THE GASTRIC SECRETION IN ANAEMIA

BY

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It is well known that anaemia of the Addisonian type is accompanied by an absence of free hydrochloric acid from the gastric juice.

In so-called secondary anaemia Davies¹ found that in the gastric juice there was excess of mucus, low peptic activity and frequently a fixed pH in contrast with the absence of mucus and peptic activity and complete fixation of the pH in pernicious anaemia. Hartfall and Witts² pointed out that in simple achlorhydric anaemia the total chlorine and peptic activity were low when there was a deficient amount of intrinsic factor. Recently Hartfall³ has stated that in the same individual free acid may be secreted at one time and not at another. He also considered that the data obtained from infants were unreliable owing to the numerous inhibitory factors likely to interfere with gastric secretion. In twenty-six adult patients with unexplained achlorhydria Pollard⁴ failed to find any significant variation from normal in the haemoglobin value and red cell count; he therefore concluded that anacidity per se did not tend to the production of anaemia. Bloomfield and Keefer⁵ as a result of their investigations into gastric secretion in adults decided that anaemia, other than the pernicious type, had little or no influence on the secretion of gastric juice. Hawksley, Lightwood and Bailey⁶ in thirteen children under ten years of age with simple iron-deficiency anaemia found achlorhydria in twelve, and consider that achlorhydria may be a causal factor. In the literature there are few other studies in children of the association of anaemia with defective gastric secretion.

During the course of an investigation into the gastric secretion in children, the following results were obtained. Thirty-four anaemic children, twenty-two boys and twelve girls, were examined; the ages varied between five months and eleven years. The method employed in examining the gastric secretion has been described in previous papers⁷. In children, as in adults, there is wide variation in the concentration of the hydrochloric acid in the gastric juice but for purposes of classification any readings of an acidity above 50 c.c. or below 12 c.c. $\frac{N}{100}$ per cent. were considered to indicate hyper- or hypochlorhydria respectively.

Results

Free hydrochloric acid.—The maximum free hydrochloric acid varied from nil to 55.6 c.c. $\frac{N}{100}$ per cent. with a mean value of 20.3 ± 2.9 , which is significantly (11.2 ± 3.3) lower than that obtained in a normal group. When the patients are considered in age groups it is clear

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that the greatest reduction in acid is present in the fourth or oldest group (nine to twelve years). In the third (six to nine years) the mean value is actually greater than in normal children of the same age. Six patients had achlorhydria at the first test, seven had hypochlorhydria and four hyperchlorhydria. None of the last group, however, showed a free hydrochloric acid content of over 57 c.c. $\frac{N}{10}$ per cent. In only seventeen was the free hydrochloric acid found to be within normal limits.

TABLE 1.
ACHLORHYDRIA.

Name	Age in years	Sex	Type of anaemia	Blood picture			Blood chlorine C.C. $\frac{N}{10}$	Gastric analysis (max. fig.)			
				R.B.C. mill-ions	Haemo-glob. percent.	C.I.		HCl. C.C. $\frac{N}{10}$	Total acidity C.C. $\frac{N}{10}$	Total Chlorine C.C. $\frac{N}{10}$	Peptic activity units
J.C. ...	1 $\frac{1}{2}$	M.	?Acholuric	2.2	35	.8	95.22	nil.	41.1	96.2	—
G.P. ...	2 $\frac{3}{4}$	M.	Nutritional	3.1	30	.5	—	nil.	20.5	97.5	62.5
								nil.	6.2	81.3	10.0
								*nil.	8.2	79.8	8.1
	2 $\frac{1}{2}$			3.9	40	.5	—	18.3	30.4	77.2	6.4
A.B. ...	2 $\frac{1}{2}$	M.	Nutritional	4.4	72	.8	70.68	nil.	42.0	69.5	1.6
A.McM.	2 $\frac{1}{2}$	F.	Haemolytic	2.1	15	.4	93.93	nil.	20.0	89.9	25.6
				3.9	42	.5	—	12.0	22.0	68.7	28.9
				4.6	78	.9	74.46	nil.	36.1	54.6	6.4
					75		—	nil.	29.6	83.1	10.0
								* nil.	24.5	69.2	14.4
J.T. ...	2 $\frac{1}{2}$	M.	Von Jaksch	3.8	45	.6	—	* nil.	21.1	67.6	40.0
								nil.	19.3	69.2	—
T.C. ...	6 $\frac{1}{2}$	M.	Nutritional (bowel deformity)	2.8	35	.6	84.80	nil.	23.3	66.3	—

* After histamine.

Of the six children with achlorhydria three had simple iron-deficiency anaemia, one acholuric jaundice, one haemolytic anaemia and one von Jaksch's anaemia. One of the children (T. C.) with iron-deficiency anaemia died a week after the test; at the post-mortem examination a mesenteric cyst and duplication of a portion of the ileum were found. Another (G. P.) at first gave no free hydrochloric acid response even after histamine but a month later a concentration of 18.3 c.c. $\frac{N}{10}$ free hydrochloric acid was found after the ordinary gruel test meal. The other patient (A. B.) made a good recovery with iron treatment. The child with von Jaksch's anaemia (J. T.) made a good recovery but owing to the fact that he was soon transferred to a convalescent home, only one test was made. The child with acholuric jaundice (J. C.) had a red cell count of 2,190,000 per c.mm., haemoglobin

33 per cent. and definitely increased fragility (occurring in 0.56 per cent. NaCl). Eventually he contracted pneumonia from which he died; only one test of the gastric secretion was carried out. The patient with haemolytic anaemia of unknown origin (A. McM.) had achlorhydria on the first test. After iron treatment for three weeks the gastric analysis showed a concentration of twelve c.c. $\frac{N}{10}$ free hydrochloric acid, but in four subsequent tests, two with histamine, it was impossible to detect free hydrochloric acid in the gastric juice in spite of treatment with iron, marmite and liver; the anaemic condition had meanwhile greatly improved the red cells having risen to five millions per c.mm. and the haemoglobin to 80 per cent.

TABLE 2.
HYPOCHLORHYDRIA.

Name	Age in years	Sex	Type of anaemia	Blood findings			Blood chlorine c.c. $\frac{N}{10}$	Gastric analysis (max. fig.)			
				R.B.C. millions	Haemo-glob. per cent.	C.I.		HCl. c.c. $\frac{N}{10}$	Total acidity c.c. $\frac{N}{10}$	Total chlorine c.c. $\frac{N}{10}$	Peptic activity units
J.K. ...	$\frac{8\frac{1}{2}}{1\frac{1}{2}}$	M.	Nutritional	5.9	50	.4	83.83	10.2	87.1	70.7	—
J.M. ...	$1\frac{2}{2}$	M.	Nutritional	4.5	58	.6	91.80	4.4	33.4	91.8	67.6
H.J. ...	$1\frac{0}{1\frac{1}{2}}$	F.	Haemolytic	4.3	70	.8	79.57	8.4	34.7	74.1	22.5
E.G. ...	$3\frac{4}{1\frac{1}{2}}$	F.	Nutritional	3.6	70	1.0	76.50	9.3	18.5	132.6	6.4
A.G. ...	$3\frac{7}{1\frac{1}{2}}$	M.	Aplastic	3.7	62	.9	—	8.5	26.8	60.1	—
A.C. ...	9	M.	Nutritional	3.9	42	.5	89.38	$\begin{cases} 5.6 \\ 3.9* \end{cases}$	$\begin{cases} 16.7 \\ 18.5 \end{cases}$	$\begin{cases} 53.4 \\ 71.9 \end{cases}$	$\begin{cases} 0.9 \\ 2.5 \end{cases}$
H.McK.	$9\frac{3}{1\frac{1}{2}}$	M.	Nutritional	4.9	60	.6	80.32	11.6	25.2	68.5	—

* After histamine.

TABLE 3.
HYPERCHLORHYDRIA.

Name	Age in years	Sex	Type of anaemia	Blood findings			Blood chlorine c.c. $\frac{N}{10}$	Gastric analysis (max. fig.)			
				R.B.C. millions	Haemo-glob. per cent.	C.I.		HCl. c.c. $\frac{N}{10}$	Total Acidity c.c. $\frac{N}{10}$	Total Chlorine c.c. $\frac{N}{10}$	Peptic activity units
D.K. ..	$1\frac{8}{1\frac{1}{2}}$	M.	Nutritional	4.4	40	.5	—	51.2	80.1	113.2	28.9
J.McN.	$2\frac{0}{1\frac{1}{2}}$	M.	Haemolytic	4.1	55	.7	—	54.5	75.6	95.4	108.9
G.M. ...	8	F.	Aplastic-haemolytic	0.6	15	1.2	96.96	50.0	66.7	76.8	19.6
R.B. ...	$10\frac{6}{1\frac{1}{2}}$	F.	Acholuric jaundice	$\begin{matrix} 2.7 \\ 3.7 \end{matrix}$	$\begin{matrix} 58 \\ 68 \end{matrix}$	$\begin{matrix} 1.1 \\ .9 \end{matrix}$	$\begin{matrix} 84.94 \\ — \end{matrix}$	$\begin{matrix} 55.6 \\ 56.7 \end{matrix}$	$\begin{matrix} 72.3 \\ 64.5 \end{matrix}$	$\begin{matrix} 111.1 \\ 99.8 \end{matrix}$	$\begin{matrix} 52.9 \\ 19.6 \end{matrix}$

There were seven patients with hypochlorhydria; five of them had simple iron-deficiency anaemia, one haemolytic and one aplastic anaemia.

In four hyperchlorhydria was found. In one of them (G. M.) there was evidence of extreme haemolytic anaemia with a red cell count of 630,000 and a haemoglobin concentration of 15 per cent. In another (R. B.) with acholuric jaundice it was found that three weeks after splenectomy there was no change in the hyperchlorhydria although there was great improvement both in the general condition and the condition of the blood. A third (D. K.)

TABLE 4.
NORMAL ACID SECRETION.

Name	Age in years	Sex	Type of anaemia	Blood findings			Blood Chlorine c.c. $\frac{N}{10}$	Gastric analysis (max. fig.)			
				R.B.C. millions	Haemo- glob. per cent.	C.I.		HCl. c.c. $\frac{N}{10}$	Total acidity c.c. $\frac{N}{10}$	Total Chlorine c.c. $\frac{N}{10}$	Peptic activity units
T. McF.	$\frac{5}{12}$	M.	Nutritional	3.3	40	.6	92.82	20.5	30.7	93.8	—
A. M. ...	$\frac{5}{12}$	M.	von Jaksch	4.2	44	.6	82.23	17.5	61.4	69.9	—
R. McR.	$\frac{8}{12}$	M.	Nutritional	4.5	46	.5	79.80	15.0	42.5	73.5	102.4
J. McI.	$\frac{10}{12}$	M.	Nutritional	3.8	24	.3	—	15.2	27.9	69.4	25.6
E. B. ...	$1\frac{1}{2}$	F.	Nutritional	5.0	62	.6	—	20.0	50.0	66.1	40.0
A. McC.	$1\frac{1}{2}$	M.	Nutritional	4.7	46	.5	82.82	18.0	45.0	73.7	176.4
C. McK.	$1\frac{1}{2}$	F.	von Jaksch	4.1	45	.9	80.01	22.4	32.0	57.7	—
G. C. ...	$1\frac{9}{12}$	M.	Nutritional	3.5	44	.6	—	30.0	44.0	81.8	22.5
J. McK.	2	M.	Nutritional	3.7	25	.3	79.68	12.7	28.6	74.9	—
H. C. ...	$3\frac{6}{12}$	M.	Nutritional	3.0	52	.9	75.14	18.1	59.3	76.0	—
D. McM.	4	F.	Nutritional	3.8	82	1.1	72.80	43.3	57.5	81.2	16.9
M. A. ...	6	F.	von Jak-sch	3.5	50	.7	81.16	38.4	51.2	—	152.1
M. V. ...	$7\frac{6}{12}$	F.	Haemolytic	2.4	50	1.1	99.45	37.1	50.7	90.3	78.4
W. W.	$8\frac{6}{12}$	F.	Haemolytic	1.7	32	.9	96.18	39.4	56.8	95.1	96.1
J. H. ...	10	M.	Aplastic ...	1.1	17	.8	—	24.2	32.3	53.9	—
J. J. ...	10	M.	Nutritional	4.9	52	.5	74.10	33.2	39.8	55.8	—
A. B. ...	11	F.	Nutritional	1.6	25	.8	90.90	15.4	33.3	88.9	—

had simple iron-deficiency anaemia dating from early infancy and probably associated with prematurity. The fourth (J. McN.) had mild jaundice with urobilinuria, a red cell count of 4,000,000 per c.mm. and a haemoglobin content of 50 per cent.

Of the seventeen patients whose gastric secretion fell within normal limits the anaemia in nine was of the simple nutritional type; in three it was considered to be of the von Jaksch type, in two haemolytic, in one aplastic

and in two it was impossible to relegate the condition into any special category. In one of the unclassified group (G. C.) there was great enlargement of the liver and a red cell count of 3,500,000 and haemoglobin 44 per cent. In the other (D. McM.) the red cells numbered 3,800,000 and haemoglobin was 82 per cent. Of the children with normal secretion two died. One of them (J. H.) had an aplastic anaemia (red cells 1,000,000 and haemoglobin 12 per cent.) which did not respond to repeated blood transfusion. The other (W. W.) had a greatly enlarged liver possibly due to a neoplasm, deep jaundice, bile and urobilin in the urine, a biphasic van den Bergh reaction in the serum and a profound anaemia of the hyperchromic, macrocytic type; this case has been classified under the haemolytic group.

From these results it does not appear that there is any relationship between the amount of free hydrochloric acid in the gastric secretion and the degree of anaemia (red cell count and haemoglobin) nor do any of the types studied show any constant change in the secretion of free acid (table 5).

TABLE 5.
SHOWING THE RELATIONSHIP OF THE TYPE OF ANAEMIA TO THE FREE
HYDROCHLORIC ACID SECRETION

	Iron deficiency	Achloruric	Von Jaksch	Haemo- lytic	Aplastic	Unclassi- fied
Achlorhydria ...	3	1	1	1	—	—
Hypochlorhydria ...	5	—	—	1	1	—
Normal secretion ...	9	—	3	2	1	2
Hyperchlorhydria ...	1	1	—	2	—	—

Total acidity.—The maximum figures varied between 16.7 to 87.1 c.c. $\frac{N}{100}$ per cent. with a mean value of 42.5 ± 3.3 which was significantly lower by 7.6 ± 2.0 than the mean of the normal group.

Total chlorine.—The maximum value for the total chlorine of the gastric secretion varied between 53.0 to 132.6 c.c. $\frac{N}{100}$ per cent. with a mean value of 79.6 ± 3.0 which was similar to that found in healthy children. The mean value for blood chlorine, however, was significantly higher by 9.29 ± 5.5 than that of the healthy group and varied inversely with the red cell count. The high mean value of blood chlorine is presumably due to the relative increase in plasma volume. It is possible, therefore, that the apparently normal values found for the total chlorine of the gastric secretion were not really the result of normal secretion but were due to the increased amount of chlorine in the blood passing through the gastric mucosa. If this is not the case one must assume that in the present series only the secretion of free hydrochloric acid was affected. This latter view is supported by the fact that the mean value for peptic activity did not differ significantly from normal. In pernicious anaemia, on the other hand, where the peptic activity is markedly deficient, Miller and Smith⁸ and Wilkinson⁹ found that the

concentration of total chlorides in the gastric secretion was below the average obtained in individuals with normal secretions.

Emptying time.—The average emptying time was longer than in the control group. In fourteen patients starch could still be detected in the gastric contents at two hours.

The relationship of the type of anaemia to the free hydrochloric acid secretion

It is recognized that the concentration of free hydrochloric acid in the gastric juice has a direct relationship to the capacity for absorbing iron. For this reason it might be anticipated that diminution or absence of free hydrochloric acid would be found in cases of simple anaemia where low haemoglobin percentage was the prominent feature. This has been found in the present series.

Of the thirteen cases in which there was defective secretion of hydrochloric acid (achlorhydria or hypochlorhydria) eleven had hypochromic anaemia as measured by a colour index which did not exceed 0.8. This suggests that hydrochloric acid deficiency strongly favours the production of hypochromic anaemia but that other causes, for example iron starvation, must play a part because ten out of eighteen cases of iron deficiency anaemia showed no diminution in hydrochloric acid secretion (table 5).

Summary

The results of fractional gastric analysis in a series of thirty-four children with anaemia show that there is in many cases a marked diminution in the secretion of free hydrochloric acid and in total acidity. The other constituents of the gastric juice do not differ significantly from those of a normal series.

No correlation was noted between either the number of red cells or the haemoglobin and the maximum secretion of free acid.

There seems to be a close association between defective secretion of hydrochloric acid and the hypochromic type of anaemia.

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