OBSERVATIONS IN CLINICAL PATHOLOGY MADE IN A SERIES OF SEVENTY FIVE CASES OF GASTRIC EROSION.

Thesis for the Degree of M.D.

By

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Observations in Clinical Pathology made in a series of Cases of Gastric Erosion.

In order to select a group of cases for observation two leading symptoms were taken:-

1. Epigastralgia at a definite interval after food.
2. The presence of blood in the vomit or faeces, or in both.

In the following cases giving a history of gastric disturbance these two symptoms were definitely present and were used to pick out the individuals from the mass of gastric cases, and to decide their being made the subject of these observations.

By epigastralgia is meant a definite pain which may be crampy, boring, cutting or burning in character. It occurs from within half an hour to four hours after a meal. It is situated in the Epigastrium, beginning anteriorly, and may radiate along the sternum or around the sides of the body reaching as high as the shoulder and as low as the sacrum. This symptom is stated by Cohnheim to be the most positive symptom of Gastric Ulcer.(1)

By blood in the gastric contents or faeces is meant the presence of blood in macroscopic quantity or in quantities determinable by chemical and spectroscopic tests.(2) In the cases observed other causes than gastric/

gastric erosion were, so far as could be determined, eliminated. The following possibilities were considered and excluded:-

1. Traumatism of stomach and intestines.
2. Carcinoma of Oesophagus, Stomach and Intestines.
3. Venous congestion and ecchymosis in cardiac disease and cirrhosis of the liver.
4. Haemophilia, Purpura, Leukaemia, Pernicious Anaemia and Splenic Anaemia.
5. Ulcerative Endocarditis, Tubercle, Typhoid, Dysentery, Colitis, Pyaemia and Septicaemia.
6. Carbonic Monoxide poisoning, Phosphorus, Corrosive poisons and Ptomaine poisoning.
7. Bleeding from fauces, pharynx, nares, larynx, bronchi and piles.
8. Contamination from menses, and vicarious menstruation from gastro intestinal canal.
9. Mucous ecchymosis and haemorrhage of general paralysis and general arteric sclerosis.
10. The recent ingestion of undercooked meat, no meat was allowed for three days before testing for occult blood, and enemata were given during this period.

These possibilities having been eliminated, whatever haemorrhage was present was limited to a gastric or duodenal source on consideration of the history and the absence of other causes. The types of/

of haemorrhage determined clinically we would now define in the following three groups.

By Hematemesis is denoted the presence of blood in the vomit in such quantity as can be detected easily from inspection and confirmed by the guaiac reaction.

By Melaena is meant the visible presence of blood in the stool confirmed by the guaiac reaction.

By Occult Blood is meant blood determined by one of the following tests:-

1. The Use of a Thorp's D. V. Diffraction Reading Spectroscope manufactured by Beck.(3) Five cubic centimetres of the stool are mixed with fifty centimetres of distilled water, a few drops of sulphuric acid are added, until the mixture turns Congo Red an intense Blue, the whole is well shaken and filtered. The filtrate is then extracted with ether. Where blood is present the ether is turned a reddish brown and gives the bands of Acid Haematin in the spectrum.

2. The Benzidin Test of Schlesinger and Holt.(4)

   A. A knife point of pure Benzidin is dissolved in three cubic centimetres of Glacial Acetic Acid.

   B. One cubic centimetre of this solution is added to two cubic centimetres of Hydrogen Peroxide Solution.

   C. A cubic centimetre of the faeces is well mixed with/

with ten cubic centimetres of distilled water and boiled in a test tube.

D. A few drops of this solution C. is added to the solution B. Where blood is present a greenish blue colour appears in a few minutes.

The following table gives a list of the 75 cases examined and states:-

1. Sex and age.
2. The total duration of gastric symptoms previous to examination.
3. The period after food at which the pain began.
4. The clinical type of Haemorrhage found as defined above.

TABLE I.

No.	Name.	Age.	Duration of gastric symptoms.	Time of onset of pain after food.	Type of Haemorrhage.
1.	Lizzie W.	22	1 Month.	Half hour.	Occult.
2.	Emily R.	40	4 years	One hour	Melaena.
3.	Harriet W.	24	1 year	Half hour	Occult.
4.	Annie V.	22	3 years	Half hour	Hematemesis & Melaena.
5.	Isabel W.	28	7 years	Half hour	Occult.
6.	Ethel H.	20	2 years	Half hour	Haematemesis & occult.
7.	Carrie J.	30	7 years	One hour	Occult.
8.	Charles S.	50	1 year	One hour	Occult.
9.	Florence S.	27	4 years	Half hour	Haematemesis & Melaena.
10.	William W.	48	13 years	Half hour	Haematemesis & Melaena.
11.	Arthur W.	43	2 months	Three hours	Haematemesis & Melaena.
12.	Henry H.	40	1 year	Half hour	Occult.
13.	Gertrude J.	17	2 years	Half hour	Occult.
14.	John S.	54	5 months	One hour	Occult.
15.	Amelia B.	31	1 year	Half hour	Occult.
16.	Elizabeth G.	32	6 months	1½ hours	Haematemesis & Melaena.
17.	Mary C.	34	3 years	¾ hour	Occult.
18.	John F.	26	4 years	Two hours	Occult.
19.	Alfred P.	21	3 days	Half hour	Occult.
20.	Gertrude S.	19	2 years	Half hour	Haematemesis & Occult.
21.	Thomas W.	38	2 weeks	Half hour	Haematemesis & Occult.
22.	Emily S.	45	30 years	Three hours	Occult in vomit & stool.
23.	Florence P.	32	7 years	Half hour	Occult.
24.	Florence D.	26	7 months	Half hour	Occult.
25.	Nell D.	29	6 months	Half hour	Haematemesis & Melaena.
26.	Emily H.	29	15 months	Three hours	Haematemesis & Occult.
27.	Anneta S.	29	8 months	Two hours	Haematemesis & Melaena.
28.	Oliver O.	71	1 year	Half hour	Occult.
29.	Nellie P.	24	5 years	Half hour	Occult.
30.	Charles P.	36	3 days	Half hour	Occult.
31.	Florence N.	24	1 year	Half hour	Haematemesis & Occult.
32.	Sarah S.	56	5 years	Half hour	Melaena.
33.	Nellie B.	19	6 years	Half hour.	Occult.
34.	Emma T.	45	6 years	Half hour	Haematemesis & Melaena.
35.	Ada C.	21	1½ years	Half hour	Occult.
36.	Elizabeth H.	34	3 years	One hour	Haematemesis & Melaena.
37.	Ada W.	25	15 years	Half hour	Haematemesis & Occult.
38.	Clara L.	29	5 years	Half hour	Haematemesis & Melaena.
39.	Rose H.	15	2 years	Half hour	Haematemesis & Melaena.
40.	Richard C.	21	1 month	¾ hour	Occult.
41.	Mary O.	40	1½ years	Two hours	Occult.
42.	Polly B.	24	5 months	Half hour	Occult.
43.	Clara B.	18	1½ years	Half hour	Occult.
44.	Arthur P.	32	1 year	Half hour	Occult.
45.	Mary D.	30	15 years	Half hour	Occult.
46.	Mary C.	39	10 years	Half hour	Haematemesis & Melaena.
47.	Alfred H.	30	5 years	Three hours	Haematemesis & Melaena.
48.	Maud P.	26	11 years	One hour	Haematemesis & Melaena.
49.					

49.	Thomas C.	34	10 months	Three hours.	Occult.
50.	Alice T.	26	2 years	Half hour	Haematemesis Melaena.
51.	Rebecca L.	48	26 years	Half hour	Haematemesis Melaena.
52.	Edith B.	15	1 year	Half hour	Haematemesis Melaena.
53.	Joseph H.	45	10 years	Three hours	Haematemesis Melaena.
54.	Hannah R.	43	2 years	Half hour	Haematemesis Melaena.
55.	Martha H.	24	9 months	Half hour	Haematemesis Melaena.
56.	Elizabeth H.	27	10 years	Half hour	Haematemesis Melaena.
57.	Florrie W.	26	5 years	Half hour	Occult.
58.	William A.	34	2 years	One hour	Occult.
59.	Joseph B.	47	2 months	Half hour	Haematemesis & Melaena.
60.	Mary P..	17	5 years	Half hour	Melaena.
61.	Hilda K.	17	1½ years	Half hour	Haematemesis & Melaena.
62.	Annie H.	26	7 years	Half hour	Haematemesis & Melaena.
63.	Violet W.	21	5 years	Half hour	Occult.
64.	Nellie E.	30	5 years	Half hour	Occult.
65.	Henry C.	34	6 months	Half hour	Occult.
66.	Richmond O..	33	7 years	One hour	Occult.
67.	Catherine B.	16	6 months	Half hour	Haematemesis & Occult.
68.	Frances C.	28	8 years	Half hour	Haematemesis & Melaena.
69.	Clara G.	21	1 year	Half hour	Occult.
70.	Gertrude M.	31	9 years	Half hour	Occult.
71.	Florence D.	24	5 years	Two hours	Melaena.
72.	Arthur L.	23	2 years	Two hours	Haematemesis & Melaena.
73.	Annie J.	21	6 years	Half hour	Haematemesis & Melaena.
74.	Emily L.	35	14 years	Half hour	Occult.
75.	Laura P.	27	2 years	Half hour	Haematemesis & Occult.

On analysing this table we obtain the following results:-

Sex distribution

Male	20	Cases
Female	55	"
	75	

Age distribution

Under 20 years	9	Cases
20 to 30 years	32	"
30 to 40 "	19	"
40 to 50 "	11	"
50 to 60 "	3	"
over 70 "	1	"
Total	75	"

Total Duration of Gastric Symptoms when examined:-

Under	1 week	2 cases
"	2 "	1 "
About	6 months	10 "
"	1 year	13 "
"	2 "	14 "
"	3 "	3 "
"	4 "	3 "
"	5 "	9 "
"	6 "	3 "
"	7 "	5 "
"	8 "	1 "
"	9 "	1 "
"	10 "	3 "
"	11 "	1 "
"	13 "	1 "
"	14 "	1 "
"	15 "	2 "
"	26 "	1 "
"	30 "	1 "
	Total	75.

From this we find 73.3 of the cases were females; the most frequent age to lie between 20 and 30; and the most common duration of symptoms to be from 1 to 2 years.

In all but three cases the duration of symptoms was at least 6 months and chronicity is the most striking feature of this group of morbid symptoms, with periods of increase and decrease of severity.

Period of onset of Pain after Food:-

Half	hour	53 cases
1	"	10 "
2	"	6 "
3	"	6
	Total	75.

Types/

Types of Haemorrhage:-

Occult Blood in Faeces	35	cases.
Haematemesis & Melaena	28	"
Haematemesis & Occult in Faeces	7	"
Melaena alone	4	"
Occult in Vomit & Melaena	1	"
Total	75.	

This last table emphasises the importance of testing for occult blood in this type of gastric case. No less than 35 out of 75 cases gave this test as the sole sign of haemorrhage or 46.6 per cent of all the cases.

The first observation made in each case was an examination of the blood as to the number of red and white corpuscles, the percentage of Haemoglobin, and the leucocytosis caused by digestion. The complete blood count was estimated half an hour before the patient's breakfast. The leucocytes were again estimated one and a half hours after that meal in all cases.

In order to have a uniformity of time relative to the symptoms the count was delayed in cases of severe hematemesis until the bleeding had apparently ceased. Then on the first day of the treatment which was in these cases by a modified Lenhartz diet given by the mouth, the digestion leucocytosis was estimated one and a half hours after the morning feed. In the other cases the observation was made on the first day after admission.

The/

The red cells per cubic millimetre were shown to vary from 5,400,000 as a maximum to 770,000 as a minimum. The latter case was one of exceptionally severe haemorrhage, the former case showed occult blood in the stool.

The Haemoglobin percentage varied from 97 to 10.

The Colour Index varied from 1.25 to .34.

The Leucocytes varied from a maximum of 17000 to a minimum of 3000.

In Digestion Leucocytosis the greatest increase was 7100 cells, the minimum 300.

The following table gives the actual result in each case. To ensure accuracy each result is the mean of three calculations, a fresh drop being put on the counting slide each time. The haemoglobin was calculated with Haldane's Haemoglobinometer.. The conclusion from these estimations agrees with that of (5) Cabot, Futcher, Da Costa, Greenough and Joslin. The Red Corpuscles are usually diminished in number. In several of the cases where repeated haemorrhage occurred the number of red corpuscles resembled the last stage of a pernicious anaemia. The Haemoglobin was in all cases decreased and the Colour Index resembled that of Chlorosis.

The digestion leucocytosis was unaffected (6) and by/

by careful examination three cases investigated, which gave no leucocytosis after digestion were proved to be carcinoma and were eliminated from this series, the diagnosis of cancer being confirmed by operation.

The amount of anaemia did not coincide with the amount of haemorrhage in these cases, as is shown on comparing tables I & II. Besides the actual loss of red corpuscles from haemorrhage, there is a loss from the action of a haemolytic factor due to the disease.

To further illustrate this last deduction the resistance of the red corpuscles to haemolysis by a standard solution of Saponin, after the method of McNeill, was determined in the last 30 cases of the series.(7) The discussion of these results will be returned to later.

Table of Blood Examinations. II.

No.	Reds.	Hb.	Colour Index.	Whites		Digestion Leucocytosis	
1.	5,400,000	45	0.41	8,000	10,200	Increase =	2,200.
2.	4,960,000	83	0.84	7,800	12,500	"	4,700.
3.	3,480,000	42	0.61	7,500	11,300	"	3,800.
4.	3,200,000	25	0.39	8,000	10,000	"	2,000.
5.	3,790,000	62	0.86	6,500	8,100	"	1,600.
6.	3,920,000	40	0.51	6,000	10,500	"	4,500.
7.	5,900,000	36	0.34	3,000	8,400	"	5,400.
8.	5,024,000	83	0.83	10,500	13,600	"	3,100.
9.	2,800,000	25	0.44	7400	10,600	"	3,200.
10.	2,750,000	33	0.61	9000	11,600	"	2,600.
11.	2,030,000	34	0.85	8600	10,400	"	1,800.
12.	5,130,000	66	0.64	4500	10,700	"	6,140.
13.	3,200,000	45	0.70	5800	6,200	"	400.
14.	4,350,000	56	0.64	8300	12,700	"	4,400.
15.	4,070,000	46	0.57	6400	11,300	"	4,900.
16.	3,200,000	23	0.36	6700	9,300	"	2,600.
17.	4,730,000	69	0.73	9000	11,500	"	2,500.
18.	4,380,000	78	0.90	8200	12,500	"	4,300.
19.	5,134,000	73	0.71	6800	9,400	"	2,600.
20.	4,300,000	58	0.67	7000	9,500	"	2,500.
21.	4,380,000	62	0.72	8700	9,900	"	1,200.
22.	4,570,000	83	0.92	7600	11,800	"	4,200.
23.	5,370,000	82	0.77	8600	10,400	"	1,800.
24.	4,870,000	65	0.66	7500	12,700	"	5,200.
25.	770,000	10	0.71	6000	6,500	"	500.
26.	4,760,000	78	0.82	9300	12,200	"	2,900.
27.	3,850,000	42	0.55	7000	9,100	"	2,100.
28.	2,700,000	34	0.63	8000	12,400	"	4,400.
29.	3,880,000	30	0.38	7300	10,500	"	3,200.
30.	5,300,000	64	0.63	9400	12,700	"	3,300.
31.	4,530,000	78	0.87	8600	9,400	"	800.
32.	3,840,000	45	0.59	5600	9.300	"	3,700.
33.	4,730,000	60	0.63	7000	9,800	"	2,800.
34.	3,611,000	32	0.44	5300	7,600	"	2,300.
35.	4,630,000	79	0.85	8800	13,600	"	4,800.
36.	3,860,000	51	0.67	13,400	15,700	"	2,300.
37.	3,970,000	41	0.52	12,500	12,800	"	300.
38.	538,000	62	0.56	9550	11,600	"	2150.
39.	4,720,000	60	0.63	9500	13,800	"	4300.
40.	5,630,000	77	0.68	11,400	13,300	"	1900.
41.	4,760,000	53	0.56	13,900	15,300	"	1400.
42.	4,000,000	40	0.50	3050	8400	"	5350.
43.	4,900,000	55	0.56	6700	13,800	"	7100.
44.	4,600,000	79	0.85	8600	11,000	"	1400.
45.	2,840,000	27	0.48	11,400	13,300	"	1900.
46.	1,500,000	19	0.63	4500	6100	"	1600.
47.	2,630,000	27	0.51	12,000	13,600	"	1600.
48./							

No.	Reds.	Hb.	Colour Index.	Whites.	Digestion Leucocytosis.		
48.	3,750,000	40	0.62	5800	7300	Increase =	1500.
49.	3,980,000	62	0.79	11,500	13,000	"	1500.
50.	1,450,000	15	0.53	3400	5100	"	1700.
51.	2,300,000	31	0.67	16,000	18,700	"	2700.
52.	3,500,000	32	0.45	4600	5300	"	700.
53.	1,683,000	40	1.25	12,300	15,800	"	3500.
54.	2,500,000	36	0.72	17,300	19,100	"	1800.
55.	1,762,000	19	0.55	5800	7300	"	1500.
56.	2,400,000	25	0.52	14,700	15,300	"	600.
57.	4,800,000	51	0.53	12,000	15,700	"	3700.
58.	2,800,000	60	1.07	8000	8300	"	300.
59.	5,143,000	64	0.63	4700	9800	"	5100.
60.	4,210,000	35	0.42	8700	12,300	"	600.
61.	2,318,000	32	0.69	6500	8400	"	1900.
62.	1,270,000	14	0.58	3300	5800	"	2500.
63.	5,040,000	47	0.47	6300	9100	"	2800.
64.	4,300,000	47	0.55	7300	9600	"	2300.
65.	5,560,000	85	0.77	9300	13,100	"	3800.
66.	4,730,000	65	0.69	5700	7600	"	1900.
67.	5,001,000	97	0.97	8800	11,700	"	2900.
68.	3,076,000	35	0.58	9400	11,000	"	1600.
69.	3,460,000	31	0.48	8000	10,300	"	2300.
70.	2,050,000	31	0.77	11,300	12,000	"	700.
71.	4,400,000	58	0.65	9000	11,500	"	2500.
72.	1,875,000	21	0.58	4300	5000	"	700.
73.	3,086,000	39	0.65	4500	7500	"	3000.
74.	5,180,000	73	0.71	7600	10,800	"	3200.
75.	4,600,000	52	0.56	6900	9400	"	2500.

Resistance to Haemolysis of the Red Corpuscles.

In applying this method about 100 c.m. of the patient's blood was received into 5 c.c. of normal saline solution containing a $\frac{1}{5}$ per cent of sodium citrate to prevent coagulation. The tube is gently mixed and then centrifuged; after pipetting off the supernatant fluid the corpuscles are again washed in normal saline, this time omitting the sodium citrate. After the second centrifuging and removal of the clear fluid the number of red corpuscles in the deposit per c.m. is determined by a Thoma Zeiss Haemocytometer. From this a standard suspension of 100 million red cells per cubic centimetre is obtained by dilution with normal saline.

A standard solution of Saponin, Merck extra pure, of a strength 0.004 grms. per 100 c.c. is made. By taking a measured amount of this solution and adding it to a cubic centimetre of suspended corpuscles in a small test tube and incubating at 37° centigrade, Haemolysis is brought about. By determining in the Thoma Zeiss slide at half hourly intervals the number of corpuscles unaffected and subtracting this number from the original number, the number of corpuscles acted upon is arrived at.

In order to show whatever change might exist in these/

these cases under investigation the test was carried out with the small amount of 0.06 c.c. of the standard Saponin solution. In McNeill's work this amount of Saponin produced in apparently healthy people a percentage of haemolysis varying from 7 to 23%, as calculated from the result in fifteen cases.

In this series of cases the last thirty alone were tested for resistance to haemolysis. The results were obtained in the manner described, viz:-

I. A standard suspension of 100 million red cells to the cubic centimetre of normal saline.

II. A standard solution of 0.004 grms. of pure Saponin to the 100 c.c.

III. An amount of 0.06 c.c. of Saponin solution was added to the cubic centimetre of suspended corpuscles.

IV. The result was taken after two hours incubation at 37° centigrade; by counting the number of red cells unaffected and calculating from this and the known value of the suspension, the percentage of corpuscles in which Haemolysis had taken place is arrived at.

Ten normal cases were taken as controls. The following table gives the result of their blood counts and the percentage of Haemolysis in two hours by the above method.

Case.	Reds.	Whites.	Hb.	Col.Ind.	Percentage Haemolysis.
Author	5,544,000	7,866	98	0.88	15%.
H. Surgeon.	5,300,000	6,950	102	0.96	9%.
2nd H.S.	5,485,000	8,400	100	0.92	12%.
A. H. S.	4,876,000	7,640	99	1.03	23%.
2nd A.H.S.	4,772,000	8,960	99	1.05	17%.
A. H. P.	5,384,000	9,480	106	1.00	14%.
Dresser	4,886,000	8,740	99	1.03	11%.
Dresser	4,730,000	7,790	100	1.06	25%.
Dresser	5,658,000	9,160	108	0.96	10%.
Porter.	5,849,000	8,750	102	0.88	19%.

Normal average Haemolysis from ten healthy individuals is thus equal to 15.5%.

The following table gives the results in thirty of the gastric cases under observation, viz. cases 46 to 75 inclusive. The observations on the cases 1 to 45 were begun before this method of estimating Haemolysis was decided upon and so did not come within this portion of the investigation.

Percentage Haemolysis in Cases 46 to 75 inclusive. Table IV.

Case.	Reds.	Haemoglobin.	Col.Ind.	Whites.	Percentage Haemolysis
46.	1,500,000	19	0.63	4500	71%.
47	2,630,000	27	0.51	12,000	63%.
48	3,750,000	40	0.62	5800	50%.
49	3,980,000	62	0.79	11,500	51%.
50	1,450,000	15	0.53	3400	78%.
51	2,300,000	31	0.67	16,000	49%.
52	3,500,000	32	0.45	4600	67%.
53	1,683,000	40	1.25	12,300	64%.
54	2,500,000	36	0.72	17,300	53%.
55	1,762,000	19	0.55	5800	61%.
56"	2,400,000	25	0.52	14,700	55%.
57.	4,800,000	51	0.53	12,000	45%.
58.	2,800,000	60	1.07	8000	62%.
59.	5,143,000	64	0.63	4700	39%.
60.	4,210,000	35	0.42	8700	47%.
61.	2,318,000	32	0.69	6500	59%.
62.	1,270,000	14	0.58	3300	78%.
63.	5,040,000	47	0.47	6300	42%.
64.	4,300,000	47	0.55	7300	54%.
65.	5,560,000	85	0.77	9300	36%.
66.	4,730,000	65	0.69	5700	41%.
67.	5,001,000	97	0.97	8800	29%.
68.	3,076,000	35	0.58	9400	55%.
69.	3,460,000	31	0.48	8000	49%.
70.	2,050,000	31	0.77	11,300	85%.
71.	4,400,000	58	0.65	9000	48%.
72.	1,870,000	21	0.58	4300	92%.
73.	3,086,000	39	0.65	4500	63%.
74.	5,180,000	73	0.71	7600	34%.
75.	4,600,000	52	0.56	6900	40%.

Mean percentage of Haemolysis in these thirty cases is therefore 55.3%.

From these two tables we see that in apparently healthy individuals the percentage of haemolysis varied from 9 to 25 and the Mean result from ten cases was 15.5%.

In/

In the morbid cases the percentage varied from 29 to 92 and the mean result from thirty consecutive cases was 55.3%. In these cases the resistance to haemolysis of the red corpuscles was lowered, as compared with healthy individuals, to the standard solution of Saponin.

We may conclude that some morbid process is present in these cases, some form of toxic material that acts upon the blood and causes a reduction in the normal resistance to Haemolysis. To the fuller discussion of this we will return in the summing up of the results of this investigation.

The presence of Bacillus Coli in the Urine.

It is well known that the kidneys can excrete bacteria in the urine without a definite lesion being present in the urinary tract. Thus Typhoid Bacilli may be present in the urine for years after an attack of the fever. The Bacillus Coli has been found very frequently in the urine and the question of bacilluria from this organism has been investigated by Bruce Clarke, Charlton Briscoe, L. S. Dudgeon, Herbert French, and others.(8)

Three stages have been recognised:-

I. Bacillus Coli and Pus in the Urine.

II./

II. Bacillus Coli, but neither pus nor epithelial cells from the urinary passages.

III. Intermittent discharge of Bacillus Coli without pus or cells.

The route of infection is disputed but it is agreed that the Bacillus Coli can pass through the intestinal wall without causing a detectable lesion. Thus in cases of cardiac ascites the Bacillus Coli may be grown freely from the fluid when freshly tapped. In three cases of cardiac ascites the fluid was drawn off by us aseptically into sterilized flasks with a view to make culture media. The entire stock had to be discarded owing to a copious growth of Bacillus Coli appearing. In several other cases we obtained sterile fluid and no growth appeared. Yet in these three cases there was no symptom of infection and the fluid appeared clear when drawn off.

In women who are constipated Bacillus Coli frequently infects the renal pelves by direct passage from the intestine when stagnation of faeces occurs. Hertz, following Professor Müller, lays stress upon this point in his book on constipation, and states that some degree of pyelitis and bacilluria is a very frequent occurrence in women and children who are constipated. Similarly, in pregnant women pyelitis often occurs as the/

the result of stagnation in the ureter from pressure of the gravid uterus. This is attributed by French in his Goulstonian lectures to the elimination of Bacillus Coli from the blood stream by the kidneys, and their subsequent infection of the stagnant ureter obstructed by pressure from the uterus. This escape of the Bacillus Coli into the blood stream and elimination by the kidney is stated by French to be not infrequent, and to be favoured by abnormalities of the intestinal canal and by stasis of its contents. The pyelonephritis of pregnancy he considers to be frequently precipitated by a bout of constipation causing this infection by the Bacillus Coli, and he quotes cases in support of his theory.

Dixon Mann points out the irregular way in which Bacillus Coli appear and disappear in otherwise normal urine. He does not give the constipation history of his cases but remarks on the absence of other subjective and objective symptoms.

Playm and Laag, on the other hand, report cases where the advent of Bacillus Coli set up a urethritis simulating gonorrhoea.

In the cases under investigation the presence of Bacillus Coli was carefully tested for in the urine. The urine was examined fresh and was obtained by catheter into sterile flasks where possible. In cases where/

where the catheter was objected to, the parts were carefully cleansed with a Lysol lotion and then with sterile water before the urine was passed. The tests used for the presence of Bacillus Coli were four.(9)

1. A drop of filtered and centrifuged urine under a cover glass showed motile bacilli.
2. A culture of the same urine in glucose litmus agar turned the blue litmus red and freed gas bubbles in a stab culture.
3. Stained films of this bacillus were decolourized by Gram's stain.
4. With McConkey's bile-salt glucose acid and gas were produced in a Durham's fermentation tube.

When these tests were complied with the urine was charted as containing Bacillus Coli.

None of the cases observed had subjective symptoms of cystitis; under the microscope occasional leucocyte cells were frequently seen, and the majority of the cases showed epithelial debris from the urinary passages. No macroscopic collections of pus, or quantities sufficient to react to the Guaiac test were found in any of the series. The infection was sub-acute and no accident such as pregnancy intervened to precipitate pyelonephritis in this series.

Bacillus Coli in the Stomach.

In order to test for the presence of Bacillus Coli in the stomach, the stomach was washed out with ten ounces of normal saline solution an hour before breakfast. This time was chosen in order to avoid the antiseptic effect of the gastric secretion excited by a test meal. The resulting fluid was tested for acidity and made neutral by the addition of decinormal sodium carbonate. The fluid was incubated for twelve hours at 37° Cent., and then tested for the presence of Bacillus Coli, the same tests being employed as in the case of the urine, mentioned above. A soft rubber stomach tube attached to a Higginson's syringe was used and in each case sterilized before passing.

Control Cases.

Twelve convalescent patients with no history of constipation and after a period of three weeks daily regulation of the emunctories had the above tests applied, in no case was there a positive result. These cases are given in the following table V. which also gives the results of the agglutination and opsonic tests. (p.30.).

The Agglutination of Bacillus Coli by the Blood Serum and the Opsonic Index of the Serum to Bacillus Coli.

Agglutinins[10] are formed in the blood serum as the result of injections of their specific antigens. Normal human serum frequently has a feeble clumping action on Bacillus Coli. In infants the amounts of agglutinins are very small but increase during life, which suggests that they may be the result of auto-inoculation from the intestine in part if not entirely. In a series of cases characterised by prolonged retention of faecal masses and their contained organisms, and in which the elimination of Bacillus Coli by the kidneys has been investigated, as well as the retrogade passage of the Bacillus Coli into the stomach, it becomes of importance to test for an increase of this power of agglutination in the Blood Serum.

Lorraine Smith has shown that the growth of bacteria in the intestine is normally kept under control by the inhibition exercised by a healthy intestinal wall but increases enormously under conditions interfering with and impairing this control. Thus Johnson and Goodall have shown that in the reduced resistance following insanity of various types, toxic effects followed the increased growth of the Bacillus Coli and as many as 60 per cent of their cases showed agglutination in excess/

excess of the normal towards this organism. Their greatest number of positive cases being obtained with a dilution of 1 in 100, the lowest dilution which they employed was 1 in 30.

On the other hand Dudgeon has stated that, in his investigation of cases with Bacillus Coli, infection of the urinary tract, Agglutination was a comparatively rare phenomenon, and in acute peritonitis out of 68 cases tested only 16 were positive; but in five cases of appendicitis he obtained positive results from each in 30 minutes with a dilution of 1 in 50. Unfortunately no mention is made of the intestinal habit in any of these cases.

Courmont has demonstrated that the most marked results in his series of cases were in the slighter degrees of infection and where the resistance of the patient was good. He extends this observation to all infections running a typical course.

In our series of cases we have the following elements present in the majority:-

1. Stasis of intestine and long retention of Bacteria and their products.
2. Retrograde passage of Bacilli as the result of this stasis.
3. Elimination of the Bacilli by other channels shown by their passage into the urine.

4./

4. A prolonged comparatively mild infection or sapraemic condition as shown by the anaemia, the lowered haemolytic resistance of the blood, the whole group of subjective and objective symptoms that are gathered into a clinical rubbish heap under the classification "gastric".

In such a series of cases the change in the blood serum, as regards agglutination and phagocytic index towards the Bacillus Coli, may be taken as an indication of the general reaction of the body to whatever assault upon its well being is the result of this intestinal stasis and increased putrefactive activity.

From this point of view the agglutination and phagocytic index for the Bacillus Coli was tested throughout the series of cases within the first three days of their coming under observation.

METHODS:-

In testing for agglutination a 24 hours culture of Bacillus Coli on Agar was used to make the emulsion. The emulsion was centrifugalised and filtered to remove unbroken masses and a hanging drop examined, until the resulting emulsion was free from clumps that might be mistaken for a reaction.

A solution of 0.1 per cent Sodium chloride and 0.05 per cent of Calcium chloride in distilled water was used in making the emulsion.

The/

The dilution was measured by using haemocytometer pipettes graduated respectively to 11, 31, and 101 in about half of the cases, for the remainder a platinum loop was employed. Hanging drop preparations were made of the following dilutions.- $\frac{1}{10}$, $\frac{1}{30}$, $\frac{1}{50}$ and where a marked reaction was obtained with the last dilution, strengths of $\frac{1}{100}$ and $\frac{1}{200}$ were also examined. In tabulating results the greatest dilution giving a positive result is alone put down of these five examinations. The time allowed in each case was one hour, the reaction was examined at the end of that period and counted positive if there was definite paralysis and clumping of the majority of the bacilli in each field examined.

In each case the following controls were performed:-

1. A hanging drop of emulsion alone was examined at the end of the hour and was found free from clumping and paralysis of movement.
2. A hanging drop of emulsion and serum from a healthy individual free from all gastric and intestinal symptoms in the dilution of $\frac{1}{30}$ was examined at the end of the hour. Either the writer or one of his colleagues furnished the serum. In all cases this control did not show agglutination at the expiration of one hour.

In/

In the table thus arrived at Agglutination was counted absent when not obtained by a dilution as low as $\frac{1}{10}$. Where present, the extent of the reaction is represented by the dilution given, which is the maximum dilution giving a definite positive result.

The Opsonic Index to Bacillus Coli.(11)

Since Wright applied his method of determining quantitatively the effect of the blood serum on phagocytosis first described by Denys and Leclef in 1895, there has been, in popular terms, a boom in Opsonins.

The technique has been described by Wright and Douglas, Fleming and Emery in the articles and text-book mentioned below, and these accounts have been carefully followed in this investigation. The important question of reliability of the test arises and this has been very seriously questioned of late.(12) The personal equation comes to the front very strongly in Opsonic determinations. We remember a paper in the British Medical Journal where the writer submitted identical samples of serum to three independent observers and the difference between their respective results far exceeded the limits of experimental error allowed in scientific work. The same slide, if counted/

counted by independent workers, will give different results to each, according to the selection of fields chosen.

In the preparation of the films the results are shown to vary with different strains of leucocytes, with the amount of injury the leucocytes receive during their preparation. The strength of the emulsion, the strain of bacteria employed, the strength and composition of the saline diluent, the length of incubation, and the variety of chances which regulate the relative positions of leucocytes and bacteria in the mixture, all unite to cause small or great variations in results. We confess that in the treatment of disease the use of the opsonic index seems to us so surcharged with unavoidable inaccuracies that we are disposed to place very little reliance upon it. By making a series of observations on a number of cases and employing standard strains of bacteria, leucocytes, and serum for control, a scale of relative values may be arrived at in healthy and in morbid conditions. This value of a series of opsonic observations is in no sense advanced as standardized and reliable, mathematical accuracy in the opsonic index as at present determined seems to us impossible.

Shattock and Dudgeon have gone fully into the question of the opsonic index towards the Bacillus coli/

coli, both in Bacillus coli infection and in a vast number of other conditions.(13) They conclude that though the immune leucocyte has an action higher than that of the normal cell, yet it may be lower or equal to it. The cells vary like the serum in value, and the only method of arriving at an accurate estimation of the index is to allow immune cells to work in the immune serum. By the ordinary method too low an index is obtained if the patient's cells are acting above the normal level and too high an index if they are acting below it. They conclude that in most chronic and acute Bacillus coli infections there is a low Opsonic index and that in normal cases the index varies from 0.6 to 1.5.

In the present series of cases the Opsonic Index was taken within the first three days of the case being under observation. Twelve control cases were observed, viz., the twelve cases given in the table of controls for the Agglutination reaction.

The same emulsion of Bacillus coli was used in each case and the same diluting fluid as in the agglutination experiment. The mixture of corpuscles and bacteria were incubated at 37°C. for fifteen minutes; and on each film 100 cells were counted. The white cells were obtained from the writer and the the/

the control serum was in the majority of cases (60) taken from him. In the remainder a pooled serum of the writer's and one of his colleagues was employed. The samples of serum from patient and control were obtained simultaneously and the experiment performed within twenty four hours in each case. The technique was that of Wright and Douglas and the description of it as quoted by Emery was followed carefully throughout, as being concise and convenient for use in a small laboratory.

The Opsonic Index of the Control cases ranged from .79 to 1.8. In the cases of the series it ranged from 0.18 to 2.6.

Reading the results from the view that a low index is indicative of (1) an infection from the organism in question or (2) a low power of resistance to that organism; that a high index is indicative of infection from the organism and a reaction against it, this table of indices shows a strong contrast between the healthy controls and those with the gastric syndrome. The twelve controls gave indices comparable with the limits in health as determined by Dudgeon and Shattock; the gastric series show the most striking divergencies from the limits of health and between each other.

As the calculations were each conducted in a similar manner and under similar circumstances by the same/

same observer, the inference from the whole series may be drawn that, in these cases, the opsonic index denoted a present or past interference with their resistance to the Bacillus Coli due to an infection from that organism.

Table of Control Cases. No Constipation present. V.

Case.	Bacilli in urine.	B.C. in stomach.	Agglutination.	Opsonic Index.
Fracture Leg	None	None	None	1.2
Fracture Hip	None	None	None	.9
Excision knee	None	None	None	1.3
Amputation arm	None	None	None	.79
Amputation breast	None	None	$\frac{1}{10}$	.8
Acute Rheumatism	None	None	None	1.6
Convalescent pneumonia	None	None	None	.85
Chronic Phthisis	None	None	None	.96
Mitral Incomp.	None	None	None	1.4
Fracture Patella	None	None	None	.88
Sarcoma Tibia	None	None	None	1.3
Double Aortic	None	None	None	1.8.

In one case, a woman with scirrhus of the breast an agglutination was obtained with a dilution of 1 in 10. None of the other controls gave an agglutination reaction.

The Opsonic index in these controls ranged from .79 to 1.8.

Bacillus Coli Infection and Reactions. Table VI.

No.	Bacillus Coli in Urine.	Bacillus Coli in stomach.	Agglutination	Opsonic Index.
1	Absent	Absent	None	0.8
2	Absent	Present	1/20	0.6
3	Present	Present	1/50	0.38
4	Present	Present	1/100	0.5
5	Present	Present	1/50	0.46
6	Present	Present	1/100	2.4
7	Present	Present	1/30	0.8
8	Absent	Present	None	1.3
9	Present	Present	1/50	0.47
10	Present	Present	1/100	0.35
11	Absent	Present	None	0.65
12	Absent	Absent	None	0.9
13	Absent	Absent	None	1.3
14	Present	Absent	None	0.76
15	Present	Absent	1/30	0.6
16	Present	Present	1/50	0.54
17	Absent	Present	None	1.5
18	Present	Present	None	0.8
19	Absent	Present	None	0.5
20	Absent	Present	None	0.49
21	Absent	Absent	None	0.93
22	Present	Present	1/100	0.57
23	Present	Present	1/50	0.35
24	Absent	Absent	1/10	1.8
25/				

No.	Bacillus Coli in Urine.	Bacillus Coli in Stomach.	Agglutination	Opsonic Index.
25	Present	Present	$\frac{1}{200}$	0.2
26	Absent	Present	None	0.86
27	Present	Absent	$\frac{1}{30}$	0.58
28	Absent	Present	$\frac{1}{10}$	0.76
29	Present	Present	$\frac{1}{100}$	0.47
30	Absent	Present	None	1.6
31	Present	Present	$\frac{1}{30}$	0.66
32	Present	Present	$\frac{1}{100}$	0.36
33	Absent	Present	None	1.3
34	Present	Present	$\frac{1}{100}$	0.52
35	Absent	Absent	None	1.8
36	Present	Present	$\frac{1}{100}$	0.45
37	Present	Present	$\frac{1}{200}$	0.58
38	Absent	Present	None	0.96
39	Absent	Absent	None	1.7
40	Present	Absent	$\frac{1}{20}$	0.73
41.	Present	Present	$\frac{1}{50}$	0.5
42	Absent	Present	None	0.61
43	Present	Absent	$\frac{1}{50}$	0.39
44	Absent	Present	None	1.1
45	Present	Present	$\frac{1}{100}$	0.62
46	Present	Present	$\frac{1}{100}$	0.18
47	Present	Present	$\frac{1}{100}$	0.75
48	Present	Present	$\frac{1}{50}$	0.35
49	Absent	Present	$\frac{1}{10}$	1.8
50/				

No.	Bacillus Coli in Urine.	Bacillus Coli in Stomach.	Agglutination	Opsonic Index.
50	Present	Present	1/50	0.27
51	Present	Present	1/50	0.53
52	Present	Present	1/100	0.76
53	Absent	Present	None	0.35
54	Present	Present	1/100	0.45
55	Present	Present	1/30	0.46
56	Absent	Present	1/100	0.36
57	Present	Absent	1/10	1. 4
58	Absent	Present	None	0. 6
59	Present	Present	1/50	0.52
60	Absent	Present	1/10	0.77
61	Present	Present	1/50	0.57
62	Present	Present	1/100	0.23
63	Absent	Absent	None	2. 6
64	Present	Present	1/30	0.45
65	Absent	Present	None	1. 6
66	Absent	Present	None	1. 9
67	Absent	Present	1/10	0.87
68	Present	Present	1/100	0.43
69	Absent	Present	None	0.74
70	Present	Present	1/100	0.46
71	Present	Absent	1/30	0.68
72	Absent	Present	None	1.5
73	Present	Present	1/50	0.37
74	Present	Present	1/100	0.64
75	Absent	Present	None	1.3

Analysis of Table VI.

Presence of Bacillus Coli.

Bacillus Coli in Urine in 43 cases out of 75.

Bacillus Coli in Stomach in 60 cases out of 75.

Bacillus Coli in Urine and Stomach in 36 cases out of 75.

No Bacillus Coli in either Urine or Stomach 8 cases out of 75.

Agglutination Results to Bacillus Coli

No reaction obtained in 27 cases.

Reaction up to $\frac{1}{200}$ Dilution 2 cases.

" $\frac{1}{100}$ " 18 "

" $\frac{1}{50}$ " 12 "

" $\frac{1}{30}$ " 8 "

" $\frac{1}{20}$ " 2 "

" $\frac{1}{10}$ " 6 "

Total number reacting 48 cases out of 75, or 64% positive reactions

Opsonic Index Results

In Healthy Cases the limits were 0.79 to 1.8.

In the Morbid Cases.

Opsonic Index below 0.8 in 51 cases,

above 1.8 " 3 "

between 0.8 and 1.8 " 21 "

Out of 75 Morbid Cases the Opsonic Index in 54 was not/

not within the limits given by healthy cases, That is 72% of cases were outside normal limits.

Ascending Infection in Intestinal Stasis. (14).

For some years past Mr Bond of the Leicester Infirmary has studied the reversed mucus current in the Alimentary Canal by introducing fine particles of Indigo into the rectum either suspended as an emulsion or as a suppository. The result of these experiments showed that in cases of intestinal obstruction, the indigo particles were carried upwards, even in cases to whom Aperients had been given, and were recoverable at the colotomy opening or caecal fistula which was present in his cases. From his experiments he concludes that Indigo particles are insoluble in the intestinal juice ; that they are carried upward in particulate masses by the mucus stream and not by phagocytic action. That in healthy animals without obstruction the flow upward is very slight and not to be compared with cases in whom obstruction exists. He gives three days as the time required in his cases for the particles to pass from Anus to Caecum.

Following the suggestion of Mr Bond, the upward flow of indigo particles was tested in a series of cases in whom marked constipation was present. These cases were, four cases of gastric carcinoma with gastrostomy openings. One Appendicostomy of old standing/

standing. One carcinoma of stomach subsequently confirmed by operation. Two hour glass stomachs and one dilated stomach with pyloric stricture afterwards confirmed by operation. Two dilated stomachs, a gastric ulcer and a case where pancreatic fistula followed pylorectomy for carcinoma.

In all these cases an emulsion of powdered indigo one drachm suspended in one ounce of mucilage was used. Each night half an ounce of the mixture was introduced into the rectum through a rubber catheter and the gastric contents or the flow from the fistula in each case was examined daily.

The gastric contents were thoroughly stirred up with filtered water and allowed to sediment in conical glasses. The indigo particles rapidly sank to the bottom and after twelve hours the super natent fluid and food particles were syphoned off and slides made from the residue. The indigo particles were easily recognised under the low power of the microscope. A similar procedure was gone through where a fistulous discharge was used.

The shortest time before indigo was recovered from the stomach was five days. The longest period was thirteen days. From the Appendicostomy opening indigo was obtained on the third day, and from the pancreatic fistula on the sixth day.

These cases had each a nightly enema of soap and water before the indigo was given, and in no case was a day passed without thus emptying the rectum. All the cases were constipated, in the cancer cases, this being partially due to the administration of morphia, and the type of constipation varied from three to seven days without natural evacuation.

Five Control Cases in whom no history of constipation was present and whose bowels had been open daily for over a fortnight in the ward were carefully selected and submitted to indigo injections with gastric lavage.

None of these controls returned indigo in the wash out from the fifth day to the end of the experiment. In none of these controls were Bacillus Coli found in the stomach contents.

These experiments go to show that there is a passage of particles through the whole length of the Alimentary Canal from the rectum to the stomach in cases of chronic constipation.

The presence of Colon Bacilli in the stomach contents is probably explained by this retrograde flow and accounts for the positive results given in the table of cases showing the presence or absence of Colon Bacilli in the stomach.

The following table VII shows the results in the constipation series and in the healthy controls in table VIII.

Table of Indigo Experiments in Intestinal Stases VII.

Case.	Disease	Operation etc.	No. Injections.	Day Indigo found
A.E.	Carcinoma Stomach	Gastrostomy	5	6th
J.D.	Carcinoma Pylorus	Gastrostomy	3	5th
C.R.	Carcinoma Pylorus	Gastrostomy	6	7th
J.T.	Carcinoma Pylorus	Gastrostomy	6	8th
J.B.	Colitis	Appendicostomy	2	3rd
M.H.	Carcinoma	Laparotomy	6	11th
E.S.	Hourglass Stomach	Inflation	5	6th
R.O.	Dilated Stomach	Inflation	6	13th
F.P.	Dilated Stomach	Inflation	5	6th
E.H.	Hourglass Stomach	Laparotomy	7	8th
A.L.	Pyloric Stricture	Gastro Enterostomy	4	5th
P.B.	Gastric Ulcer		6	7th
M.B.	Carcinoma and Pancreatic Fistula after operation	Gastro Enterostomy	5	6th

Table Control Cases where Constipation Absent VIII.

Case	Disease	Injections	Last day examined
R.C.	Fracture Tibia	9	10th
M.H.	Neurasthenia	11	12th
H.J.	Chronic Eczema	11	12th
W.R.	Convalescent Pneumonia	11	12th
R.B./			

Case	Disease	Injections	Last day examined
R.B.	Convalescent Pneumonia	14	15th

In each of these controls the gastric contents were examined from the 5th day onwards. In none of these cases were Indigo grains present in the gastric wash out.

Oral Sepsis and the Pancreatic Reaction of Cammidge.

An investigation in these cases was made as to the existence of oral sepsis, and of the Pancreatic reaction of Cammidge.

The cause for this grouping was due to the author having had an association of these two factors in his personal experience.

While junior Assistant to Sir Thomas Fraser in the Royal Infirmary, the writer had the alarming experience of developing a glycosuria.

Dr Chalmers Watson kindly did the Cammidge reaction and found it positive. During this period, the writer suffered from Alveolar Suppuration round two carious stumps and slight pyorrhoea and sponginess of the adjacent gums. A constant discharge of pus and organisms seemed to him to be a possible source of infection and irritation to the duodenum and by ascent through /

through the duct to the pancreas. This pyorrhoea was carefully attended to and the gums disinfected daily with Hydrogen Peroxide before meals and all food particles carefully removed after each meal, The reaction disappeared from the urine together with the glycosuria and have not returned, although no care is taken to eliminate carbohydrates from the diet.

Oral Sepsis, (15).

In the healthy human mouth the gums are closely applied to the necks of the teeth, small processes project between contiguous teeth filling up the space between the necks of the teeth, the transverse diameter of the crowns being greater at their point of approximation than at the gum margin. The alveolar process between adjacent teeth is thicker than at other portions of its circumference, it contains a little marrow, and is nearer the free surface than elsewhere. The gums are applied closely to the teeth but not attached along their free edges, the line of attachment being a little lower and blending with the dento alveolar periosteum where the cementum covering to the roots begins. When the gum margin is inflamed the local congestion causes an increase in the depth of this natural pocket, debris may accumulate in it, and if the congestion persist, bacterial infection will follow. The slight sensory nerve supply to the gum/

gum margin allows of many small abrasions and a considerable amount of irritation to pass unnoticed, and the onset of pyorrhoea is insidious and becomes chronic before it is detected.

In the early stage of Pyorrhoea Alveolaris the gums are slightly swollen, and red, the margins appear thicker and rounded. A feeling of tenderness may be experienced along the roots of the teeth when chewing. The teeth may feel tender to hot and cold fluids. This stage if allowed to progress is followed by the formation of pockets between the fang of the tooth and the gum, and the periosteum of the tooth is gradually stripped. The deeper layers of the gum are infiltrated by round inflammatory cells, the alveolar margin is attached and a rarefying osteitis sets in. Most important from the point of our argument, debris, pus cells and organisms in large numbers collect in the ever deepening pockets and in the spongy granulations of the gum margins. This infective matter is continually being expressed mixed with the food and saliva and swallowed.

Pyorrhoea Alveolaris is therefore equivalent to a constant flow of septic organisms and their products into the stomach and intestine. That disease follows Oral Sepsis is suggested by Hunter in his work in Anaemia by Jones in his book on Rheumatoid Anthritis, by Goadby and numerous other observers.

In/

In the cases investigated in this series the following symptoms were noted most strongly marked in the cases which showed most chronic Pyorrhoea.

Anaemia occasionally with a slight leucocytosis of a secondary type, as shown by the chart of blood counts. Depression and malaise approaching a melancholia in some of the cases. Acne and impetiginous eruptions of the skin which was sallow, clammy or scurfy. Such were the general symptoms accompanying the dyspeptic symptoms and the pyorrhoea in these cases. The question of cause and effect will be discussed later.

Here we wish to emphasise the point of continued administration of septic material connected with symptoms of general toxaemia and in particular with the presence of Cammidge's Pancreatic Reaction.

Cammidge has worked out a test for the presence of a pentose which appears in the urine during the course of an inflammatory disease of the Pancreas. (16)

Following Cammidge's results Chalmers Watson, Taylor and others have showed the presence of some degree of pancreatitis in cases which have been labelled clinically as neurasthenia, intestinal indigestion, gout, rheumatoid anthritis, glycosuria, duodenal ulcer, gall stones, colitis, constipation, gastric ulcer and a host of other conditions where the common factor in each case is the presence of some infective condition that /

that has reached the pancreas and caused an acute sub acute or chronic inflammatory change and disturbance of function in that organ.

In a series of cases such as the present where the multitude of symptoms labelled gastric in the text book occur in every variety of combination, and where in so many of the cases a pancreatic reaction was also present, the question of relationship cause and effect again rises.

A full discussion of these symptoms is not in the direct path of this inquiry. Our object is to clearly show out of a series of gastric erosion cases how many had a constant supply of septic material sent from the mouth to the stomach, and how many gave the Cammidge reaction which indicates an infected pancreas.

The reaction as done in these cases was carried out as follows. We are indebted to Dr Chalmers Watson for having instructed us in the technique.

Method of Pancreatic Reaction.

1. A twenty four hour's specimen of urine was filtered and tested for albumen, sugar, bile and Indican.
2. Twenty c.cm. of clear filtered urine free from sugar and albumen is taken. In our cases no glycosuria was present in any of them, in a few a slight albumen uria was present, the albumen was removed by boiling and filtering. This amount is mixed with 1 c.cm. of strong Hydrochloric Acid and the whole gently boiled on/

on a sand bath, with a condensing funnel in the neck of the flask, for ten minutes.

3. The flask is well cooled in running water and the contents made up to 20 c.cm. with distilled water. The excess of acid is neutralized by adding 4 grams of lead carbonate. After standing for a few minutes and being again cooled, the contents are filtered repeatedly through the same paper till the filtrate is entirely clear.

4. This filtrate is shaken well with 4 grams of tribasic lead acetate and again filtered till clear.

5. The lead in solution is now removed by shaking with 2 grams of powdered sodium sulphate, the mixture is heated to the boiling point and then cooled as low as possible in running water, and again filtered till clear.

6. Ten c.cm. of the clear filtrate is made up to 18 c.cm. with distilled water and 0.8 grams of phenyl hydrazine hydrochloride, 2 grams of powdered sodium acetate and 1 c.cm. of 50% Acetic Acid are added. This mixture is boiled in a flask with funnel condenser on the sand bath for ten minutes and then filtered hot into a test tube having a 15 c.cm. mark. Should the filtrate fail to reach this/

this mark it is made up to 15 c.cm. with hot distilled water.

This tube is allowed to stand over night and the deposit is examined microscopically next morning.

If the reaction is positive long, light yellow, flexible hair like crystals are seen arranged in sheaves. By introducing 33 per cent sulphuric acid under the cover glass these melt and disappear in from ten to fifteen minutes from their contact with the acid.

Control Test. To exclude traces of sugar 20 c.cm. of urine are treated in the same way as above with the exception of adding the Hydrochlorie Acid.

Should a trace of sugar be discovered from the control it would be necessary to remove it by fermentation after the boiling with the acid, the excess acid having been first neutralised with soda solution.

The following Table shows.-

1. The type of constipation in days gone habitually without a stool.

2. The presence or absence of Pyorrhoea.

By slight is meant a case where the disease has not progressed beyond the stage of redness and sponginess of the gum with perhaps

a/

a trace of pus on firm pressure. Where the term Marked is used, the Pyorrhoea was extensive with numerous pockets containing pus with absorption and granulation round the alveolar margins.

3. The presence or absence of a positive result to the above reaction of Cammidge. By a positive result is meant the finding of definite sheaves of the crystals as described and their disappearing to the sulphuric acid test under the microscope.

The type of constipation is put in here to show whether the positive reactions correspond with the degree of constipation in more than an accidental manner.

In the observations elsewhere on retrograde mucus flow in the intestine, and the presence of Bacillus Coli in the stomach. This table of degree of Constipation becomes of importance, and is there referred to.

That the Pancreas is liable to infection by ascending organisms along the duct is proved by the experiments of Bond and others elsewhere referred to.

Powdered Indigo placed in the duodenum or swallowed by the mouth can be detected microscopically in the ramifications of the pancreatic ducts, thus showing that an inert powder can be carried against the descending current. Robson and Cammidge similarly/

ly show the effects of ascending infection from the duodenum and in cases of gall duct infection.

Table showing Type of Constipation degree of Pyorrhoea and the result of Pancreatic Reaction. IX.

Number	Type Constipation	Type Pyorrhoea	Pancreatic Reaction.
1	2-3 Days.	None	Negative
2	3-4	None	Positive
3	2-5	Very Slight	Negative
4	2-3	Marked	Positive
5	3-5	Very Slight	Negative
6	2-5	Marked	Positive
7	3-4	Slight	Positive
8	1-2	Very Slight	Negative
9	3-5	Marked	Positive
10	3-6	Marked	Positive
11	3-5	Marked	Positive
12	2-4	Marked	Positive
13	1-2	None	Negative
14	3-4	Marked	Positive
15	3-4	None	Negative
16	2-4	Slight	Negative
17	2-3	None	Negative
18	2-5	Marked	Positive
19	2-5	None	Negative
20	2-3	Slight	Positive
21	1-2	Marked	Positive
22/			

Number	Type Constipation	Type Pyorrhoea	Pancreatic Reaction .
22	3-5	Marked	Positive
23	3-4	Marked	Positive
24	4-6	Marked	Positive
25	4-6	Marked	Positive
26	2-3	None	Positive
27	2-3	None	Negative
28	4-7	None	Negative
29	3-5	None	Negative
30	4-6	None	Negative
31	2-3	Slight	Negative
32	3-4	Marked	Positive
33	2-4	Marked	Positive
34	3-5	Marked	Positive
35	2-3	None	Negative
36	4-7	Marked	Positive
37	3-5	Marked	Positive
38	2-3	None	Negative
39	2-3	Slight	Positive
40	3-4	Very Slight	Negative
41	2-3	Marked	Positive
42	4-7	None	Negative
43	5-7	None	Negative
44	3-5	Marked	Positive
45	4-6	Marked	Positive
46	2-5	Marked	Positive

47/

Number	Type Constipation	Type Pyorrhoea	Pancreatic Reaction.
47	3-5	Marked	Positive
48	3-4	None	Positive
49	2-5	Marked	Negative
50	5-7	Slight	Positive
51	3-5	Marked	Positive
52	2-4	Marked	Positive
53	3-7	Marked	Positive
54	4-5	Marked	Positive
55	3-6	Marked	Positive
56	2-5	Marked	Positive
57	3-4	Slight	Negative
58	2-3	Marked	Positive
59	2-3	Marked	Positive
60	1-2	None	Negative
61	3-5	None	Positive
62	5-7	Marked	Positive
63	1-2	Very Slight	Negative
64	5-6	Marked	Positive
65	2-3	None	Negative
66	1-2	None	Negative
67	2-3	None	Negative
68	3-5	Marked	Positive
69	2-5	None	Negative
70	4-7	Marked	Positive
71	1-3	None	Positive

72/

Number	Type Constipation	Type Pyorrhoea	Pancreatic Reaction.
72	3-7	Slight	Positive
73	2-4	None	Negative
74	1-2	Marked	Positive
75	2-3	Marked	Positive

Analysis of Table for Pyorrhoea and Pancreatic Reaction.

Pancreatic Reaction Positive in 47 out of 75 cases.

Pyorrhoea Absent in 24 cases.
Pancreatic Reaction in 5 cases of these positive.

Pyorrhoea Very Slight in 5 cases.
Pancreatic Reaction Absent in all of these.

Pyorrhoea Slight in 8 cases.
Pancreatic Reaction in 5 of these positive.

Pyorrhoea Marked in 38 cases.
Pancreatic Reaction in 37 of these positive.

Total Pyorrhoea Cases 51
Pancreatic Reaction in 42 of these positive.

Conclusion.- The Pancreatic Reaction is much more frequent in the cases of Gastic Erosion which suffer from marked Pyorrhoea.

The Reaction is present in 62.6% of all the cases and in 82.3% of the cases with Pyorrhoea.

The Bacillus Coli is stated by Bosanquet in Allbutts system of Medicine to be the most frequent cause/

cause of subacute and chronic pancreatitis. Carnot found the gland was frequently invaded by this organism after injury to the gland itself or following inflammation and infection of the duodenum.

One road of infection of the pancreas has been proposed in the preceding investigation viz. from organisms brought from septic gums to the duodenum in the process of swallowing.

In the present series of cases the reflux of Bacillus Coli into the stomach has been tested, and where the organism is present in the stomach it may be taken for granted that it is also present in the duodenum to an equal and most probably greater extent. It is therefore necessary to compare the number of cases with Bacillus Coli invasion of the stomach with those in which the Pancreatic Reaction appears and to note those in which both phenomena appear simultaneously.

The following table shows the relationship between the presence of Bacillus Coli in the stomach and the Pancreatic Reaction.

X Table of Bacillus Coli in Stomach and Pancreatic Reaction.

Case	Bacillus Coli in Stomach	Pancreatic Reaction.
2	Present	Positive
3	"	"
4/		

Case	Bacillus Coli in Stomach	Pancreatic Reaction
4	Present	Positive
5	"	
6	"	Positive
7	"	Positive
8	"	
9	"	Positive
10	"	Positive
11	"	Positive
16	"	
17	"	
18	"	Positive
19	"	
20	"	Positive
22	"	Positive
23	"	Positive
25	"	Positive
26	"	Positive
28	"	
29	"	
30	"	
31	"	
32	"	Positive
33	"	Positive
34	"	Positive
36	"	Positive
37	"	Positive
38/		

Case	Bacillus Coli in Stomach	Pancreatic Reaction.
38	Present	
41	"	Positive
42	"	
44	"	Positive
45	"	Positive
46	"	Positive
47	"	Positive
48	"	Positive
49	"	
50	"	Positive
51	"	Positive
52	"	Positive
53	"	Positive
54	"	Positive
55	"	Positive
56	"	Positive
58	"	Positive
59	"	Positive
60	"	
61	"	Positive
62	"	Positive
64	"	Positive
65	"	
66	"	
67	"	
68	"	Positive
69	"	

70/

Case	Bacillus Coli in Stomach	Pancreatic Reaction.
70	Present	Positive
72	"	Positive
73	"	
74	"	Positive
75	"	Positive

From this Table we get the following result.-

Cases with Bacillus Coli in Stomach	60
Pancreatic Reaction Positive in	41 of these
Total Positive Pancreatic Reactions	47
Total combining Bacillus Coli Invasion of Stomach with Pancreatic Reaction	41
Percentage of Pyorrhoea Cases giving Pancreatic Reaction	82.3%
Percentage of Bacillus Coli Invasion Cases giving Pancreatic Reaction	68.3%

We thus find that the Percentage of Pyorrhoea associated with Pancreatic Reaction exceeds the Percentage of Bacillus Coli Invasion of the Stomach combined with Pancreatic Reaction by 14%.

The Cammidge Reaction is thus more frequently associated in this series with Pyorrhoea than with Bacillus Coli Invasion of the Stomach.

In order to further trace the possible route of Pancreatic infection a number of cultures were made from the Pancreas Post Mortem, and also from cases of Pyorrhoea as follows.

1./

1. Cases of Pyorrhoea Alveolaris Cultures from the peridental pockets.
2. Cases not giving the Pancreatic Reaction during life. Cultures from the Pancreas within 12 hours of death.
3. Cases giving the Pancreatic Reaction during life, Cultures from the Pancreas within 12 hours of death. Cultures from the gums taken before death.

XI Table of Group I.

Cultures from 8 Pyorrhoea Cases of the Series.

Case of Series	Organisms from Gums.
22	Staphylococcus Albus and Aureus, Micrococcus Catarrhalis.
23	Staphylococcus Aureus, Pneumococcus.
24	Streptococci, Staphylococcus Aureus.
33	Streptococcus Micrococcus Catarrhalis Staphylococci
41	Streptococci and Staphylococci Micrococcus Catarrhalis

52/

Case of Series	Organisms from Gums.
52	Diphtheroid Bacilli Staphylococci and Micrococcus Catarrhalis
59	Streptococci and Staphlococci
68	Staphylococci and Micrococcus Catarrhalis

Result - Staphylococci found in 8 out of 8 cases
Micrococcus Catarrhalis 5 " " " "
Streptococci 4 " " " "
Pneumococcus 1 " " " "
Diphtheroids 1 " " " "

XII. Table of Group II.

Cultures from Pancreas in cases where Cammidge Reaction Negative.

Case	Organisms in Pancreas.
Rhoda C. 60 Mitral Disease	Bacillus Coli
Walter M. 32 Empyema	Bacillus Coli Staphylococci
Susan P. 62 Mitral	No growth
Alice L. 37 Pneumonia	Bacillus Coli
Harry C. 29 Hydatid Liver with abscess.	Streptococci and Staphylococci

Percy/

Case	Organisms in Pancreas.
Percy S. 35 Pneumonia	No Growth
Christopher C. 18 Phthisis.	Bacillus Coli
George T. 27 Mitral Stenosis	Bacillus Coli
Dinah N. 64 Pneumonia	No Growth
Charles R. 28 Cerebral Tumour	Bacillus Coli

Result.- Bacillus Coli in 6 out of 10 cases.
Staphlococci in 2 " " " "
Streptococci in 1 " " " "
No Growth in 3 " " " "

As far as a limited series can show, the Bacillus Coli is a frequent inmate of the Pancreas without causing a Cammidge Reaction.

XIII. Table of Group III.

Cultures from Gums and Pancreas in cases of combined Pyorrhoea and Cammidge Reaction.

Case	Gums	Pancreas.
Henry K. 40 Aneurysm	Staphylococci	Bacillus Coli
James/	Micrococcus Catarrhalis.	Staphylococci

Case	Gums	Pancreas.
James W. 24 Pernicious Anaemia	Streptococci Staphylococci Micrococcus Catarrhalis.	Streptococci & Staphylococci
John T. 49 Gastric Ulcer	Streptococci Staphylococci Pneumococci	Streptococci Staphylococci
Thomas H. 31 Cirrhosis Liver	Staphylococci Streptococci Gram Positive Bacilli	Streptococci Gram Positive Bacilli. Bacillus Coli

Result.- In 4 cases of Pancreatic Reaction during life combined with Pyorrhoea similar organisms were obtained from the pockets around the teeth, and from Cultures from the Pancreas within 12 hours of death from intermittent disease.

These 4 cases tend to show that an infection of the Pancreas is possible from organisms swallowed from septic gums.

A Cutaneous Reaction to Bacillus Coli. (14)

Von Pirquet described his Cutaneous test for tubercle in 1907. Working on similar lines, Professor Chantemesse investigated the effect of Bacillus Typhosus toxins on the conjunctiva in typhoid fever, and Dr S.J. Deehan has described a cutaneous reaction/

reaction in typhoid analogous to that of Von Pirquet. It seemed a reasonable inference that in Bacillus Coli infection of chronic constipation a similar reaction might be obtained.

Mixed strains of Bacillus Coli were grown on Agar-Agar for 24 hours. The growth was then washed off with sterile normal saline solution and an emulsion prepared by shaking this mixture with glass beads in a test tube for half an hour. This fluid was next incubated at 37° centigrade for four days. At the end of this time the fluid was almost clear and the bacilli chiefly disintegrated. The fluid was then sterilized at 60° for three quarters of an hour on three successive days. The mixture was then centrifugalised for half an hour and the supernatant fluid pipetted into glass capsules, after its sterility had been tested by several cultures, and the number of bacilli to the cubic centimetre standardised by Wright's method for standardising vaccines. A strength of five billions of bacilli to the cubic centimetre was used. This fluid was used within two weeks of its preparation, and at the end of that time discarded, and a fresh mixture prepared.

A drop of this fluid was placed on the skin over the biceps on the arm of the case being investigated and the skin lightly scratched through the drop with a sharp Hagedorn's Needle sterilized by a flame.

A /

A similar lesion was produced a few inches away through a drop of normal saline. The abrasion was made sufficiently deep to open the superficial lymph vessels, but stopped short of drawing blood.

The reaction was classified as follows.-

1. Feeble. An area of hyperaemia and slight hardness of the skin to the touch 3 to 5 millimetres in diameter.
2. Medium. A larger zone of redness with a definite elevation of the skin into a papule.
3. Strong. A more marked redness with oedema of the skin, marked papule formation and resistant area of skin.

The reaction, where it occurred, began in from 18 to 24 hours after the inoculation. The redness and papule faded away completely in from 6 to 48 hours according to the severity of the reaction.

Thirty Control Cases with no history of constipation or gastric disease were inoculated and in no case gave any reaction.

Controls healthy

These cases were as follows.-

Fractures of Leg	5
Fractures of Arm	3
Chronic Bronchitis	2
Acute Rheumatism	4
Cardiac Disease	7
Phthisis	8
Uterine Carcinoma	1
Total Controls	30 with negative results,

The/

The results in the cases of this investigation are given in the following table.

XIV. Table of Cutaneous Reaction to Bacillus Coli.

No.	Result	Onset	Duration of Reaction.
1	None		
2	Feeble	18 hours	12 hours
3	Medium	18 hours	24 hours
4	None		
5	Medium	18 hours	36 hours
6	None		
7	None		
8	None		
9	Medium	18 "	36 "
10	Feeble	24 "	6 "
11	Feeble	24 "	24 "
12	None		
13	None		
14	None		
15	None		
16	Feeble	18 "	6 "
17	None		
18	Feeble	18 "	12 "
19	None		
20	Feeble	24 "	36 "
21	None		
22	Medium	18 "	48 "
23/			

No.	Result	Onset	Duration of Reaction.
23	None		
24	None		
25	Strong	18 hours	60 hours
26	Feeble	24 "	12 "
27	Medium	18 "	36 "
28	Medium	18 "	48 "
29	Feeble	24 "	12 "
30	None		
31	None		
32	Feeble	24 "	6 "
33	None		
34	Medium	18 "	36 "
35	None		
36	Feeble	24 "	6 "
37	Feeble	24 "	12 "
38	None		
39	None		
40	None		
41	None		
42	None		
43	Feeble	18 "	12 "
44	None		
45	Medium	18 "	36 "
46	Medium	18 "	48 "
47	Medium	18 "	36 "
48	Feeble	24 "	12 "
49	None		

50/

No.	Result	Onset	Duration of Reaction.
50	Medium	18 hours	54 hours
51	Feeble	24 "	6 "
52	Feeble	18 "	6 "
53	Medium	18 "	48 "
54	Medium	18 "	36 "
55	None		
56	Feeble	24 "	6 "
57	None		
58	Feeble	18 "	12 "
59	None		
60	None		
61	Feeble	24 "	12 "
62	Medium	18 "	36 "
63	None		
64	None		
65	None		
66	None		
67	None		
68	Feeble	18 "	6 "
69	Medium	18 "	48 "
70	Medium	18 "	36 "
71	None		
72	Medium	24 "	48 "
73	None		
74	None		
75	None		

Summary/

Summary of Result.

No Reaction	38 cases
Feeble	19 "
Medium	17 "
Strong	1 "
Total Positive	37 out of 75 cases.

Conclusion, - That in almost 50% of the cases under examination there is a positive reaction to the Cutaneous inoculation of Bacillus Coli Vaccine.

Control Cases of Abdominal and Renal Infections with Bacillus Coli.

Appendix Abscesses from which Bacillus Coli was obtained, ruptured duodenal ulcers, and cases of Cystitis with Bacillus Coli in large numbers and pus in the urine were chosen as controls.

XV. Table of Controls.

Case	Time Inoculated	Result.
Appendix	4 days after operation	Reaction moderate.
Appendix	4 days after operation	Reaction marked
Appendix	Before operation	Reaction moderate
Appendix	2 days after operation	Reaction negative
Appendix	4 days after operation	Reaction moderate
Appendix/		

Case	Time Inoculated	Result.
Appendix	4 days after operation	Reaction marked
Cystitis	Two months history	Reaction moderate
Cystitis	Four months history	Reaction marked
Cystitis	One year's history	Reaction marked
Cystitis	Three week's history	Reaction slight
Duodenal Ulcer	6 days after operation	Reaction marked
Duodenal Ulcer	2 days after operation	Reaction slight

Analysis of Controls.-

Twelve cases of Bacillus Coli Infection		12
Reaction obtained in		11
No Reaction	1 case	
Slight Reaction	2 "	
Moderate Reaction	4 "	
Marked Reaction	5 "	
Total	12 "	

The Presence of Areas of Hyperaesthesia, (18) and a pathological Cause for their Presence. (19)

Mackenzie and Head have pointed out that in cases of Gastric Ulcer, hyperaesthesia of the skin may be found to pinching and pricking in the epigastric region, other areas such as the scapular regions and over the tenth rib posteriously are often the seat of similar hyperaesthesia.

It/

It is unnecessary for our purpose to give the distribution of this pain in all our series of cases, the symptom was carefully determined in each case with the following result.-

Cases showing definite Epigastric Hyperaesthesia to pinching the skin gently.	66
Cases in whom Hyperaesthesia of the skin was entirely absent	9
Total	75

This shows that there is hyperaesthesia of the skin in the areas for referred gastric pain in 88% of the series.

It may be assumed that this symptom of hyperaesthesia of certain areas of the skin is a constant feature in cases of gastric erosion. Its absence depends on the stage of the disease. During the progress of the case to recovery we universally noted that the skin hyperaesthesia was the first to disappear, then the pain to moderate pressure in the epigastrium. The subjective pain frequently disappeared several days before this hyperaesthesia to pinching.

We will now endeavour to furnish what we believe to be an original explanation of this symptom.

A suggested explanation of Referred Gastric Pain based on Pathological Changes in the Spinal Cord.

The question of visceral pain has been exhaustively investigated by Head, Mackenzie, Lennander, Langley/

Langley, Sherrington and others as tabulated in the bibliography (18). We will first briefly state the present views with regard to visceral pain.

It is suggested that under certain circumstances the afferent nerves of the autonomic system react upon the cerebro spinal nerves and stimulate them. As an immediate result, pain, hyperalgesia and muscular contraction in the external body wall appear.

On testing the various organs and tissues of the body for sensitiveness to pain, they are found to vary widely in their susceptibility. The viscera are found to be insensitive to stimuli which produce pain in the superficial and deep layers of the body wall. The tissues sensitive to pain from pricking and pinching are found to be those supplied by the cerebro spinal nervous system, those which are insensitive are supplied entirely by the autonomic system. Pain arising from visceral stimulation is therefore produced by a different mechanism to that of the tissues supplied by the cerebro spinal system.

When a cerebro spinal nerve is stimulated in any part of its course, the pain is localised to the peripheral distribution of the nerve. Where the stimulation is severe, as in whitlow, there is a wider radiation of pain through the superficial and deeper structures, not only in the neighbourhood of the lesion, but often referred to distant parts . This radiation is explained by supposing a violent stimulus/

ulus to affect not only the nerve cells of the affected nerve in the cord, but to affect neighbouring groups, and thus cause pain to be referred to their peripheral distribution.

In the body wall we find three layers of extreme sensitiveness to pain, viz. the skin, the voluntary muscles and the sub-peritoneal layer of connective tissue.

The viscera on the other hand are insensitive thus Haller demonstrated that the viscera could be cut and burnt while the animal ate its food without pain. Harvey has described the insensitiveness of the heart. Mackenzie and Lennander have tested the various viscera by pinching burning and pricking and found them insensitive.

The mechanism of visceral pain is then of a special order. The above observers describe it as follows.- When a nerve to a sense organ is stimulated in any part of its course, the brain receives the same impression that would arise from a stimulation of its periphery. Similarly a sensory nerve stimulated at a part of its course refers the resultant sensation to its periphery. If a morbid stimulus arises, the increased stimulation affects neighbouring centres in the cord or brain, and thus stimulates sensory, motor and other nerves that issue from this part of the cord. Such stimulation will result in a sensation or a contraction referred to the periphery of/

of the centres affected. Visceral pain is thus a viscero sensory reflex, and where a skeletal muscle is affected, a viscero motor reflex.

Where visceral pain diffuses over a wider area than that occupied by the lesion, as for instance in the wide hyperaesthesia associated with disease of the gall bladder or stomach; it is due to an extension of the irritation affecting the central ends of sensory nerves in the spinal cord. A large area of hypersensitive centres in the cord may be established and stimuli which in health would pass unnoticed will now on reaching this area in the cord cause marked sensory phenomena referred to the peripheral distribution from these centres. These areas in the cord may become so irritable in visceral disease that peripheral stimuli will give exaggerated responses, thus we arrive at the hyperalgesic areas of skin and hypertonicity of the recti and other abdominal muscles in cases of gastric ulceration.

This irritable focus of the cord is of great frequency in stomach disease. Not only will pinching of the skin in the related areas cause pain, but a stimulus reaching the focus from any source will cause pain, for this reason, we get the phenomena of localized gastric pain after food which was taken as a leading symptom in this series of cases.

The epigastrium is the place where this referred hyperalgesia is most common, and the upper part of the/

the left rectus is the muscle most frequently contracted. The nerve supply involved comes from the sixth and seventh thoracic. When the symptoms are severe the regions supplied by the fifth and fourth nerves develope referred pain.

The vagus stimulation is thought by Mackenzie to be the source of the referred pain in the fifth cervical and upper regions.

To sum up these views. Epigastralgia and hyperalgesia, the hyperalgesia in the scapular region, over the tenth rib near the spine, and whatever other areas of hyperaesthesia are present in a stomach case are examples of a viscero sensory reflex. The stimulus from a gastric ulcer is carried by afferent nerves to the cord, round their termination in the cord an irritable focus is established affecting both sensory and motor cell areas. When a peripheral stimulus is carried along the peripheral nerves to this focus a painful sensation is experienced and referred to the peripheral distribution of the focus. The skin for instance is hyperaesthetic to pinching over the epigastrium. Such we understand to be the explanation given by Mackenzie, Head and the other workers in this field, of hyperaesthesia and pain in visceral disease, more especially in the present case of the hyperaesthesia and epigastralgia of gastric ulcer.

Pathological Changes in the Cord (19).

There is a certain vagueness about the explanation of sensory phenomena by neurologists. Research along modern lines with the microscope and improved methods of staining nervous tissue have dissipated the old terminology to a certain extent. An explosive discharge of nervous stimuli may explain epilepsy, and morbid stimuli acting on hyperaesthetic areas of the cord may explain the pain of gastric ulcer, but an infinitely more satisfactory explanation would be found if some tangible evidence of change in the cord was visible under the microscope. With this object in view we will first inquire briefly into certain phenomena observed in the spinal cord in infective conditions and endeavour to formulate certain deductions bearing, it seems to us, upon this question of referred pain.

A most important fact, which is emphasised by Adami, is that the lymphatics of the peripheral nerves are continuous from the periphery to the cord and independent of the lymphatics of the tissues through which they pass. There is a continuous lymph canal from the periphery of each nerve, from its termination to its entrance into the cord.

Orr and Rows in 1904 emphasised and corroborated the observation that the lymph flows in an ascending direction to the cord along the nerves, and that the main/

main current lay at the periphery of the nerve bundles immediately under the fibrous sheath.

Tetanus and Rabies spread to the cord by the nerves. Marie and Morax found that if the nerve to a limb was cut, tetanus toxin could be injected into the paw of an animal without any convulsions following a lethal dose.

Homen and Laitinen injected streptococci into the sciatic nerve and traced the organisms upwards into the meninges of the cord. Pironne experimented with pneumococci and found changes of a similar nature corresponding to the nerve injected. Guillain injected ferric chloride into the sciatic and subsequently potassium ferrocyanide into the circulatory system and found Prussian Blue in the posterior roots.

Sicard and Bauer using China Ink found after injection into a nerve the particles ascending along the perineural lymph stream to the cord. Arguing from these premises it was thought possible that in cases where a septic focus existed, the nerve supply to that focus might convey in its lymph stream organisms and toxins to the cord.

Orr and Rows examined the cords of cases having septic bedsores, pelvic cellulitis, empyema, caries of vertebrae with psoas abscess, suppurating knee joint, chronic cystitis and other cases having localized septic disease. In all cases they found that in peripheral nerves, spinal roots and cranial nerves, there/

there is a constant stream of lymph ascending towards the central nervous system whose main current lies in the inner meshes or lymph spaces of the fibrous perineural sheath. Toxins follow this channel and penetrate with the nerve roots into the substance of the cord. In the extramedullary portion the nerves are protected by the neurilemma sheath, but after losing this in their intramedullary part they at once show degeneration. The first change being a primary degeneration of the myelin, the axis cylinders and nerve cells being affected later.

In tabes and general paralysis there are degenerations in the posterior columns of the cord, which resemble one another, which also commence in the intramedullary portion of the sensory fibres immediately after the neurilemma sheath is lost.

The toxins in Orr and Rows' cases were shown to flow chiefly along the sensory roots and to a much less extent along the motor roots, the degeneration being always greater in the posterior columns. Homen also states that toxins reach the spinal cord more easily by the posterior roots. The posterior roots are nearly three times as large as the anterior and pour a larger quantity of lymph along their channels.

Following out these clinical facts experimentally lesions resembling those of tabes and the degenerations in/

in cases of septic foci, were produced by placing celloidin capsules containing virulent bacteria under the sciatic nerve in dogs. The toxin filtered through the capsule ascended the nerve and from the termination of the neurilemma sheath entered the nerve and cord producing degeneration.

Lesions of lymphogenous distribution in the cord have been found in tabes dorsalis, general paralysis, septic foci in the body and limbs, and also by experimental infection along a peripheral nerve.

What does this then lead to. In a series of cases following infection along nerve lymph canals, we get degenerations of the posterior columns in the cord, and to a less extent in the anterior motor root distribution in the cord.

We have thus an area of disturbance and irritation in the cord. In cases of low virulence there is long standing irritation with slow atrophy and degeneration so often met with in nervous disease. We have slow and rapid types illustrated in the varying durations of cases of tabes and general paralysis.

The common feature of these nervous degenerations during their early stages is the occurrence of peripheral areas of pain and hyperaesthesia. The causation of this pain has been attributed by Mott and other modern workers to the gradual liberation of/

of chemical irritants from the degenerating posterior root neurous.

The pain symptoms can exist for a very long time and the degeneration of the myelin be prolonged almost indefinitely in some cases before the axis cylinder is attacked. The disease may possibly intermit.

Adami in his Pathology lays stress on the minute chemical interchanges within and without the cell that can form the basis and be the result of disease. In mild infection constantly supplying minute doses of toxin along the nerve lymphatics we get a prolonged stage of chemical irritation to the sensory columns and to a less extent to the motor columns of the cord.

Reasoning from these premises it seems to us that the irritable foci in the cord of Mackenzie and Head are really the centres of toxic action conveyed along the lymphatic channels from the diseased viscus.

In the comparatively gross lesions of tabes the hyperalgesic symptoms follow the distribution of the portions of the cord that are successively attacked.

In gastric erosion there is a septic focus exposed to the varying septic contents of the alimentary tract. Along the visceral nervous lymphatics a steady stream of toxin ascends to the cord, irritation is set up in the sensory and to a less extent in the motor areas and the viscero sensory and motor reflexes of Mackenzie are the result. The hyper sensitive areas/

areas of the cord are due to the chemical action of bacterial toxins and not merely the result of the summation of peripheral stimuli from irritated nerve endings.

The question of the existence of degeneration in the cord in these cases remains to be investigated. If there are degenerations to be found among the myelin sheaths in the region of the dorsal roots five to eight of a type comparable to those described, then this theory is legitimate.

This investigation is still in progress. The difficulty of securing cords from cases of old standing gastric ulcer is considerable. However, one such case we were fortunate enough to secure.

A man aged 47 suffering from gastric pain and hyperalgesia for a period of over twenty years. Death following severe haematemesis. Post Mortem a very old ulcer surrounded with much induration and fibrous tissue formation was found; in the base were sclerosed vessels, one of which had been eroded and whose walls were held apart by the thickening of the vessel and the cicatricial tissue around.

On examination of the cord by Marchis method degeneration was found in the posterior columns from D 5 to D 9 most marked in D 6 and D 7 sections and gradually shading off. The left side of the cord was somewhat more marked than the right. The degeneration/

degeneration as a whole was much less marked than in those cases which Dr Rows showed us in his series of septic lesions at the laboratory of Lancaster Asylum.

In cases of less standing, the degeneration would probably be much less marked, or the cord might be in a predegenerative condition of irritation that would give the sensory visceral reflex without the microscopic change.

The comparison of Mackenzie's work with that of Orr and Rows is most suggestive and gives a clue to the pathological source of Referred Pain.

The whole question of the cord in gastric ulcer we hope to more fully work out as material arises, and we are convinced that in observations of this nature much that is now unexplained in referred pain, and visceral disease will be made clear to the greater benefit of diagnosis in abdominal and thoracic disease.

Discussion of these Investigations. (20).

The cause of Gastric Ulcer is not known. What then are its associations, is it a symptom of a more general disease or is it a distinct entity?

Gastric Ulcer occurs frequently among the poorer classes ill nourished and ill clad living in badly ventilated surroundings, it occurs frequently among the servants of the wealthier classes who are well/

well fed and in these days frequently a pampered portion of the community.

In association with certain diseases gastric erosion is common especially in chlorosis, amenorrhoea, syphilis, tubercle, malaria, scurvy, chronic valvular disease of the heart, chronic nephritis, and septicaemic disease of every kind.

Gastric and duodenal ulcers are often multiple, and may be associated in the same case; they may be accompanied by ulceration of the tongue, gums and cheeks, even of the oesophogus. There is hardly any toxaemic and infective condition in which gastric and duodenal ulcers may not occur. These statements are the commonplaces of the textbooks, what do they point to? The inference is that gastric erosion is not a disease in itself, but rather a local expression of some dyscrasia, of some floating poison, as Hort puts it, of some gastrolytic substance that acts locally on the mucous membrane of the stomach, and causes ulceration.

Bolton has produced gastric ulcers in animals by injecting a cytolytic serum made by immunising an animal of a different species with an emulsion of gastric mucosa. He thus injected the macerated mucosa of guinea pigs into rabbits and produced a serum cytolytic to the gastric mucosa of the guinea pig.

Turck/

Turck by introducing cultures of streptococcus Pyogenes aureus and Bacillus Coli into the stomach of dogs produced typical gastric ulcers. Weinland has postulated the presence of fixed antipeptic and antitryptic bodies antagonistic to peptic and tryptic bodies normally present in gastric and pancreatic secretions.

Hort in his recent work on gastric haemorrhage holds the view that some forms of gastric ecchymosis, gastrostaxis and gastric ulcer are local expressions of a general blood disease; that ecchymosis may be associated with gastrostaxis and both with gastric ulcer; that as a symptom of an unnamed general blood dyscrasia ulcer may occur without preceding ecchymosis or gastrostaxis; and that ecchymosis and gastrostaxis are due to the presence of endotheliolytic bodies in the blood, and that gastric ulcer itself is due to the presence of floating haemorrhagins, mucolysins and other cytolysins in the blood.

Considerations such as these suggest that in cases of gastric erosion clinical observations should be directed to the discovery of evidence of infection and general toxaemic conditions. Without recourse to elaborate laboratory equipment a certain number of observations are possible where an incubator and a microscope are available, and a moderate supply of test tubes and reagents.

The/

The present investigation aims at applying the resources of a minor laboratory to the observation of cases from this point of view.

In all 75 cases the records were made within the first three or four days from the patients coming under observation. The conditions accompanying gastric erosion, and not the progress and cure of the lesion were investigated. If there is a generalised infection in these cases, facts pointing to its existence must be looked for in untreated cases. Also the more full the clinical investigation at this stage the better the indications for the plan of campaign with regards to treatment. The results obtained are not offered as explaining the cause of gastric erosion, but are taken as indications of the general condition that accompanies this lesion, and of the possibilities for general infection and toxaemia to be found in these cases.

The results of the various observations may be here summed up.

1. A series of cases complaining of gastric symptoms over a long period of time in the great majority of instances were examined. A series of 75 cases were picked out because they displayed the two leading symptoms of gastric erosion viz. Epigastralgia and Haemorrhage. Employing every precaution

to/

to eliminate other sources of haemorrhage, the vomit and stool was tested for macroscopic and occult blood.

2. A complete Blood Count was performed to determine the degree of Anaemia in each case. The digestion leucocytosis was determined and where it was decreased or absent special care was taken to exclude cancer. This resulted in three cases being proved cancerous and eliminated from the series.

3. The resistance to Haemolysis was determined in 30 of the cases to determine if the resistance of the red cells was lowered to haemolysis by a standard solution of a haemolytic agent.

The result of this blood examination showed a degree of anaemia, and a decrease in haemoglobin that could not be accounted for by loss of blood from haemorrhage. The resistance to haemolysis was also weakened as compared with that of healthy individuals.

4. A determination of the presence or absence of Bacillus Coli in the Urine and Stomach was made.

While the writer was Resident to Sir Thomas Fraser in the Edinburgh Infirmary all gastric cases admitted to the wards were given olive oil enemas on admission. As a result the axiom/

axiom might have been propounded that all gastric cases especially those with gastric ulceration are constipated. No matter how strongly the patient averred regularity of defaecation the result of the enema was to disclose constipated masses.

If then there is intestinal stasis in these gastric erosion cases, and careful inquiry shows it present in almost all of this series, how far does this stasis lead to infection and toxaemic absorption.

The Bacillus Coli is easily traced, where it passes other infection may also pass; leaving for the present the specific action of its toxins aside, the presence or absence of the Colon Bacillus seemed a just indication of the extent of infection possible from the retention of putrefying faeces in a sluggish intestine.

The result was that out of 75 cases only 8 were entirely free from Bacillus Coli in either the Urine or Stomach or in both.

5. In order to discover if this presence of Bacillus Coli had a specific influence on the individual infected the agglutination and Opsonic Index were tested, and compared with the results in healthy controls. This investigation showed an agglutination reaction/

action in 48 out of 75 = 64% and an opsonic index outside the limits given by the control cases in 54 out of 75 cases = 72%.

6. In order to test whether intestinal stasis could cause sufficient reflux mucus carriage of bacilli to account for their presence in the stomach, a number of experiments were made with powdered Indigo after the method of Bond. By introducing Indigo particles into the rectum and examining the stomach contents at intervals it was proved that Indigo particles in cases of intestinal stasis can travel in the mucus currents of the intestine from the rectum to the stomach in from 5 to 13 days, while in the healthy acting intestine such a reflux is not found.

In cases of constipation from intestinal stasis there is therefore a possibility of upward infection of the stomach from the lower reaches of the intestine owing to these reflux currents of mucus loaded with bacteria. There is also a greater tendency to the long retention of bacteria in the upper regions of the intestine and a greater opportunity for their passage out through the walls of the intestine into the circulation as shown by their elimination by the kidneys, and a greater chance of gall and pancreatic duct infection.

7./

7. As a most frequent source of sepsis in gastric disease exists in Pyorrhoea Alveolaris a series of observations was made on the cases in the series.

In 51 out of 75 cases Pyorrhoea was found to exist, or 68%.

As Pyorrhoea is a possible source of Pancreatic infection, the relationship of Pyorrhoea and the Cammidge reaction was tested. The result was, that 47 cases out of the 75 cases gave a Pancreatic reaction while of these no less than 42 suffered from Pyorrhoea. Otherwise 82.3% of the gastric cases with Pyorrhoea, who were examined had some degree of Pancreatitis.

8. As a control to the inference made concerning the relation of Pancreatitis and Oral Sepsis three series of observations were made.

In 8 of the cases combining Oral Sepsis with Pancreatic Reaction the organisms in the gums were examined. These cases showed the presence of cocci, staphylococci and streptococci and the micrococcus catarrhalis, with an occasional bacillus and pneumococcus.

In 10 cases free from Cammidge Reaction the pancreas was examined and cultures made within 12 hours of death. This showed that the Bacillus Coli was frequently present without causing the/

the reaction. In two cases Cocci were also found.

Lastly in 4 cases of combined Oral Sepsis and Positive Cammidge Reaction, similar organisms were grown from the gums during life and from the pancreas after death.

The number of cases in which post mortem examination was possible is unfortunately small. The result of the few cases examined goes, however, towards confirming the inference already drawn, viz. that in cases of oral sepsis the pancreas may be affected by organisms swallowed and as a result pancreatis may be established and the pancreatic reaction appear in the Urine.

The Pancreatic Reaction may therefore be taken as an indication of gastric and duodenal sepsis.

9. As a further test for Bacillus Coli infection in the cases of this series an attempt was made to get a cutaneous reaction to the Bacillus Coli analogous to the reaction of Von Pirquet in tuberculosis. The cases were subjected to the test and two series of controls were also examined. As a result 37 cases out of 75 reacted to the inoculation, and in the controls who were known to be infected 11 out of 12 cases gave a positive reaction, while the healthy/

healthy controls remained unaffected.

This observation therefore showed a distinct tendency towards a reaction analogous to the tuberculin test, and gave additional weight to the suspicion of a bacillus coli infection.

10. Epigastralgia was employed as one of the two main symptoms for the selection of cases for this investigation. The presence of areas of skin hyperaesthesia was found in 88% of the cases.

A comparison was drawn between the hyperaesthetic areas of the cord created by peripheral stimulation according to the theory of Mackenzie and Head and the areas of degeneration following a lymphogenous distribution as found clinically and experimentally by Orr and Rows. Similar degenerations were found in the cord of one case of gastric ulcer and are being searched for in an investigation which is not yet complete.

This part of the research tends to bring the subjective symptoms of gastric ulcer under the general theory of an intoxication from bacterial toxins.

The conclusions we would arrive at from a consideration of these results are as follows.

Gastric Ulcer has been produced experimentally by feeding animals on virulent organisms such as Streptococci and Bacillus Coli.

Gastric/

Gastric Ulcer appears rather as a symptom in a general dyscrasia than as a morbid entity.

On looking for symptoms of septic infection and its consequences in cases of gastric ulcer we find the following.

I. An anaemia unexplained by haemorrhage.
A decreased resistance to haemolysis.

In this connection we remember that the Gastrotoxic serum of Bolton is also a haemolytic agent, and that the products of bacterial action in the body give rise to haemolytic agents as for instance the Colilysin formed by the Bacillus Coli.

II. The presence of Bacillus Coli in the stomach is more frequent in the cases of gastric erosion than can be explained by accident. The presence of Bacillus Coli in the Urine is also frequent, and points to infection from intestinal stasis.

III. From the agglutination and opsonic index to Bacillus Coli it was shown that in gastric ulcer these tests are more frequently in favour of an infection than can be possibly explained by experimental error or chance selection of cases.

IV. By experiments with Indigo intestinal stasis was proved to be the chief factor in infection of the stomach with Bacillus Coli and other products of the lower intestine.

V./

V. Another source of bacterial infection is present in cases of Pyorrhoea. The activity of this infection may be judged from its relationship to pancreatis.

VI. In gastric ulcer a considerable number of cases give a cutaneous reaction to the Bacillus Coli thus favouring the theory of infection by that organism.

VII. The subjective hyperaesthesia of gastric ulcer is capable of explanation by the theory of bacterial infection conveyed along the nerve lymphatics to the cord causing foci of irritation and degeneration in the cord.

We can therefore find clinical and pathological evidence in cases of gastric ulcer of bacterial invasion and infection.

By the action of bacterial toxins and their products in the circulation and lymph stream we can explain the symptoms and clinical facts of gastric ulcer.

These results therefore tend to further the view that gastric ulcer is not an entity of disease but is a symptom of a systemic infection.

A further clinical support for this view is found in the treatment advocated by Hart for cases of gastric and duodenal ulcer. Hart argues that these ulcers are a local expression of some dyscrasia

and/

and suggests the action of a floating mucolytic poison. So long as this poison is present, recurrence will take place, when this factor is removed cure follows by cicatrization and exclusion by this means of the ulcers base and sides from the lymph stream. In an untreated case we find periods of suffering alternating with periods of comfort or absolute ease. In quiescent intervals we have sometimes evidence of the ulcer not being healed as by the appearance of haemorrhage. Yet manifestations of activity producing suffering may only appear at certain seasons of the year or during periods of depression mental or physical. The eroding influence of gastric juice and the presence of food substances have been constantly present, the clinical change is due to another unknown factor that determines the change from quiescence to activity.

It is reasonable to suppose a fresh activity of specific poisons in these cases and it is essential to raise the resistance of the cells and the nutritional defences of the body to combat this activity.

Proceeding on these lines Hart has treated more than 200 cases of ulceration in the stomach and duodenum as follows.

In acute cases with haemorrhage he gives subcutaneous injections of sterile normal horse serum and feeds chiefly on meat.

In /

In chronic cases he gives full meat diet with repeated doses by the mouth of an antilytic serum specially prepared. Of his cases 2 have had temporary relapses and 1 was a failure due to inability to pursue the treatment.

The rationale of the treatment is best given in Hart's own words.

"If it be true that duodenal ulcer is a symptom and not a disease, the absorption of adequate protein cannot but increase the resistant powers of the body as a whole to the determining cause of the disease. Local repair will moreover be assisted.

"If protein food be presented to a case of ulcer in which we know that the digestive fluids exhibit a high degree of peptic and tryptic avidity, a certain proportion of these peptic and tryptic molecules will be saturated by the protein. If now at the height of digestion, be added a serum with a high antipeptin and antitrypsin content, some of the unsatisfied residue of peptic and tryptic bodies will combine therewith and the ulcer itself be thus indirectly shielded by diversion of these bodies.

"If an ulcer is being constantly bathed in secretions laden with trypsin and other proteolytic ferments set free from disintegrated leucocytes, other tissue cells and from bacteria, the administration of a serum charged with antipeptic, antitryptic/

tic, antibacterial and other inhibitory bodies cannot but have great value. That is to say the eroding activity of ferments from these sources must to a great extent be kept in check by such serum."

Taken in connection with the foregoing, the results of Dudgeon with normal and immune horse serum, as regards agglutination, phagocytosis, and bacterial action assume considerable importance. Similar results are quoted from various authors by Emery in his recent work on Immunity. Horse serum has a marked effect in agglutinating the bacilli, in increasing the opsonic index with human corpuscles, and in exerting a bactericidal action, these results are enormously increased by immunising the animal to the Bacillus Coli. Similar effects are displayed towards staphylococci in the experiments quoted.

The rationale of Hart's treatment is thus supported by these properties of horse serum.

The conclusion from this series of observations we would express as follows.-

During the active period of gastric erosion as determined by subjective and objective clinical evidence we have an unknown poison at work.

During this phase we have also evidence of bacterial invasion of the stomach itself, and of the body at large, from the presence of bacteria in abnormal places, and from the altered reactions of the blood serum.

Sources/

Sources of this bacterial infection lie in chronic constipation and in oral sepsis.

The subjective and objective symptoms of gastric ulcer can be completely explained by the action of these bacteria and their products on the body fluids and the spinal cord.

The cure of gastric ulcer will best be arrived at by attacking this systemic infection and raising the resistance of the organism as a whole while means are also taken to allay the local symptoms.

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We have endeavoured to make this investigation as free from quotations as possible and to lay most stress on the results of clinical and pathological observations.

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