

increased consistency and diminished sensitiveness of one or both testicles, to indurative atrophy of the base of the tongue, leukoplakia and the like, and scarring and deflection of the epiglottis, to scars of the pharyngeal vault, to perforation of the nasal septum, to the presumptively syphilitic nature of aortic regurgitation, to the ophthalmoscopic signs of chorioretinitis pigmentosa, and similar discoverable signs of syphilis, any one or any combination of which, as the case may be, is less apt to lead one astray than the results of a Wassermann reaction. These and like signs were sought by the clinicians of the generation that passed with Delafield and the elder Janeway; but the generation that holds the responsibility of the future is being inculcated with an almost reverential respect for artificial methods that neither clinician nor pathologist can explain or control.

#### CONCLUSIONS

1. Depending on the antigen employed, the Wassermann reaction in the living patient, as carried out at Bellevue Hospital, gives a negative result in from 31 to 56 per cent. of cases in which the characteristic anatomic signs of syphilis are demonstrable at necropsy.

2. The Wassermann reaction in the living patient is positive in at least 30 per cent. of cases in which it is not possible to demonstrate any of the anatomic lesions of syphilis at necropsy.

### THE DIAGNOSIS OF INFARCTION OF THE ENTIRE SPLEEN

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Total infarction<sup>1</sup> or necrosis of the spleen has received little attention in medical literature. Even the larger systems of medicine devote only a line to its consideration. From scattered reports of colliquative necrosis, coagulation necrosis, thrombosis of the splenic vein, etc., it is evident that a definite symptomatology is associated with these specific affections of the spleen. The purpose of this paper, in addition to adding four instances of total infarction or necrosis of the spleen to the literature, is to point out the possibility of the diagnosis of this condition.

The symptoms are pain, tenderness in the left hypochondrium, enlargement of the spleen, occasionally fever, and vomiting of blood due to rupture of dilated gastric veins. A glance at the literature reveals the regularity with which these symptoms are recorded. The added examples in this report are a repetition of the former.

Whenever the spleen becomes totally infarcted, enlargement occurs, the weight varying from 300 to 1,300 gm., and the dimensions reaching such proportions as 25 by 15 by 8 cm. The enlargement in all of the new cases reported here was noted on physical examination, but was often misleading, it being assumed that such an enlargement must be due to a leukemia or other condition. This fallacy is demonstrated by the fact that infarction of the spleen may

result in a huge enlargement, such as occurred in no less than ten instances in this report.

Pain in the left hypochondrium likewise is present, though variation in the site of the pain differs somewhat. In three cases the pain was described as diffuse throughout the abdomen, then localizing in the left hypochondrium, and in a fourth as "in the region of the stomach." The character of the pain varied from a dull ache to a sharp colic, with all degrees of gradation between. The pain is usually superficial and spontaneous, but may be deep and provokable. It is frequently exaggerated by changes in position, and may radiate along the phrenic nerve or into the left shoulder.<sup>2</sup> A sensation of weight in the left hypochondrium was often complained of, a violent hauling to the left exaggerated by inspiration, or a tingling, shooting or beating sensation in the same region.<sup>3</sup> The pain is probably due to irritation or interference with the structures immediately surrounding the spleen, since this organ is not very sensitive. Total infarction of the spleen may occur, however, without any pain, as in one case here reported and in three of those in the literature.

Tenderness is usually associated with the pain, and is present in the left hypochondrium. The tenderness may come on suddenly and may continue for many days, or there may be occasional tenderness in the left side.<sup>4</sup>

The presence of fever apparently depends on the disease to which the spleen alterations are concomitant. When this is due to an obstruction of the splenic vessels by thrombi or emboli that are sterile, fever is absent. But after the spleen has undergone degenerative changes, bacteria which were already present<sup>5</sup> or which make their entrance from some source such as the colon<sup>6</sup> multiply rapidly, the organ finally resembles a bag of pus, and fever occurs. In one of the four cases here reported, the *Proteus mirabilis*, in another the colon bacillus was isolated from the spleen, and in each instance a rise in temperature of from 1 to 2 degrees was present intermittently. Many times the splenic changes result from or are accompanied by inflammatory changes elsewhere in the body, and under such conditions the fever is often attributable to such factors. In one of our instances a gangrenous cystitis, in another a suppurative pyelophlebitis and in a third an amebic dysentery was present and would account for the rise in temperature.

The vomiting of blood, bright red at times, and resembling coffee grounds at others, is of frequent occurrence. It was present in one of our instances and in several from the literature. Ewald<sup>7</sup> recorded an example of a large spleen resulting from a thrombosed splenic vein, the patient dying as the result of a hemorrhage from the stomach. Following the hemorrhage there was a marked reduction in the size of the spleen. The reasons for bleeding from the stomach following splenic infarction or necrosis are well known, and have been substantiated by experiments. The splenic changes are accompanied by extensive anastomoses between the splenic and gastro-epiploic vessels. The dilatation of these gastric veins often becomes extreme, and the possibility of their rupture

2. Lefevre: Bull. Soc. anat. de Paris, 1848, p. 193.

3. Durand, M.: Contribution à l'étude des infarctus de la rate, Lille, 1903, Mason.

4. Saundby: Brit. Med. Jour., 1908, 2, 1155.

5. Carrière and Vanverts: Arch. d. méd. exper. et d'anat. pathol., 1899, 11, 48.

6. Balacescu: München. med. Wehnschr., 1901, 48, 35.

7. Ewald: Deutsch. med. Wehnschr., 1913, 39, 398.

1. The term "total infarction" is here used because the condition is discussed in the literature, as a rule, under this title. Strictly, total infarction is very rare, most infarcts being "mixed," the blood by imperfectly anastomosing vessels infiltrating the edges to make a red margin about the place of more total infarction. "Infarction of the entire spleen" is, therefore, a better term.

is imminent. However, the bleeding in the instance recorded by Ewald was through a mucous membrane of the stomach which did not present gross lesions. This, too, has been described before. Experimentally, Troell<sup>8</sup> found that following ligation of the splenic veins, a second procedure is necessary, namely, ligation of the dilated anastomosing vessels in the ligamentum gastrosplenicum. Likewise, Warthin<sup>9</sup> found that after ligation of the splenic vessels proper, anastomoses of the spleen with veins of the gastrosplenic omentum and of the stomach allowed small islets of the spleen to live.

In the etiology of total infarction of the spleen, vascular obliteration has been held responsible; but the cause of the vascular obliteration must be determined. The important factors here concerned are pressure on the walls of the splenic vessels by tumors; torsion of these vessels in instances of ectopic spleen; thrombosis of the splenic vessels, and embolism. The emboli may be (1) exogenous, including microbes, and (2) endogenous, as atheromatous plaques. In one of our instances, thrombosis of both the splenic artery and the splenic vein was found; in another, an embolus in the splenic artery from a mitral endocarditis, and in a third an extension of a carcinoma into the splenic

whether the thrombosis was primary in the portal or splenic veins. Sometimes, in a general arterial sclerosis, the portal vein is markedly sclerosed. Or a portal sclerosis may be present even without a general arterial sclerosis.<sup>11</sup> In such instances, Simmons believes that the sclerosis is due to bacterial poisons, and the primary splenic enlargement is the result of blood stasis. Syphilis and trauma also have been held as productive of a primary portal sclerosis,<sup>12</sup> and may be responsible for a portal thrombosis which backs up into the splenic vein. The thrombus in the portal vein does not necessarily mean death to the patient, as is generally believed, since the thrombus may become canalized.<sup>13</sup> Or the portal vein may remain completely obliterated without causing death, as Umbra<sup>14</sup> found.

A displaced spleen or torsion of the splenic vessels may give rise to splenic infarction. In a series of twenty-six instances of ectopic spleen collected from the literature, Durso<sup>15</sup> found seven in which there had been complete infarction of the spleen. To these he added one instance of his own, the body of the organ being necrotic and surrounded by a narrow strip of healthy splenic tissue which obtained its nourishment from the capsule. He found that rotation of the spleen in dogs produced infarcts of the character of

TABLE 1.—EXAMPLES IN AUTHOR'S SERIES

Case	Cause	Symptoms	Pathology of Spleen	Cause of Death
1.....	Obturator thrombus of splenic artery and vein	Pain in left hypochondrium; vomiting at times; anorexia and headache for eight weeks; large spleen; intermittent fever, 1-2 degrees; both bright and "coffee ground" blood in vomitus	Spleen much enlarged and entirely necrotic	"Diphtheria and gangrenous cystitis"
2.....	Embolism of splenic artery from mitral endocarditis	All symptoms referable to an ulcerative, amebic colitis	Wt., 300 gm.; "a soft, yellow, necrotic mass not normal at any point."	"Ulcerative stenosis of rectum; amebic dysentery"
3.....	Extension of carcinoma into splenic vein	Enlargement of spleen; pain under costal arch	Wt., 600 gm.; size, 13 by 9 by 8 cm.; entirely necrotic	Carcinoma of stomach with perforation into lesser peritoneal cavity
4.....	Not determined; overlooked at necropsy	Pain in left hypochondrium	Wt., 210 gm.; organ entirely necrotic	"Suppurative pyelophlebitis; multiple abscesses of liver"

vein. Thrombosis of the splenic vein was the causative factor in nine instances recorded in the literature; arterial plugging was responsible in five. Occlusion of both the artery and the vein was present twice. Torsion of these vessels produced a total infarction in nine instances. Pressure on the vein or invasion of it by neoplasms was found twice. In five, the condition of the splenic vessels was not determined.

Thrombosis of the splenic vein has resulted, therefore, in a total splenic infarction more frequently than any other single factor. Usually the thrombus is primary in the splenic vein, Bonne<sup>10</sup> reporting the first example of this. His explanation is frequently quoted, and is as follows: An infectious process in the spleen results in a splenitis, which in turn produces an endophlebitis. This endophlebitis causes a proliferation of the endothelial cells, and leads to thrombus formation. The splenic induration and the circulatory disturbances which follow aid in an extension of the thrombus formation.

In a few examples of totally infarcted spleen, a portal thrombosis has been found associated with the splenic thrombosis, and it was difficult to determine

embolic infarcts, and that as a result, severe symptoms became manifest. He determined that the infarction resulted from the circulatory disturbance in the branches of the splenic veins.

An embolus lodging in the splenic artery only rarely gives rise to total infarction, in spite of the fact that this artery is an end artery. In one of our instances, however, total infarction resulted from an embolus coming from thrombi on the mitral valve.

The pathology of total infarction of the spleen does not differ from infarction in any viscus that has a "terminal" blood supply. Softening of the infarct is sometimes mistaken for abscess formation, and cannot be differentiated without the aid of the microscope. In each of our four instances, the changes in the spleen had reached this stage, the organ being entirely necrotic and resembling a bag filled with purulent material. In two of the four instances, bacteria of low virulence were isolated from this material. In approximately one half of the examples in the literature, a similar condition was found. In others the spleen was

8. Troell: Ligation of the Splenic Vessels as a Substitute for Splenectomy in Blood Diseases, *Ann. Surg.*, 1915, **63**, 88.

9. Warthin: Experimental Ligation of the Splenic and Portal Veins with the Aim of Producing a Form of Splenic Anaemia, *Proc. Soc. Exper. Biol. and Med.*, 1907, **4**, 127.

10. Bonne: Ein Beitrag zur Kenntniss der Thrombosen der vena lienalis, *E. Huth, Göttingen*, 1884.

11. Simmons: *Virchows Arch. f. path. Anat.*, 1912, **207**, 360.

12. Heller: *Verhandl. d. deutsch. path. Gesellsch.*, 1904, **41**, 182.

13. Edens: Ueber Milzvenenthrombose, Pfortaderthrombose und Bantische Krankheit, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1908, **18**, 59.

14. Umbra: Beitrag zur Pfortaderobliteration, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1901, **7**, 487.

15. Durso: Studio clinico e sperimentale dello infarto splenico nella rotazione della milza, *Policlinico, Rome*, 1896, **3** C, 63; abstr., *Atti d. r. Accad. Med.-Chir. di Napoli*, 1895, **49**, 214.

a "gigantesque" (gigantic) cicatrix, fibrous and infiltrated with blood pigment, the third or final phase of infarct formation having been reached.<sup>3</sup> In some, the three phases of infarct formation were represented, portions of the infarcted spleen being brownish and

tumified, other regions having softened and become cysts filled with necrotic material, and still other portions of the same organ, fibrous and retracted.<sup>16</sup>

16. Lefevre: Etudes physiologiques et pathologiques sur les infarctus viscéraux, Paris, 1867, p. 125.

TABLE 2.—EXAMPLES FROM LITERATURE

Case	Author Reference	Cause	Symptoms	Pathology of Spleen	Cause of Death
1	Bonne, G.: Ein Beitrag zur Kenntnis der Thrombosen der Venen, Göttingen, 1891-1892, 43, 49	Thrombosis of splenic vein and its branches; also of portal vein	Seized with abdominal pain; spleen became enlarged; diarrhea and headache developed	Spleen 18 by 11 by 15 cm.; necrotic	Peritonitis
2	Rollleston, H. D.: Tr. Path. Soc. London, 1891-1892, 43, 49	Thrombosis of splenic vein	Not stated	Weight of spleen, 36 oz.; filled with extensive, anemic, infarcted areas	Chronic diarrhea
3	Same	Carcinoma growing into and occluding splenic vein	Not stated	Not stated	Peritoneal carcinomatosis, originating in cecum
4	Christomanos, A. A.: Beitr. z. path. Anat. u. z. allg. Path., 1898, 24, 519	Torsion of pedicle and thrombosis of splenic vein	Diffuse abdominal pain localizing to left of epigastrium	Spleen weighed 1,300 gm.; entirely necrotic	Operation with recovery
5	Horch: Verhandl. d. deutsch. Gesellsch. f. Chir., 1885, 10, 63	Torsion of pedicle with thrombosis of vein	Enlargement in left hypochondrium; pain on standing or walking; vomiting of blood	Weight, 2,700 gm.; vein filled with dark clot due to torsion of pedicle; cut surface gave appearance of infarct	Recovery following splenectomy
6	Heurtaux: Bull. et mém. Soc. d. chir., 1893, 19, 752	Rotation of spleen with torsion of vessels	Tumor in abdomen, intermittent fever	Weight, 615 gm.; a rim of healthy tissue surrounded bulk of the organ, which was necrotic	Operation with recovery
7	Vetlesen, H. J.: Forh. med. Selsk. i Kristiania, 1889, p. 84	Infarction due to malignant endocarditis	Four attacks of pain in region of left costal margin, each associated with splenic enlargement	"Spleen large"; contained four distinct large infarctions corresponding to clinical history	Malignant endocarditis with hemorrhagic nephritis
8	Weber, F. P.: Med. Press and Circular, 1908, 37, 14	Complete occlusion of splenic artery by recent thrombus	None	Weight, 12 oz.; organ converted into one large infarct	Pulmonary tuberculosis
9	Saundby: Brit. Med. Jour., 1908, 2, 1155	Splenic thrombosis following pregnancy	Tenderness and occasional pain in left side with enlarged spleen	Not demonstrated	Did not die
10	Edens: Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1908, 18, 59	Old thrombosis of splenic and portal veins, the former canalized	Not stated	Spleen 25 by 15 by 8 cm.; firm consistency; marked increase in fibrous tissue throughout	Peritonitis
11	Same	Not known	Sudden pain in left hypochondrium; enlargement of spleen; fever for 3 weeks	Not known; diagnosis of splenic thrombosis or septic infarct	Recovered
12	Fisher, W. E.: Proc. Roy. Soc. Med., London, 1908-1909, 2, Clin. Sec., 128	Wandering spleen	Not stated	Wandering spleen engorged, owing to traction on vessels and with large infarcts	Splenectomy; recovered
13	Watson and Stewart: Lancet, London, 1912, 2, 877	Associated with tonsillitis	Tenderness in left side with enlarged spleen	Spleen converted into a sac filled with turbid bloody fluid; streptococci found	?
14	Goldman: Deutsch. med. Wchnschr., 1913, 39, 1542	Endocarditis resulting in infarction of the spleen and thrombosis of the splenic vein	Pain in region of stomach; large spleen; vomiting of blood	Spleen 2 by 14 by 7 cm.; tough consistency; organ filled with old, fibroid infarcts	Portal thrombosis?
15	Ewald: Deutsch. med. Wchnschr., 1913, 39, 398	Thrombosed, partially canalized splenic vein	Large spleen; fatal hemorrhage from stomach, followed by reduction in size of spleen	Spleen 30 by 7 by 6 cm.; same increase of fibrous tissue	Hemorrhage
16	Lavastine and Bloch: Bull. et mém. Soc. anat. de Paris, 1914, 79, 352	Atheromatous splenic artery	Not stated	Weight, 500 gm.; spleen pulp entirely filled with infarcts of various ages; one, size of orange	Bronchopneumonia
17	Unger: Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1901, 7, 487	Complete obliteration of splenic and portal veins	Not stated	Marked enlargement; increase in fibrous tissue	?
18	Hektoen, L.: Med. News, 1894, 1, 325	Extensive primary thrombosis of all of the splenic veins following typhoid	None referable to the spleen	Spleen 14 by 9 by 5 cm.; weight, 250 gm.; firm; filled with anemic and hemorrhagic infarcts, and all of the vein thrombotic.	Bronchopneumonia
19 to 26	Durso, G.: Policlinico, Rome, 1896, 3-c, 1, 63	Reports one of his own and 7 cases collected from the literature of ectopic spleen associated with infarction and due to torsion of the splenic vessels	In most instances pain in the left side	Spleen enlarged, in one instance weighing 1,050 gm.	
27	Lefevre: Etudes physiologiques et pathologiques sur les infarctus viscéraux, Paris, 1867	Infarction resulting from aortic valve disease	Local manifestation hidden by an acute rheumatism and a subacute peritonitis; severe pain in splenic region, however	Spleen enlarged, adhering to surrounding structures, pulp filled with infarcts, four of which had softened and become comeocysts filled gangrenous material	Pericarditis; peritonitis
28	Durand, M.: Contribution à l'étude des infarctus de la rate, Lille, 1903, Mason	Infarction resulting from an old typhoid fever	Tenderness on pressure in left hypochondrium	Spleen a "gigantesque" cicatrix, fibrous and infiltrated with blood pigment	Cerebral hemorrhage

Following thrombosis or embolism sufficient to cause complete occlusion of either the splenic artery or the splenic vein, the vessel itself undergoes degenerative changes and becomes obliterated from the point of its occlusion onward to its finer terminals.

From our examples it is evident that an occlusion of either the splenic artery or the splenic vein is sufficient to produce total infarction of the spleen. Simultaneous occlusion of both of these vessels, however, is apt to result in immediate necrosis of the entire spleen, and a fatal outcome may follow from the absorption of toxins. The first of our examples illustrates this. An obturating thrombosis of both the splenic artery and the splenic vein resulted in a much enlarged and entirely necrotic spleen. Death followed in six weeks from continuous absorption of toxic material.

Similar conclusions have been drawn from experiments. Carrière and Vanverts<sup>17</sup> ligated both vessels in dogs and rabbits, and found that in most instances gangrene resulted, the spleen becoming a pus sac. They held that the spleen normally contains bacteria, but that these are of low virulence or of none at all. Among these organisms are colon bacilli, diplococci, staphylococci and streptococci. In ligation of the splenic artery alone, gangrene did not result; and they concluded that since the circulation was not completely interfered with, the spleen cells were able to take care of the bacteria without pus formation. Balacescu<sup>18</sup> likewise found that when both the artery and the vein were tied, many animals died of absorption of toxins from a gangrenous spleen. When one vessel was tied, he found that many adhesions form and that gradually bacteria from the intestinal tract gain admittance into the spleen.

Any discussion of splenic thrombosis is incomplete without a consideration of the possibility of a relationship between this condition and the so-called Banti's disease. The exact status of Banti's disease has not been determined. Banti<sup>19</sup> assumes that a toxic agent produced in the spleen brings about the changes in the splenic and portal vessels, finally the three stages of a typical Banti's syndrome resulting. The first stage includes an enlargement of the spleen; the second, urinary changes and marked anemia; the third, liver changes with ascites and a gradual increase in the severity of all the symptoms. We now know that some mechanical conditions, such as circulatory disturbances in the splenic and portal systems, can produce an illness very similar to Banti's disease. Senator<sup>19</sup> is authority for the statement that splenic anemia cannot be differentiated from Banti's disease during the first stage of the latter. Gilbert and Lereboullet,<sup>20</sup> after a review of the subject, decide that Banti's disease does not exist. They maintain that the histology of Banti's disease is only that of a chronic passive hyperemia of the spleen, and that portal hypertension can make a good example of splenomegaly and can also cause the liver changes found in Banti's disease. As a result of these and similar conclusions, Isaac<sup>21</sup> wonders if Banti's disease is rather a

complex of symptoms which may be caused by various etiologic factors.

The importance of recognizing infarction of the spleen of sufficient degree to produce symptoms is evident in considering the treatment. Whether medical attention is sufficient or whether surgical procedures are called for depends on several factors. Among these are the reaction of the patient to the toxic material absorbed from a necrotic spleen, and the presence of hemorrhage from dilated gastric veins. Usually in the total infarction of the spleen, the organ is bound to the surrounding structures by firm, fibrous adhesions. This increases the difficulty of surgical intervention. Perhaps improved methods from recent experiences with splenectomy in pernicious anemia will help to overcome these difficulties.

#### SUMMARY

1. Total infarction or necrosis of the spleen has been infrequently reported.

2. Total infarction of the spleen may result from an embolus or a thrombus in either the splenic artery or the splenic vein; from the extension of a thrombus backward from the portal vein into the splenic vein; from pressure on the splenic vessels by a neoplasm; from torsion of the splenic vessels when the spleen is displaced, or from an inflammatory process originating within the spleen and involving the terminal branches of the splenic artery and vein (Bonne's view).

3. Total infarction of the spleen gives rise to definite enlargement of the spleen, pain and tenderness in the left hypochondrium, fever, and occasional vomiting of blood, and from these a correct diagnosis may be made.

4. The treatment, whether medical or surgical, depends on many factors, such as the condition of the patient and the underlying disease of which the splenic infarction may be either the chief expression or only a minor part.

## EXCRETION OF INGESTED PURINS IN CHRONIC GOUT

### A STUDY OF TWO CASES

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It is generally accepted that less exogenous uric acid is eliminated by persons subject to gout than by normal persons. It is still disputed whether or not this lessened excretion of exogenous uric acid can be used for diagnosis.

Vogt, Reach, Soetbeer, Pollak, Mallory, Weinberger and Yavein have found that in gout the excretion of exogenous purins is diminished and delayed. This is not always the case according to Magnus-Levy, Weintraud, Rommel and Pratt.

In a recent article, McClure and Pratt<sup>1</sup> present tables showing a summary of all the previous observations on the exogenous uric acid excretions of normal persons, of patients with chronic arthritis, and of gouty patients. They have studied the uric acid excretion in two cases of gout after the feeding of sweetbreads.

They believe that the retention of uric acid is a symptom of questionable importance in the diagnosis of gout.

1. McClure, C. W., and Pratt, J. H.: A Study of Uric Acid in Gout, *Arch. Int. Med.*, October, 1917, p. 481.

17. Carrière and Vanverts: Etudes sur les lésions produits par le ligature expérimentale des vaisseaux de la rate, *Arch. de méd. exper. et d'anat. path.*, 1899, **11**, 498.

18. Banti: The Treatment of Banti's Disease, *Folia haemat.*, 1910, **10**, 33.

19. Senator: Ueber Anaemia splenica mit Ascites (Bantische Krankheit), *Berl. klin. Wchnschr.*, 1901, **38**, 1145.

20. Gilbert and Lereboullet, quoted by Cauchois: Splénomégalie chronique d'origine pyéthrothrombotique, *Thèse de Paris*, 1908, p. 92.

21. Isaac: Das Bantische Symptom Komplex und seine Stellung unter den Splenomegalien, *Jahrb. d. ges. Medizin (Schmidt's)*, 1912, **215**, 122.