producing a litre of milk daily, which is a high yield (Morrison, 1952), and assuming that the calorie requirements of an infant are 115 calories per kg. body weight (Smith, 1951), then one-fifth of the lactating population will be incapable of adequately nourishing an infant beyond a weight of 11 lb. (5 kg.). The mother who explains her lactation failure by saying "my milk was too thin" may, in fact, be telling the truth.

The reason for these individual differences in fat content is at present obscure. That it should be a peculiarly human characteristic is understandable, since alternative methods of rearing an infant have probably always been available, either by wet-nursing or by artificial feeding, so that selective breeding for the ability to breast-feed, which has occurred in other mammals, has been avoided. However, although the level of fat production is an individual characteristic, it does not appear to be entirely genetically determined, since it is not always maintained in subsequent lactations.

In a later publication the relation of the fat content to a number of physical attributes of the mother, and also to some environmental factors, will be examined.

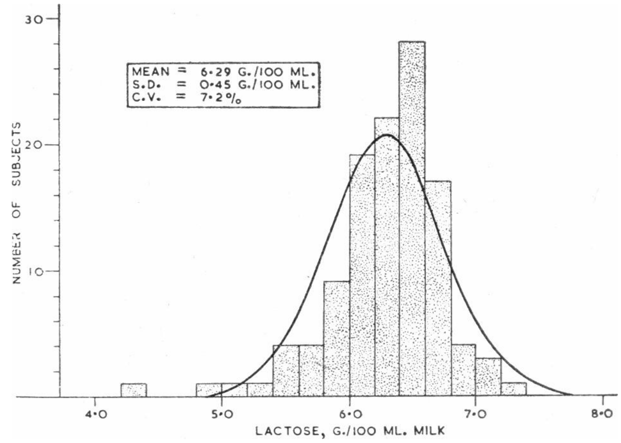

FIG. 3.—The frequency distribution of lactose content of seventh-day milk. The normal curve is superimposed.

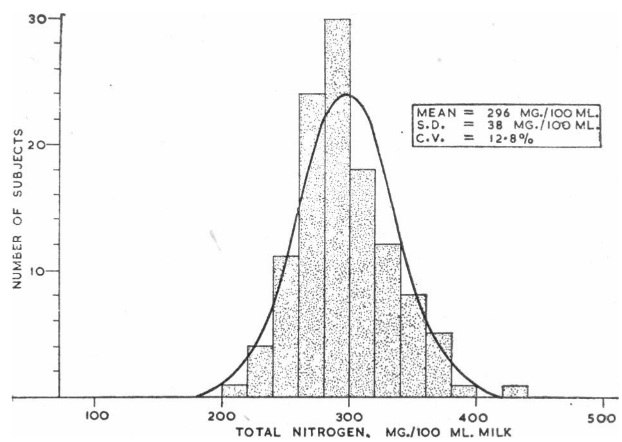

FIG. 4.—The frequency distribution of total nitrogen content in seventh-day milk. The normal curve is superimposed.

*The regression equations are:

(i) Fat = 1·90 (protein) + 0.0010 (volume)
± 0.33 ± 0.0004

(The effect of lactose was negligible). The standard deviation about the regression line was 0.70, compared with 0.78 for the standard deviation for fat content about its mean.

(ii) Lactose = −0.0062 (total N) + 0.00086 (volume) + 0.0014 (N.P.N.) + 6.80
± 0.0011 ± 0.00020 ± 0.0003

The standard deviation about the regression line was 0.34, compared with 0.45 for the standard deviation for lactose content about its mean.

Summary

The differences occurring in the composition of milk on the seventh day of lactation have been studied in 150 women, 121 of whom were primiparae.

There is no statistically significant difference between the milk of primiparae and multiparae in this series, but evidence is presented to show that the same individual, in two lactations, may produce milk differing greatly in fat content.

There is a wide range of values for all the major constituents as well as for the total yield at this stage of lactation. The variability of the lactose and protein seems to be due to differences in speed of maturation of the milk.

There is a wide range of fat content, and consequently of calorie value. The fat content is not apparently related to the content of other constituents, and seems to be an individual characteristic. In some milks the fat content is so low that, even with a high milk volume, the child may be undernourished.

I am grateful to Professor Dugald Baird and to the staffs of the Midwifery Department and the Aberdeen Maternity Hospital for invaluable help; to Dr. I. Leitch, of the Commonwealth Bureau of Animal Nutrition, Bucksburn, for criticism and advice; and to Dr. F. H. C. Marriott for statistical assistance.

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IODODERMA OF THE FACE AND MARKED EOSINOPHILIA

BY

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Iodine has a long-established place in the history of medicine. There are few drugs which have been used more freely in the treatment of coughs, syphilis, and thyrotoxicosis, apart from its popularity as a skin disinfectant. Relatively few cases of iodism have been reported despite the commonness of its use and importance in radiological contrast substances.

The present case draws attention once again to the dangers of iodine intoxication and demonstrates two features of some interest—an unusual skin lesion and a pronounced eosinophilia.

Case Report

A 60-year-old white man of French extraction, resident in British Columbia for over 30 years, was admitted to the Vancouver General Hospital on February 27, 1952. Asthma had troubled him at infrequent intervals for many years without producing any severe disability. During 1951 he had two major surgical procedures—a suture of a perforated gastric ulcer in April and a transurethral prostatectomy in November—and during this period his general health deteriorated and his asthma became increasingly severe.

In October, prior to his prostatectomy, he was submitted to intravenous pyelography, and developed a severe but temporary reaction to the iodine-containing contrast substance. In November, for a four-week period following his operation, he was given 5 gr. (0.32 g.) of potassium iodide three times a day in an attempt to avoid any fibrous contraction of the prostatic bed. During January, 1952, his asthma became more troublesome. Towards the end of the month he treated himself with proprietary asthma tablets, each containing about 1½ gr. (0.1 g.) of potassium iodide. He took an average of six tablets daily. A few days after beginning this treatment he noticed red vesicular raised spots appearing on his arms and trunk. He described them as being like "pimples from which no pus came." By the middle of February he had developed several spots on each malar region, and these gradually spread and coalesced to form fungating tumour-like masses. These lesions and his severe asthma caused his admission to hospital.

Physical examination on admission showed a firm raised reddish mass with an irregular surface over each malar region of the face; severe asthma with an emphysematous chest; hypertension (B.P. 190/108); and a few vesicular spots on the upper trunk and arms.

Laboratory studies on February 28 showed: Hb, 97%; W.B.C., 32,950 (P. 22%, staffs 1%, lymphs 6%, monos 4%, eosins 66%, basophils 1%); N.P.N., 38 mg. per 100 ml. Urinalysis: Sp. gr. 1022; protein +++; W.B.C. ++; R.B.C. ++; and an occasional hyaline cast seen.

During the week February 28 to March 6 the patient's condition steadily deteriorated and oxygen was given continuously. Treatment included adrenaline, aminophylline, penicillin, and potassium iodide—5 gr. (0.32 g.) three times a day. Bacteriological examination of the facial lesions on three occasions revealed the presence of only coagulase-negative *Staphylococcus albus*.

A sternal puncture and haemogram were performed on March 4, the findings being:—(1) Peripheral blood: Hb, 98% (14.2 g.); R.B.C., 5,300,000; platelets, 350,000; reticulocytes, 1%; haematocrit, 44%; W.B.C., 31,800 (neut. polys 16%, neut. staffs 2%, eos. polys 55%, eos. staffs 15%, lymphs 8%, monos 4%). (2) Bone marrow: On a 300-cell differential count 37.3% were lobed eosinophils, 11.3% staff eosinophils, 4.3% metamyelocyte eosinophils, 5% myelocyte eosinophils, and 0.6% promyelocyte eosinophils. The marrow was not as hypercellular as one would expect in a leukaemic condition, and in view of this, the absence of splenomegaly, and the excessive rarity of eosinophilic leukaemia it was felt that the latter was probably not the diagnosis.

On March 6 the patient was seen with a view to the possible administration of A.C.T.H. as a life-saving measure. His condition was critical. The striking lesions on the face had extended and the surface was now a blackish-red colour (Fig. 1). He was in an oxygen tent, his breathing was asthmatic and very laboured and noisy, and he was roused only with difficulty, his answers to questions being irrational. In addition to hypertension he had a marked tachycardia (pulse rate 160) with numerous extrasystoles. Examination of the upper trunk and arms revealed the presence of numerous rounded raised red papular spots of varying size, while similar spots were evident on the chin and ears.

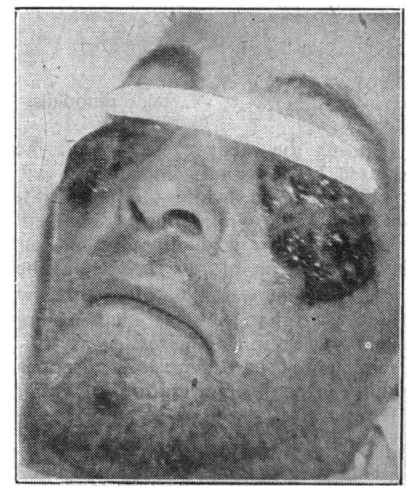

FIG. 1.—Photograph of patient showing facial lesions.

The patient was put at once on intravenous A.C.T.H., digitoxin, pethidine hydrochloride, and diphenhydramine hydrochloride, the pre-