The undersigned, acting as a Committee of
the Graduate School, have read the accompanying
thesis submitted by Egerton Lafayette Crispin
for the degree of MASTER OF SCIENCE. They ap­
prove it as a thesis meeting the requirements
of the Graduate School of the University of Minne­
sota, and recommend that it be accepted in partial
fulfillment of the requirements for the degree of
MASTER OF SCIENCE.

Christopher Graham,
Chairman

H. L. Ullrich

A. F. Hamilton

May 23, 1917.
REPORT
of
Committee on Thesis

The undersigned, acting as a Committee of the Graduate School, have given the final oral examination to thesis submitted by Egerton Lafayette Crispin for the degree of MASTER OF SCIENCE. They approve it as a thesis meeting the requirements of the Graduate School of the University of Minnesota, and recommend that it be accepted in partial fulfillment of the requirements for the degree of MASTER OF SCIENCE.

[Signatures of Committee Members]

May 23, 1917.
Clinical Studies in Abdominal Disorders

A Thesis
Submitted to the Faculty
of the
Graduate School
of
The University of Minnesota

by

E. L. Crispin

In partial fulfillment of the requirements for

the degree
of
Master of Science

1917
CLINICAL STUDIES IN ABDOMINAL DISORDERS

E. L. Crispin, M. D.
Los Angeles, California
While the development of gastric surgery has proved ulcer to be the most frequent cause of bleeding from the stomach and duodenum, the coincident development of pathology in the living has emphasized the fact that frequently there may be gastric hemorrhage without any demonstrable surgical gastric lesion. The opinion is prevalent among the laity that hematemesis means ulcer requiring operation, and hemorrhage from the stomach is often too readily accepted by physicians as sufficient evidence to warrant surgery. I wish to call attention to the hemorrhages occurring from other than true surgical lesions, and to the importance of differentiating the causes of bleeding that are medical from those that are surgical.

The calloused ulcer derives greatest benefit from surgery. However, gastric surgery has been too often resorted to without benefit to the patient. Particularly is this true in cases in which hemorrhage was the principal cause of exploration. Often when an abnormal constitutional condition is not obvious, bleeding from the upper gastro-intestinal tract is considered as coming from a so-called hidden or non-symptomatic chronic ulcer, and the patient carries a gastro-enterostomy for

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ulcer for which there was not sufficient evidence before operation and no evidence at the time of operation. The burden of differentiating hemorrhage due to chronic ulcer from hemorrhage due to non-surgical conditions rests with the internist.

It is true that we occasionally see ulcers, benign and malignant, of which the histories are meager and alone are not sufficient for clinical conclusion. The proportion of these will decrease with a more general knowledge of the varying clinical factors that are helpful in the recognition of the atypical group, and roentgenology will further assist in their diagnosis. Clinical study supplemented by the diagnostic efficiency developed in gastric roentgenology has made it possible to determine the presence or absence of the bleeding gastric lesions that can be benefited by surgery in a very large percentage of the cases of hemorrhage from the stomach.

To designate the oozing of blood from the stomach in the supposed absence of chronic ulcer, Sir Edwin Cooper Perry suggested to Hale White the term "gastrostaxis," which is similar etymologically to "epistaxis." White advanced the opinion that there might be a clinical group of this type among young women having pain, vomiting, and hematemesis, without ulcer symptoms, and in whom spontaneous recovery was the rule. The suggestion brought out considerable discussion in regard to gastric hemorrhages of obscure origin by White, Bolton, and Hort. As the conditions in which such hemorrhages usually occur are toxic, the term "toxic gastric
hemorrhage" suits our purpose better and will be used in referring to them here.

Blood that is vomited and tarry stools do not always mean hemorrhage from chronic gastric ulcer. Blood from the lungs and pharynx may be swallowed and later vomited. Bleeding from esophageal varices, particularly when associated with the toxic state in cirrhosis of the liver, may be severe and have the appearance of gastric hemorrhage. In the purpuræ, leukemias and anemias, especially anemias associated with enlargement of the spleen and liver, there may be severe bleeding from the stomach. In constitutional diseases and toxemias associated with hepatic and renal disease, it is common to find on necropsy that the gastric mucus membrane is intact, though vomiting of blood occurred during life. Blood may be vomited during exacerbations in states of hypertension and in secondary congestions of the liver and spleen. Endocarditis may be a remote cause of gastric hemorrhage. Also, exudative erythemic states of the viscera are possible causes of bleeding. Arteriosclerosis of the abdominal vessels with aneurysmal dilatation and rupture into the stomach has been reported. During the attacks of gastric crises in tabes, there is often coffee-ground vomitus and at times bleeding may be severe. Young females may have extensive hemorrhages with no proof of chronic ulcer and with usually spontaneous recovery.

With infections of the gall bladder and appendix there are
occasional hemorrhages for which no adequate cause in the stomach is found at operation. In an operated series studied in a large middle western clinic, the Mayo Clinic, bleeding was associated with infections of the gall bladder and gastric symptoms in 5 per cent., and with appendicitis and gastric symptoms in 2 per cent. Deaver mentions infections in the fallopian tubes as a causative factor in some cases of gastric hemorrhage. Bleeding from follicles or superficial erosions in the stomach permitting hemorrhage may be secondary to acute infections in the tonsils. Rosenow has shown the association of various streptococccic infections with bleeding from hemorrhagic points and superficial ulcers in the gastric mucosa. These may become so extensive that large patchy areas of the mucosa ooze blood, though when wiped off, individual points are made out with difficulty.

Dieulafoy has called attention to gastric bleeding from the two following varieties of non-chronic ulcer: (1) Simple erosions consisting of mere abrasions of the surface epithelium. These, though so small as to be scarcely perceptible to the naked eye, may give rise to alarming hemorrhages. At necropsy they may be easily overlooked, but during the course of the hemorrhage the mucous membrane appears to be studded with numerous bleeding points. (2) Ex-ulcerative simplex. The lesions of the type to which Dieulafoy applies this term are rather more extensive, and the surface layers are removed to such an extent that the
arterioles running under the muscularis mucosae are exposed. This form may give rise to severe hemorrhages that may even prove fatal. When the stomach is opened, the condition appears as small bleeding fissures, small patchy areas oozing blood, or thick hemorrhagic infiltrations from which blood literally seeps.

Deaver, in discussing hemorrhagic disease of the stomach not associated or closely related to gross ulcer, says: "Excepting extrinsic poisons, I believe the violent congestion of the gastric vessels is primarily dependent on an intra-abdominal, or more rarely, remote, focus of infection." This focus of infection he believes is most commonly the appendix or gall bladder. According to Mayo Robson the gastric lesions after death in some cases of sudden severe hemorrhages, particularly in the young in whom there is no clinical evidence of ulcer, seem altogether inadequate to explain the nature of the serious hemorrhages. It is his opinion, also, that: "Capillary oozing or bleeding from arterioles is much more common and accounts for many more cases of gastric hemorrhage than has hitherto been supposed." Hemorrhages of this kind, parenchymatous hemorrhages in the apparently healthy male, hemorrhagic gastralgias and the large group of variously defined bleedings from the stomach in which there is sudden onset, absence of symptoms and usually spontaneous recovery, are of infective or toxic origin, and for these surgery will be of doubtful benefit.

Typical acute gastric ulcer may be the source of repeated hemorrhages if there is erosion of the vessels at its base, but rarely
causes fatal bleeding. At operation these ulcers may be shallow and not visible or palpable through the wall of the stomach. When secondary to gross infection elsewhere, mucous ulcers may be multiple. Chronic gastric and duodenal ulcers as a rule do not bleed copiously. Bleeding from malignant disease usually is small in amount like that from ulcer, and more or less continuous.

In seeking a cause for gastric hemorrhage a history of ulcer should be sought and, when necessary, diagnostic evidence should be brought out by every adjunctive means available. If evidence indicating ulcer is not strong, effort should be made to prove or exclude all the numerous conditions that might be underlying causes of the hemorrhage.

In general, surgery offers the best results for ulcer of the chronic calloused type. In this condition the symptoms of ulcer are marked and the patient goes to the physician usually because of the distress from the ulcer rather than because of the hemorrhage. A second group of patients with gastric hemorrhage lays greater emphasis on the bleeding and complains only of gastric symptoms that are more or less indefinite. In such cases effort must be made to determine the presence or absence of calloused ulcer or of a toxic or infective condition as the cause of the hemorrhage. A third group of patients are those who come for examination because of the hemorrhage, but whose gastric symptoms are of minor importance. They believe they have an ulcer, frequently have been told that they have an ulcer, and have often resorted to gastric
surgery which has not prevented subsequent hemorrhages.

Speaking broadly, cases of hemorrhages without gastric symptoms, either before or after surgery, should be considered toxic. The nonsurgical nature of the causative factors, such as the blood diseases and secondary congestions, are, usually easy to determine. Medical observations will further develop the exact nature of many hemorrhages of the toxic group and relegate them to their proper medical sphere. When an infective source, either intra-abdominal or remote, is found, the possibility of an association between the gastric hemorrhage and this infected atrium should be considered. In many cases the hemorrhage is probably toxic. When medical observation determines the presence of abnormal constitutional states such as diseases of the blood, renal toxemias, disproportional varices, pathologic vascular tensions, multiple angomas, syphilis or tuberculosis, the hemorrhage should be considered of toxic nature.

Correction, when possible, of the underlying conditions, and waiting, rather than surgery, is advisable. Any surgery in these cases should be only in the nature of exploration without promise as to results. Spontaneous hemorrhage occurring in young women and parenchymatous hemorrhages in which evidence does not point to chronic ulcer, should also be considered toxic. They are not surgical; spontaneous recovery is the rule.

Patients giving a history of repeated severe hemorrhages over many years, with an ulcer history, which though not clear-cut, is strengthened by adjunctive evidence, and in whom no constitutional cause can be
found, should have an exploratory operation. In such cases, the hemorrhage is probably due to a surgical condition. Well-nourished patients who have had one or a few hemorrhages, and for whom the clinical or contributory data is very poor, may be considered toxic until medical observation proves the absence of a constitutional condition as a factor, or time brings out evidence of ulcer. If surgery is indicated at all for gastric hemorrhages occurring in the presence of intra- or extra-abdominal infection, and accompanied by indefinite gastric symptoms, it should be applied to the focus of infection rather than to the stomach.

Patients who have had repeated hemorrhages for many years, who are past middle life, whose general appearance is below par and for whom the history and evidence of ulcer is indefinite, should also be carefully studied for toxic causes. The following abstracts of histories will serve to illustrate various types of gastric hemorrhage.

**CLINICAL EVIDENCE ALONE INSUFFICIENT FOR ULCER.** 
**EXPLORATION BECAUSE OF POSITIVE ROENTGEN FINDINGS.**

Case 146581, M.C.D., traveling salesman, age 52 years. Examined November 20, 1915. Patient had been having hemorrhages from the bowel, black and tar-like, for thirty years; in all, about twenty; in bed after each attack. The last hemorrhage occurred in June, 1915. Three hemorrhages in 1913. No clear-cut gastric history, though he had had distress for days at a time, and on a few occasions for a couple of weeks.
Food relief variable; never used soda; never had colic. Present trouble with stomach of about two weeks' duration. He dieted for two years, but did not obtain relief. In present attack he had had a little distress at night, varying from 11:00 P. M. to 5 A. M., and some distress after meals. Most of the hemorrhages "have come out of a clear sky when he was feeling his best." Epistaxis frequent in youth, but never put him to bed. Examination: A healthy-looking man, 5 feet, 9 inches in height, weighing 145 pounds; no weight loss. Mucous membranes somewhat pale. Multiple pea-sized, raspberry angiomas over body. Haemoglobin 70 per cent. Gastric analysis: acids 58, 44, 14; no food remnants. Wassermann negative. Coagulation time three minutes. Blood pressure 128, 90. Eye grounds negative. Urine negative. Proctoscopic findings negative. Roentgen findings: Cap deformity; duodenal ulcer.

A history covering thirty years with slight symptoms except for bleeding, clinical absence of obstruction at the pylorus, and the angiomas over the body, made diagnosis doubtful. An exploratory operation was performed because of the roentgen evidence. A duodenal ulcer was found one-half inch below the pylorus.

CLINICAL AND ADJUNCTIVE EVIDENCE INSUFFICIENT FOR ULCER. CONSIDERED TOXIC AND NOT NOW SURGICAL.

Case 141079, T. A. C., advertising manager of a newspaper, aged 50 years. Examined September 15, 1915. Patient has been in the habit of eating fast; he worked hard; burned the candle at both ends. Formerly
a printer. Twenty-five years ago he had anemia, which he thought was
due possibly to lead poisoning. In the last twenty-five years he had
had a few attacks of gastric trouble lasting a week or two. Symptoms
meager. In October, 1914, he fainted one day while in the toilet;
soon vomited food and blood. Vomited clots three times within a short
period. Had tarry stools for the following three or four days. Was
put on a Von Leube diet, and rapidly regained his health; well since.
Came for examination 11 months later because an ulcer had been diagnosed
at the time of the hemorrhage. No symptoms since hemorrhage except a
little discomfort without food relation, in the left hypochondrium.

Examination: Height 5 feet, 10½ inches; weight 195 pounds; no weight
loss; skin somewhat highly colored. Blood pressure 178, 100. Gastric
analysis: acids 66, 56, 10. No food remnants. Haemoglobin 89 per cent.
Differential blood count normal. Coagulation time eight minutes. Wassermann negative. Negative fundi. Urine showed a few hyalin casts.
Roentgen findings: Stomach indeterminate.

On account of lack of evidence of ulcer, and because of the
blood pressure, urine findings, coagulation time, and patient's generally
well-nourished condition, diagnosis was made of toxic hemorrhage. He
was advised about caring for his general health, and sent home for obser-
vation.
NEGATIVE GASTRIC EXPLORATION. CONSTITUTIONAL STATE.

VISCERAL ANGIONEUROTIC EDEMA BELIEVED TO BE CAUSE OF BLEEDING.

Case 101588, W. H. S., paper hanger, aged 40 years. Examined March 4, 1914. This patient had been urged a number of times to have operation for gastric ulcer. He had had gastric trouble intermittently for twenty-three years. When 17, the cramps were so severe as to double him up. He used to tie a towel tight around his waist, and a number of times was rolled over a barrel to relieve the cramping pain. These attacks came frequently for a few weeks and then disappeared for weeks or months. Only occasional trouble between the ages of twenty and thirty. In an attack when about 31, he vomited a large handful of clots of blood. No clear-cut food relation to gastric pain. Present attack three weeks. No regularity. For three months has had most marked angioneurotic disturbances. Large plaques came out on his skin each night. Roentgen findings: "Lesion of the stomach at or near the pylorus." The patient had angioneurotic swellings. At exploration (C.H.Mayo) neither lesion nor cause for hemorrhage was found in the stomach. The gall bladder, showing doubtful pathology, and the appendix, were removed.

The attacks of pain have continued since operation without any material change in nature. They are regarded as visceral manifestations of angioneurotic edema. Because of the constitutional condition the
hemorrhages may be considered toxic.

YOUNG WOMAN. HEMORRHAGE. TREATMENT FOR ULCER. NO SYMPTOMS OR EVIDENCE OF ULCER. SPONTANEOUS RECOVERY.


She complained of gastric trouble and hemorrhage. Eighteen months before a severe hemorrhage occurred in the stomach; melena persisted for a number of days. She was put to bed and kept on milk diet for seven months. Her physician said the bleeding came from an ulcer in the stomach. She had been away at school, had eaten irregularly and injudiciously a large amount of candy; enjoyed social activity, dancing, tennis, etc. Indefinite distress in the stomach began a month or two before the hemorrhage, about the middle of the school year. Stomach always tender, with pain and soreness after eating ordinary foods; never free periods. No food relief. Menstruation irregular, increased flow for three years; for two weeks at each period a profuse flow. Patient said she had had grippe three or four times. Wrenched her back four years ago and it "had been sore ever since." Examination: A thin, somewhat pale young girl. Very nervous. Weight 104 pounds. Blood pressure 100, 78. Urine negative. Haemoglobin 89 per cent. Gastric analysis: Acids 20, all combined. No food remnants. Roentgen findings: Stomach negative. At the hotel the patient ate everything and forgot all about her stomach.

Because of the hemorrhage, she firmly believed that she had an
ulcer, as did her mother and her brother, a physician. Her physician had advised operation for ulcer. The seven months in bed on ulcer treatment had made her a marked neuroathenic. There was neither clinical nor laboratory evidence of ulcer. Patient was told that there was no evidence of ulcer and operation was not advised.

**GASTRIC ATTACKS WITH HEMORRHAGES, FOLLOWING TONSILLITIS.**

Case 145217, Mrs. R. T., aged 24 years. Examined November 8, 1915. Epigastric pain, hemorrhages from stomach. She has had repeated attacks of tonsillitis and rheumatism. Distress in stomach at times for eight years. Cramp-like pains lasting five or ten minutes associated with nausea. Vomited during the first five years, but seldom vomited food. Has had numerous hemorrhages from stomach, in one of which she lost a quart of blood. Gastric symptoms lasted ten days to two weeks; she was then relieved for a period of months. No definite food relationship. The pain was present, even when a strict diet was maintained. About three attacks of tonsillitis each winter. Gastric attacks always followed tonsillitis. In a remission four weeks before there was a hemorrhage from the stomach. **Examination:** Short, soft, systolic blow heard at cardiac apex. Blood pressure 122, 82. Pulse 68. Temperature 99.2. Urine negative. Haemoglobin 70 per cent. Gastric analysis: Acids 46, 28, 20. Roentgen findings: Chest negative; stomach indeterminate. **Consultant's note:** "Not typical ulcer. History suggest superficial type of acute lesion with hemorrhage. The frequency with which
tonsillitis has preceded attacks is interesting." Tonsillectomy by
Dr. Matthews. Culture from tonsils by Dr. Rosenow showed streptococci, and animals injected showed multiple hemorrhages and superficial ulcers of the stomach, due to streptococci. Hence these hemorrhages, which seemed to be toxic, were apparently due to the localized hematogenous infections of the mucous membrane of the stomach, following tonsillitis.

GASTRIC SYMPTOMS WITH HEMORRHAGES. EXPLORATION: CHRONIC APPENDICITIS. NEGATIVE GALL BLADDER AND STOMACH.

Case 126387, E. C. P., contractor and builder, aged 46 years. Examined March 12, 1915. This patient had had myalgias, followed by ecchymoses that put him in bed for three or four days. For fifteen years he had had trouble with his stomach, which came on in spells, formerly lasting for months. Trouble now continuous. Had had some food relief and relief by alkalies and vomiting. A burning sensation was felt in the stomach usually from 10:00 to 11:00 P.M. Hemorrhage from the stomach. Vomited a large quantity of blood during a period of two days. Four months ago had another hemorrhage, and at that time tarry stools. Described pain radiation as being "most anywhere" in the upper abdomen. Patient very nervous; continuous headaches for last two months.

ulcer (W.J. Mayo). **Findings at operation:** "Sub-acute appendicitis. Appendicitis apparently would account for symptoms, as it was rather unusually well-marked. Gall bladder and duodenum normal. Gall bladder somewhat adherent, but empties easily and contains no stones." Appendix removed. After negative exploration of upper abdomen, the hemorrhages were believed to be toxic, secondary to the infection in the diseased appendix.

GASTRIC SYMPTOMS, HEMORRHAGE, CAME FOR "ULCER" CHOLECYSTITIS AND PANCREATITIS. NEGATIVE STOMACH AND DUODENUM.

Case 124020, Mrs. N. M., aged 36 years. Examined February 8, 1915. Trouble with stomach began four years ago. First attack, four months. One free period of three years. Second attack began one year before; was ill nine months. She had pain nearly continuously except when eating. Vomited sour water. Once she had delayed vomiting. Slight food relief. Soda relief formerly. Had sharp cutting pain in left epigastrium, for which her physician had given morphia. Tarry stools. Coarse and sour foods caused distress. Patient referred to the Mayo Clinic, with a diagnosis of ulcer and hemorrhage. **Examination:** A very neurotic, fairly well-nourished woman. Area complained of the left epigastrium. Slight tenderness to deep pressure in right lower abdomen. Blood pressure 125, 80. Urine negative. Haemoglobin 85 per cent. White blood cells, 7000. Gastric analysis: Acids 28, 12, 16. No food remnants. Roentgen findings: Stomach indeterminate. The physician at home and the patient were sure that ulcer was the cause
of her distress and bleeding. She was under observation a week, then sent for exploration of the stomach, gall bladder and the appendix. Cholecystectomy and appendectomy were done. Findings at operation: (E. S. Judd) "Definite chronic cholecystitis and chronic pancreatitis. Head of pancreas twice its normal size; chronic appendicitis; stomach and duodenum negative."

NEGATIVE EXPLORATION — TOXIC CONSTITUTIONAL CONDITION —

CARDIO RENAL SYNDROME WITH TRANSIENT HYPERTENSION.

Case 135561, H. R. T., bank cashier, aged 60 years. Examined July 17, 1915. Patient had had hemorrhages from the bowels (tarry stools) seventeen years, ten years and five years ago. In September, 1914, also vomited blood; collapsed. In years past had to be careful of his diet and had intermittent discomfort. A clear history was difficult to obtain. A diagnosis of ulcer was made after each hemorrhage. In the Fall of 1914 a gastrojejunostomy was done for "ulcer on anterior duodenal wall one inch below the pylorus." Four weeks before coming for examination he had collapsed, and the next day had profuse tarry stools. Examination: Five feet, seven inches in height; weighed 130 pounds; underweight. Appeared weak, and had marked pallor. Some bagginess under eyes. Solera pearly; looked nephritic. Heart five inches to left. Diastolic murmur at aortic area. Blood pressure 185, 85. Haemoglobin 45 per cent. Coagulation time six minutes. Differential blood count normal. Gastric analysis: Acids 64, 54, 10. No food remnants. Wassermann negative.
Old patches of hemorrhages in fundi. Phenolsulphosphthalein functional test 43 per cent. in two hours. Roentgen findings: Gastroenterostomy functioning; otherwise negative. Patient gained on ulcer diet; was kept under observation for three weeks. Believed to be gastrotoxic, but because of reported presence of ulcer at the time of gastroenterostomy done elsewhere, and in order to clear up the nature of the condition, an exploratory operation was performed (W. J. Mayo). Surgical report:

"Two inches of the stomach and two inches of the duodenum were resected. Gastroenterostomy in good condition. Site of supposed ulcer on duodenum resected. Patient in wretched condition." Pathological report: Pyloric ring of stomach normal; on section scar of ulcer could not be found.

The patient gained rather slowly after operation. About three months later he had a very severe hemorrhage. Was found unconscious in a pool of blood in the bathroom. A letter from his home physician stated that a blood pressure of 250 systolic had been recorded a few days before the hemorrhage. It is probable that all of the bleedings were the result of a constitutional state, toxic in type, and of a nature that surgery could not benefit.

SUMMARY.

Toxic gastric hemorrhage is essentially a medical condition. Hemorrhage does not always mean chronic ulcer. Surgery should be resorted to for the calloused type of ulcer, and for this type only will it give the best results. Recognition of the true cause of hemorrhage from
the upper gastrointestinal tract is sometimes most difficult. At times evidence will warrant exploration to prove or exclude peptic ulcer as a cause. The presence of a constitutional disease without sufficient evidence of ulcer, makes medical observation and study, rather than surgery, advisable. In cases of hemorrhage of obscure origin, search for infected foci should be made and the possibility of their association with the cause of the hemorrhage should be considered. In addition, studies of blood diseases associated with bleeding, and further studies in blood pressure, with recognition of transient hypertensive states, will help to define and separate hemorrhages having their origin in surgical ulcer from gastric hemorrhages of acute infective and toxic origin.
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DUODENAL ULCER WITH ACHLORHYDRIA.

E. L. Crispin, M. D.
Los Angeles, California.

In duodenal ulcer the total and free acids are usually high. The free acid frequently has a higher relative proportion than normal. Subnormal acidities are occasionally recorded. In gall bladder disease subacidity and achlorhydria are quite common. When the clinical history is not distinctive of either lesion, and particularly when there are no direct roentgen findings, the gastric analysis is used to influence the weight of evidence in making the diagnosis. Gastric analysis showing an achlorhydria with the usual test breakfast technique should not too strongly prejudice against a diagnosis of duodenal ulcer, if the evidence given by the patient indicates ulcer.

The following is a brief review of the history of 11 cases in the Mayo Clinic of operatively proved duodenal ulcer in which the gastric analysis showed an absence of free hydrochloric acid.\(a\)

The analyses were made by the routine technique used in the Clinic. Patients sent for gastric analysis are instructed to eat an evening meal of bread, meat, potatoes, etc., to be followed later by about


(a) This number is less than 1 per cent. of the total number of duodenal ulcers demonstrated at operation.
twenty raw raisins. In the morning they are given a test breakfast consisting of 30 grm. of arrowroot biscuit and 400 c.cm. of water. The water is served in two portions, one warm and the other cold. The test breakfast is withdrawn after from fifty to sixty minutes and any remnants of the evening meal are noted. The gastric content is filtered and titrated with phenolphthalein and dimethylamidoazobenzol. When the amount of free hydrochloric acid is below 20, Gunzburg's test is done. This is delicate to .005 per cent. for free hydrochloric acid. The Rehfuss acidity curves and short-time motor meals are not done as part of the routine examination.

Ten of the eleven patients in this series were males. The one female, aged thirty-seven, was the youngest. The oldest patient was sixty-six. The average age was fifty-four years. Four of the patients had used alcohol moderately, i.e., 1 on a basis of 0 to 4. Seven had been moderate users of tobacco. In no case was there history or evidence of syphilis. In all there was weight-loss, the greatest being 94 lb., the least 5 lb., and the average, not counting the very excessive loss of 94 lb. in one case, 15 lb.

It is interesting to note that as regards previous illnesses, four of the patients (36 per cent.) had had typhoid fever on an average of twenty-four years before. Three of the patients had had abdominal operations; in two the appendix had been removed eight and six years before, respectively; the third patient had been operated on for gallstones four
years before; stones were not found; the gall bladder was drained and the appendix removed.

The average duration of gastric history in these cases was 6.9 years. The duration of attacks when the patients presented themselves for examination had varied from three weeks to five months. In three instances there was complaint of continuous trouble for a year or more; in nine there was a history of spells and free periods. The appetite was variable, being given by different patients as poor, fair, and good. In only one case was a cause ascribed for the attack; in this it was attributed to chill or cold.

All the patients had pain or distress. In two instances it was located in the stomach, in five in the epigastrium, in one in the left epigastrium, in one in the right epigastrium, and in two in the epigastrium and right costal margin and through to the back. The intensity varied from a dull aching to a burning, gnawing pain lasting until food was taken. The time of pain or distress was variable, beginning from one-half to four hours after meals. Night pains were recorded in three instances. The methods used to control distress were given as food taking in 8 cases, alkali in 6, gastric lavage in 2, and morphine in 1. The type of pain indicated perforation in one case. Nine patients gave a history of vomiting, varying in character from hot scour water to delayed vomit. Two patients had hematemesis. Nine complained of gas
belching and bloating. Eight were constipated; three had had diarrhea; and three reported blood from the bowel.

In none of these cases was free hydrochloric acid found in the gastric content. The lowest acidity was 4-0-4, the highest 38-0-38; and the average 15-0-15. Food remnants from the evening meal were withdrawn with the test breakfast content in 6 of the cases. The largest amount of retention was 1,200 c.cm.

Ulcer was diagnosed clinically in 6 cases; ulcer or cancer, with a question mark, in 2; cancer of the pylorus in 1; and cancer of the stomach in 1. One case was marked "for exploration." Gall bladder disease was recorded in the clinical diagnosis in 3 cases and carcinoma of the pancreas in 1. Disease of the appendix was recorded as a part of the diagnosis in one instance. The roentgen examination, made in 10 of these cases, was correct in 5, indeterminate in 2, negative in 1, and in error in 2.

In operating on these cases of duodenal ulcer, it was found that 1 was associated with empyema of the gall bladder; 2 had perforated; in 3 there were also gastric ulcers (in two instances on the posterior wall, and in one on the lesser curvature). In 5 cases there was no disease in the upper abdomen other than the duodenal ulcers. In 6 of the cases marked obstruction of the duodenum was found at operation. In 1 there were two ulcers on the anterior surface of the duodenum. In 5 of the 11 cases the appendix was removed at the time of operation. Because of the ulcers a gastroenterostomy was done in all.
VISCERAL CRISSES IN ANGIONEUROTIC EDEMA

E. L. Crispin, M. D.
Los Angeles, California.

A large number of the patients suffering from visceral crises, particularly of the erythemic, purpuric, angioneurotic group, are advised to have surgical operations and many of them sooner or later submit to abdominal surgery from which they do not obtain desired relief. I wish particularly to call attention to this group of cases and to discuss the diagnostic importance of visceral crises more from the standpoint of value in negating or avoiding surgery which does not give relief, than from the standpoint of too closely differentiating interrelated medical conditions. I shall only mention visceral crises of syphilitic origin for which surgery is occasionally done and the abdominal pains of nephritis, particularly of the hemorrhagic type, to which Osler has called attention. Surgery is advised in these conditions only when examination has been incomplete.

The more or less widely varied manifestations of these affections with which are associated visceral pains have never been sharply differentiated, and are probably all members of the same group. It is probable that most of the allied conditions as the urticarias, erythemas

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and purpuras, have as an underlying condition an angioneurosis. Some of them may be caused by chemical irritation; others may be toxic in origin; and yet others may have resulted because of the nature of the individual and from faulty metabolism. It is probable too that anaphylaxis may be a basic cause of many of these angioneurotic conditions. In each of this entire group, localised vascular dilatation occurs and is associated with a serous or hemorrhagic exudation. Caspary\(^1\) says the erythemas as well as the urticarias may result from the action of different toxins on the nerve centers. Osler\(^2\) suggested that the entire group of angioneuroses may depend on some poison which, in varying doses in different constitutions, excites in one urticaria, in another a peliosis rheumatica, and in a third a fatal form of purpura.

One of the conditions forming this group, a purpura with a more definite symptom complex than many of the others, was described by Henoch.\(^3\) This condition is characterized by recurrent attacks of purpura and crises of abdominal pain, often accompanied by diarrhea and vomiting. Arthritis is present in the typical form of the disease. This type occurs most often in the young. Abdominal manifestations similar to those in Henoch's purpura, as Osler has shown, occur in erythema and urticaria. He also calls attention to the variability of the lesions of the skin and reports cases in which some of the attacks of agonizing colic have occurred with no cutaneous manifestations.

Some of the French writers have grouped both the purpuras and
urticarias under the erythemas. Wagner\textsuperscript{4} would have the exudative erythemas to include three forms at least: Erythema nodosum, Erythema multiforme exudativum and urticaria. Osler regards purpura rheumatica as the hemorrhagic type of an exudative erythema and considers Henoch's purpura in the same group. In recording the variability of the lesions of the skin in these conditions, he shows that it is possible to diagnose at different times in the same patient simple purpura, simple urticaria, exudative erythema, arthritic purpura and angioneurotic edema. Jacobi\textsuperscript{5} has shown the close affinity that exists between exudative erythema, Henoch's purpura and angioneurotic edema. Advances in experimental medicine will in time separate such clinical grouping as Wagner has made. Within the past year Rosenow\textsuperscript{6} has experimentally produced erythema nodosum and from his studies recorded a streptococcus as the etiologic agent in his experimental series.

General attention was called to angioneurotic edema by Quincke's\textsuperscript{7} description in 1882. Since then a number of cases have been reported of the exudative erythemic state which indicates that the condition is fairly common. Graves\textsuperscript{8} described the condition in 1848, and Milton,\textsuperscript{9} in 1876, reported cases under the name of giant urticaria. Quincke's name for the condition is most generally used in this country and in England, though the literature abounds with synonyms. Most of the cases not showing purpura or joint affections are grouped under this head though, as has frequently been noted, different attacks in the same
patinet may present a wide range of skin manifestations. Osler has called these varied skin manifestations angioneurotic dermatoses, noting that they are characterized by a marked disturbance of vascular tonus in addition to a more or less inflammatory condition of the skin, due to its abnormal tendency to react to slight and varied irritants, with resultant dilatation of the vessels and exudation. This sensitivity of the skin and the abnormal reaction, the result of a general neurotic disturbance, must be distinguished from the action of inflammatory irritants.

All members of the erythema group may have visceral manifestations, or there may be visceral manifestations in the nature of crises associated with any or none of these varied angioneurotic external conditions. These visceral or gastrointestinal crises may be so severe at first sight as to cause concern and they may be without external clues in the nature of lesions of the skin. If the history is not carefully taken, the hurriedly called physician may easily be misled into thinking that the trouble must be due to the gall bladder, or appendix or at least something that should be taken out. Because of the variability of the skin conditions or of their absence in some of the attacks, often patients do not associate the conditions and, unless they are carefully questioned, clues may not be obtained. Under visceral lesions of the erythema group Osler has reported twenty-nine cases of
these interesting conditions.

Of greatest diagnostic importance in these cases is the indefiniteness of the nature of the abdominal pain. The point most impressive in taking a history is that these pains, apparently of great severity, do not conform to the types usually observed and known to be of a surgical nature. In children, particular care should be taken to get a full history which may bring out previous attacks either of lesions of the skin, inflammation of the joints, abdominal colic or crises. In adults, one is often struck with what is called a neurotic tendency of the patient. In questioning the patients who present themselves for examination and diagnosis between attacks, a wide oscillation will often be noted in their story and too strong a reaction to external stimuli. The crises of which they complain are described as being severe abdominal pain. One patient described her pain as "intense suffering;" another said that she had doubled up with the pain and rolled about on the floor. The abdominal pains come without food time relation, usually at any time. The nocturnal exacerbations are frequent. In one instance I observed a suggestion of regularity in the return of pain about the same time each night. There may be diarrhea, vomiting of blood, or there may be slight melena. The location of pain is usually mid-abdominal or it may be general and described as "all over the abdomen." The usual radiations of lesions causing surgical conditions, however, are not found. Attacks in the various
individuals are usually of about the same duration; from six to eight hours. They vary in intensity from mild aching to such severity that it may be necessary to give morphia.

In cases in which attacks of pain are of a few hours duration differentiation from disease of the gall bladder, in which there is high epigastric location of pain, and the sudden onset and cessation of pain in some of the attacks are diagnostic; in anal colic the radiation, localisation, urinary findings, cystoscopic and roentgenologic findings may be used to clear up differential conditions. In obstructions of the intestine, the prolonged condition in single or few attacks and the causes for obstruction with the general symptoms should prevent confusion. It should be borne in mind that visceral crises of the types under discussion are caused by the results of vasomotor changes and that with the onset sufficient time must elapse for exudation to reach the painful stage and likewise for its disappearance. There is more constancy in time of onset, duration of pain and in the way pain disappears in different attacks than in the various surgical conditions with which these crises may be continued. Disease of the gall-bladder probably is most often confused with the attack of a few hours duration, though peptic ulcer is sometimes confused with it, particularly when vasomotor conditions have occurred in the stomach and permitted sanguinous seepage. It is then the cases of few hours duration that must be differentiated from upper abdominal surgical conditions.
There is another type probably resulting from the same primary cause that is occasionally mistaken for appendicitis or appendiceal abscess in which the onset and disappearance of pain are more gradual. A swelling often appears in the lower right abdomen, which suggests appendiceal abscess. There may be increased temperature; the symptoms, usually of comparatively short duration, are out of proportion to the patient's general condition which is fairly good. In operating on these patients a brawny induration often of the whole cecum and appendix, thick walled and somewhat hard, is found. Occasionally the big gut above the cecum is involved for several inches. The appendix does not show sufficient changes to be the primary cause of the condition. One of the most striking features is the rapidity with which the patients recover. A day or so after operation they are well except for such discomfort as may be present from the abdominal incision. Further inquiry into the history may disclose the presence of swellings in the skin at various times. In the exudative types of longer duration the cecum seems to be more involved than other parts of the viscera, partly because the frequency of appendicitis and the presence of tumefaction permit more frequent exploration.

Often attacks of abdominal pain occur which last for some time with no other suggestive diagnostic clues; but in some of these cases inquiry brings out a history of hives, swellings (hard, white, burning,) in the skin, purpura, puffing of face, eyelids, cheeks, cold hands and
feet, etc.; also, a history of swelling in the throat causing dyspnoea and danger of suffocation is occasionally obtained. Attacks of transient bronchorrhea occurred in one of the cases observed. This bronchorrhea should always be looked for. That there is swelling in the viscera analogous to that in the skin has been quite definitely proved. It is believed that the exudation of serum and distention of the visceral coats produce pain and, when sufficient to cause pseudo-obstruction in the intestines, the pain is peristaltic. When there is great distention of the visceral wall, not only may there be severe pain but considerable exudation of blood into the stomach which may be vomited. In these cases a diagnosis of ulcer is sometimes made. Morris, when giving a lavage at the beginning of an attack, brought out a piece of gastric mucosa thickened with a simple, non-inflammatory edema. Harrington, when operating during an attack of colic, found an urticarial swelling of the gastrointestinal wall. Lenander says that either serous or hemorrhagic infiltration of the wall of the stomach or intestine, if sufficient to produce stretching of the parietal (mesenteric) attachment, will produce colic. Osler cites three cases in which laparotomy was done without definite findings. He quotes cases of Sutherland and Burrows confirming the view that colic may be due to infiltration of the intestinal wall with blood and serum. Some of the indurative, edematous conditions occasionally found at the operating table in which histories have not been definite undoubtedly are of this type, and surgery is of doubtful benefit. Rigg
Dr. Crispin cites four cases of thickening of the ileum and cecum that he regards as visceral manifestations of the condition having for its outward signs erythema, angioneurotic edema, etc. Three cases of induration of the cecum and adjacent gut have been observed in the operating room by W. J. Mayo.° Before operation, because of the tumefaction, these cases had suggested appendiceal abscess. The induration was found in the cecum and in the appendix without sufficient cause. These patients got well with striking rapidity. A history of swelling of the skin was obtained afterward.

Patients in the angioneurotic group with visceral crises have repeated attacks, sometimes for years, that cause great discomfort.

Of the entire group of exudative erythemas 50 were diagnosed angioneurotic edema. The abstracts of illustrative cases are appended.

Case 1. (137701) L. M. Unmarried woman, aged 60 years. Examined August 14, 1915. This patient complained of chronic constipation and hives. The constipation had existed many years; the hives began eighteen months before and had appeared every night for some months. She had swelling over her entire body, lasting five or six hours, then gradually fading away. At times her head and face swelled so she could hardly see; her lips were swollen and protruded. The swelling was sometimes accompanied by hives, which were raised red blotches sometimes covering the entire body. The itching was almost unbearable. She complained of "intense suffering in abdomen;" no localization, but all through
the abdomen, which lasted a few hours and then subsided. She had been told that she had appendicitis or peritonitis and that the large bowel was contracted to the size of a lead pencil. She was neurotic; her brother said they never crossed her because of her nerves. She was well nourished, had gained weight the last year. **Physical examination:**

Gastric analysis practically normal. Roentgen examination of the bowels showed no abnormality other than incompetent ileocecal valve. At one observation there was a raised red, circumscribed area, irregular in outline and the size of a half dollar, in the posterior left lumber region. This was a type of the hives that came out profusely each night. The adjunctive special examinations gave no added information as to the cause for her condition. A diagnosis of angioneurotic edema with visceral manifestations and colonic urticaria was recorded.

**Case 2.** (133719) T. M. S. Married woman, aged 37 years.

Examined June 21, 1915. This patient complained of recurrent cramps in the upper abdomen with loss of strength. For many years she had been easily exhausted. For the last four years she had had frequent cramps in the abdomen lasting from one to four hours. The attacks were of gradual onset, came irregularly and could not be relieved. After the pain was over there was soreness; no relation to food; no radiation. She would lie on the floor and double up when the cramps came on. With the severe pain in the abdomen she was sometimes nauseated, but never vomited. For four years there had been swelling coming at any time over body, face
and extremities, sometimes about joints. Her face had been so swollen as to have been hardly recognizable. The swelling sometimes lasted from one to three days; itched and stung; it was often circumscribed. The patient was very sympathetic, did everything with great zeal, feeling joy, sorrow, etc., with intensity. She did not associate the lesion of the skin with the abdominal condition and it was brought out only by questioning. Physical examination: The right side of the patient's face was greatly swollen; this was painless, though it felt stiff to the patient. Examination of intestinal tract clinically and with the Roentgen ray did not reveal anything of value. Many adjunctive examinations made for record and completeness gave no further information. A diagnosis of angioneurotic edema with visceral crises was made. The patient came to the clinic expecting to have an operation on the gall bladder.

Case 3. (101588) W. H. S. Man, aged 40 years. Paperhanger.

Examination March 4, 1914. This patient had been urged a number of times to have operations for gastric ulcer. He had had gastric trouble off and on for twenty-three years. When seventeen, he had had cramps so severe as to double him up. He used to tie a towel tight around his waist and a number of times was rolled over a barrel to relieve the cramping pains. These attacks came frequently for a few weeks, then disappeared for weeks or months. Only occasional trouble between the ages of twenty and thirty. When about thirty-one he had an attack and vomited a large handful of clots of blood. Sometimes the pain came while
eating, at other times when he was hungry; apparently no clear-cut food
relation. Nothing relieved the pain. Small clots were vomited again
about two years later. For three years prior to examination there had
been a series of attacks, — about one a year. Present attack had
lasted about three weeks. No regularity; stomach better midway between
meals. For three months he had noticed great blotchy swellings come
out on his skin. Swellings usually came about eight in the evening and
lasted until about one in the morning. Skin became thick and hard, and
stung. At times the skin at the joints was so thickened that the normal
use of the joint was impossible. Slight swelling on the face, but swell-
ings on the back and thigh areas as large and thick as a man’s hand ap-
peared in a few minutes and were gone the next day, leaving only a little
tenderness in the skin. He gave a history of profuse expectoration at
nights, spitting a quart or more in an hour or two and coughing up large
quantities of watery mucus so that it would run out of his mouth. The
patient lost eight pounds within four days while under observation. He
had no pain during this time, but disturbances of the skin were marked
each night. He said he sometimes lost forty pounds in two months while
having this trouble, but soon gained it back. Appetite good while losing
weight. Physical examination: Roentgenograms showed considerable fibro-
sis of the lungs; and a lesion of the stomach at or near the pylorus.
After this examination of the stomach and while still in the dressing room,
the swellings were observed coming out. Within ten minutes thick raised,
hardened areas the size of half a dollar were noted on the thigh.

Further examination revealed areas nearly as large as the palm of the hand over his back. While the angioneurotic condition was recognized, because of history of hematemesis and present roentgen findings, exploration was advised. At the operation nothing was found in the stomach. The gall bladder was removed but, when opened, revealed doubtful pathology. An obliterated appendix was also removed. One year later the symptoms were the same as before operation without noticeable change in any characteristics. The lesion at or near the pylorus reported by the roentgenologist was probably a visceral swelling. Seventeen months later the patient's physician reported attacks of both abdominal pain and skin manifestations, the same as before. The last attack of pain which was of the usual type, being in mid-epigastrum, severe, lasting from seven in the evening until half past one, during which time the patient was given one-half grain of morphia. Swollen areas in the skin were large and numerous. It is interesting to note that a little alcohol will always precipitate these attacks of angioneurotic edema and crises.

**Case 4. (177381)** A. J., man, aged 39 years. This patient first came to the clinic December 16, 1912. Bronchitis and asthma were diagnosed. Nasal polypi were removed and the antra irrigated. He returned February 17, 1913, feeling much better. On July 2, 1914, he again returned complaining of attacks of abdominal pain coming on soon after meals and causing much discomfort. Repeated examinations did not
reveal the nature of this pain and the patient was referred to the hospital where he remained forty days. Severe pains in the epigastrium at 10:00 p.m. lasted three hours and required morphia. During this time, spells of angioneurotic edema were recorded, varied in distribution and lasted from a few minutes to a day. Purpuric hemorrhages were noted a number of times. Coagulation time of two minutes was recorded. The abdominal pains persisted usually during the night. No relation to meals. There was an eosinophilia for which no cause was found. Though the angioneurotic edema and purpura had caused the patient to be under observation for weeks and the nature of the pains was believed possibly due to same cause, yet some features of the patient's illness made exploration advisable. And August 26, 1914, a cholecystectomy was done for enlarged gall bladder, "showing an indefinite cholecystitis." The appendix, which was ruptured at the tip and sealed by the small intestine, was removed. The pancreas was apparently normal. Three months later his home physician stated that the symptoms continued, differing in no way from those before operation.

Case 5. (76027) W. T., man, aged 39 years. Examined November 13, 1912. About ten days before admission to the clinic the patient had had an attack of general cramping abdominal pain. Soreness became localized in the right lower abdomen. Three years before he had had a similar attack accompanied by blue-black spots thought to be acetanilid poisoning. In November, 1914, another attack of pain occurred to the right of the
navel with severe vomiting, gas distress and marked tenderness, in right iliac fossa. Operation note November 14, 1915. On opening the abdomen a quantity of free fluid without flakes of lymph and without odor came out. The coil of the ileum fourteen inches in length, 2.5 feet from cecum, was thickened, purplish red and distended. The intestine above and below was normal. A diagnosis of angioneurotic edema was recorded. Peritoneum shiny; no evidence of necrosis. Intestinal wall greatly diminished in lumen by reason of thickening. There was a subacute condition of the appendix which evidently was the cause of the attack ten days ago. The appendix was removed.

CONCLUSIONS

1. Severe abdominal pains which do not conform to the true surgical types may be confused with visceral crises for which surgery would be of no benefit.

2. When a history of severe abdominal pain is given which does not conform to true surgical types, careful inquiry should be made as to the presence at any time of urticarias, erythemas, purpures and swellings of angioneurotic edema types.

3. A history of recurrent severe abdominal pains with constancy in the nature and duration of the attacks, with skin manifestations of any of the exudative erythematous forms, with or without noticeable association with the abdominal pains, should excite suspicion as to the presence of crises of angioneurotic type.
4. A diagnosis of visceral crises of angioneurotic type should not be made until careful examination has excluded or made independent surgical causes. In this, roentgenologic examination of the gastrointestinal tract is valuable negative evidence. Syphilis and tuberculosis should be excluded.

5. The constancy in the recurring attacks of pain not conforming to surgical types in patients who have had skin manifestations of the exudative erythema group and whose general condition does not account for the suffering they have had to bear will warrant a diagnosis of visceral angioneurotic edema.

6. Repeated or even single attacks of intestinal colic with tympanation in which the patient's general condition is too good for the extent and severity of the trouble and in which history of swellings can be obtained, may be of this type. To wait is good surgery. The rapid return to health is strongly suggestive of visceral angioneurosis.

7. Having determined the medical nature of these angioneurotic visceral crises or even in these cases of angioneurotic edema or the entire exudative erythema group, we should endeavor to work out the causes of toxemia. These may be: Feel of pus in the upper respiratory tract and sinuses, bacterial absorption, idiosyncrasies to heat, cold, chemicals, parasites, carbohydrates or proteins that are the causes for anaphylaxis.

8. Removing the causes for anaphylaxis, whether it be idiosyncrasy, in one patient for ice cream, banana in another, alcohol in a third or any
anaphylactic base or source of exogenous or endogenous irritation or poison, may give the patient relief that the advised surgery would not have given him.
REFERENCES


