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clinic the values lay within normal limits. The lesions tended to run a chronic course, and neither local therapy nor, in the case of diabetics, general management tended to speed their healing. In some cases the lesions slowly receded and left depressed scars.

Two ideas regarding the pathogenesis of this condition have been considered: (1) that which assumes the occurrence of a primary vascular injury, possibly by circulating toxins, with secondary thrombosis, necrosis, and fat imbibition and (2) that which assumes a local lipoid disturbance in the skin, based on a general disturbance in fat metabolism. Neither hypothesis has proved satisfactory in the light of studies made both here and elsewhere. Therefore, the pathogenesis of this condition remains obscure.

BANTI SYNDROME (FIBROCONGESTIVE SPLENOMEGALY)

DEFINITION, CLASSIFICATION AND PATHOGENESIS

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The Banti syndrome is still an unsolved problem. The question of cardinal importance is whether the splenomegaly is primary or secondary to portal or hepatic changes.

Banti [1] stated the belief that the trouble lay primarily in the spleen and that the portal and hepatic changes were dependent on the splenic ones. The idea that the splenomegaly was the consequence of circulatory disturbances was put forward by Dock and Warthin [2] and further developed with the description of the thrombophlebitic splenomegaly.[3] This theory occupied a position of definite advantage when it was recognized that the structure of Banti splenomegaly was chiefly congestive [4] and that

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2. Dock, G., and Warthin, A. S.: A Clinical and Pathological Study of Two Cases of Splenic Anaemia, with Early and Late Stages of Cirrhosis, Am. J. M. Sc. **127**:24, 1904.

3. (*a*) Cauchois, A.: Splénomégalies chroniques d'origine pyléthrombosique, Thesis, Paris, no. 422, Paris, G. Steinheil, 1908. (*b*) Dévé, F.: Splénomégalie chronique avec anémie d'origine pyléthrombosique, Normandie méd. **23**:109 (March) 1908. (*c*) Warthin, A. S.: The Relation of Thrombophlebitis of the Portal and Splenic Veins to Splenic Anaemia and Banti's Disease, Internat. Clin. **4**:189, 1910. (*d*) Eppinger, H.: Hepato-lienale Erkrankungen, Berlin, Julius Springer, 1920. (*e*) Frugoni, C.: La splenomegalia tromboflebitica primitiva, Arch. di pat. e clin. med. **3**:574 (Dec.) 1924; La splénomégalie thrombophlébitique, Rev. belge sc. méd. **10**:227 (April) 1938. (*f*) Ceconi, A.: La splenomegalia tromboflebitica, Gazz. d. osp. **50**:265 (March 3) 1929. (*g*) Klemperer, P.: Cavernomatous Transformation of the Portal Vein, Arch. Path. **6**:353 (Sept.) 1928.

4. (*a*) Greppi, E.: Il tumore di milza contrattile emorragiparo come probabile forma di splenoangiopatia primitiva, Minerva med. **2**:644 (Sept. 22) 1928; Die contractile Milztumor und seine Beziehungen zur thrombophlebitischen Splenomegalie, Verhandl. d. deutsch. Gesellsch. f. inn. Med. **40**:615, 1928. (*b*) Villa, L.: Il significato semiologico della contrazione di volume della milza mediante adrenalina par la diagnosi delle splenomegalie voluminose, Boll. d. soc. med.-chir., Pavia **2**:479, 1928; Cuore e circolaz. **12**:465, 1928. (*c*) Larrabee, R. C.: Chronic Congestive Splenomegaly and Its Relationship to Banti's Disease, Am. J. M. Sc. **188**:745 (Dec.) 1934. (*d*) Rousselot, L. M.: The Role of Congestion (Portal Hypertension) in So-Called Banti's Syndrome, J. A. M. A. **107**:1788 (Nov. 28) 1936.

the pressure in the splenic vein was highly increased.[5] But these same signs of portal hypertension were found to be present when an obstructive factor was missing. This fact was responsible for the widest gap in the support of the theory of venous congestion as the causative agent and formed an apparent paradox of great interest.[6]

It is my opinion, however, that this apparent contradiction may be explained if the portal congestion is considered to be the effect of an increased flow of blood into the spleen ("primary acute congestion"). In 1936 I published a detailed study[7] in which I suggested this interpretation. I believe that some important recent contributions by other observers and my successive experience have brought further evidence to the support of this view.

The object of this paper is to correlate these various arguments, thus bringing up to date an idea which may have some bearing both on the understanding of the physiology of the spleen and on the clinical management of its circulatory dysfunctions. Before proceeding, it seems advisable to suggest a definition and a scheme of classification of the Banti splenomegalies; these preliminary considerations should be constantly borne in mind, as they form the premises of any discussion on the pathogenesis of the syndrome.

DEFINITION

Banti's conception of a symptom complex which is dominated by chronic splenomegaly, characterized by certain particular anatomicohistologic changes, due to an unknown agent and recognizable as a separate, clearcut disease can no longer be maintained. Many conditions presenting the clinical and pathologic features described by Banti have been shown to be dependent on various known causative agents.[8] The term "Banti's disease" has thus been discarded and "the Banti syndrome" used in its place, though even recently an author,[8'] with

5. Thompson, W. P.; Caughey, J. L.; Whipple, A. O., and Rousselot, L. M.: Splenic Vein Pressure in Congestive Splenomegaly (Banti's Syndrome), J. Clin. Investigation **16**:571 (July) 1937.

6. (*a*) Whipple, A. O.: The Combined Spleen Clinic, Surg., Gynec. & Obst. **64**:296 (Feb.) 1937; (*b*) The Medico-Surgical Splenopathies: Introduction, Bull. New York Acad. Med. **15**:174 (March) 1939. (*c*) Rousselot, L. M.: Congestive Splenomegaly, ibid. **15**:188 (March) 1939.

7. Ravenna, P.: La splenomegalia fibroso-congestizia primitiva con cirrosi epatica e la sua sistemazione fra le sindromi bantiane, Minerva med. **1**:225 (March 10); 255 (March 17); 276 (March 24); 306 (March 31) 1936.

8. (*a*) Micheli, F.: Contributo clinico ed anatomopatologico allo studio della varietà luetica del morbo di Banti, Soc. ital. per il progr. delle sc. **7**:962, 1913. (*b*) Dürr, R.: Bantimilz und hepatolienale Fibrose, Beitr. z. path. Anat. u. z. allg. Path. **74**:418, 1924.

8'. Patrassi, G.: Il morbo di Banti inteso come cirrosi splenomegalica a decorso protratto, Arch. per le sc. med. **69**:259 (April) 1940.

remarkable lack of criticism, insisted on the term Banti's disease, in spite of the fact that he admitted the multiple etiologic considerations. Even the idea of a Banti syndrome has been the object of repeated criticisms until recently.

It must be granted, however, that chronic splenomegalies not related to any typical disease of the blood, to intrasplenic deposits of lipoids or to tumors are a matter of universal experience, though their existence has been noted more often in certain countries than in others. Banti[1] and several other Italian authors[9] emphasized that this type of splenic enlargement is more or less frequently associated with hepatic cirrhosis. As to the relation between splenomegaly and cirrhosis, it was noted that the same degrees of splenic enlargement are found without any lesion of the liver, or with diverse stages of typical cirrhosis. There was enough evidence, it was believed, to warrant the assumption that this splenomegaly is either autonomous or coordinated with, but not dependent on, the hepatic lesion.

This intimate relation between splenomegaly and cirrhosis of the liver, in which the splenic enlargement constitutes, apparently at least, the primary lesion, forms the basis of the modern idea of the Banti syndrome.[10] To the Banti syndrome can therefore be ascribed the conditions in which the morbid picture is dominated by a considerable chronic splenic enlargement, nonhemolytic anemia and leukopenia. The clinical course is often punctuated by repeated severe hematemeses and sometimes by transitory or permanent ascites. More or less constantly these symptoms are coupled with cirrhosis of the liver. Splenomegalies due to diseases of the blood, to intrasplenic deposit of lipoids or to tumors must not be confounded with Banti syndrome. Splenic anemia, a term which from Griesinger's times up to recent years[11] has pooled all these and other various morbid conditions, is really void of any particular meaning.[12] Almost all chronic splenomegalies are, in point of fact, associated with such a type of anemia.

9. (*a*) Micheli, F.: Sul morbo di Banti, Arch. per le sc. med **33**:351, 461 and 495, 1909; Sistemazione e patologia delle splenomegalie primitive, Turin, *Unione tipografico editrice torinese*, 1910. (*b*) de Vecchi, B., and Zanotti, P.: Su di una particolare splenomegalia primitiva, Sperimentale, Arch. di biol. **32**:217, 1928.

10. (*a*) Greppi, E.: La maladie de Banti. Evolution et état actuel du problème, Rev. belge sc. méd. **10**:237 (April) 1938. (*b*) Ravenna.[7]

11. Hanrahan, E. M.: Splenic Anemia: A Study of End Results With and Without Splenectomy Based on Thirty-Five Cases, Arch. Surg. **10**:639 (March) 1925. Mayo, W. J.: Certain Blood Dyscrasias Dependent on Pathologic Conditions of the Spleen, J. A. M. A. **88**:815 (Sept. 13) 1924.

12. (*a*) Naegeli, P.: Blutkrankheiten und Blutdiagnostik, ed. 5, Berlin, Julius Springer, 1931, p. 560. (*b*) Klemperer, P.: The Pathologic Anatomy of Splenomegaly, Am. J. Clin. Path. **6**:99 (March) 1936; The Spleen, in Downey, H.: Handbook of *Hematology*, New York, Paul B. Hoeber, Inc., 1938, vol. 3, pp. 1591-1728.

CLASSIFICATION

Actual classifications are mainly founded on morphologic bases. Macroscopic and histologic examinations have decided whether the splenomegaly had to be classified as fibrous or fibroadenic,[1] congestive[4] or siderotic.[18] Naegeli's [12] and McNee's [14] classifications were based on *which tissue* was prevalently damaged. The concomitant presence of hepatic cirrhosis or of thrombophlebitis gave rise to other classes (Eppinger [84] and Rousselot [46]). All these classes do not differentiate nosologic entities but merely point to characteristics and courses which may depend either on the same or on different causative agents.

In syphilitic patients with the Banti syndrome, for instance, all the aforementioned aspects have been recorded (Micheli [85] and Minot [15]), either with or without histologic signs of syphilis (Ravenna [7]). The only correct diagnosis would be that of Banti syndrome of syphilitic origin, which offers a comprehensive definition of the disease and not only one particular aspect.

One of the best schemes for classification was suggested by Klemperer,[12b] and it was based on pathogenetic criteria. But a lasting classification should be based on the etiology. Only conditions of which the cause is not determined may be divided, somewhat arbitrarily, from the standpoint of morphologic aspects. It would then be correct to make a diagnosis of primary or cryptogenetic splenomegaly with prevailing congestion (hemorrhages or siderosis) or with prevailing fibrosis (fibroadenia or cirrhosis). The latter class evidently includes instances presenting all the etiologic and morphologic characters described by Banti, and it therefore may conserve the name of Banti's disease.

The following scheme may be suitable for a simple classification.

A. Of known origin	infective	syphilis leishmaniasis schistosomiasis malaria tuberculosis
	toxic	alcohol lead phosphorus
B. Of undetermined origin (primary fibrocongestive splenomegaly with cirrhosis)	with prevailing congestion	
	with prevailing fibrosis (Banti's disease)	

13. Gamna, C.: Contributo alla conoscenza della splenomegalia primitiva, Haematologica **4**:129, 1923.

14. McNee, J. W.: The Spleen: Its Structure, Function and Diseases, Lancet **1**:951 (May 2); 1009 (May 9); 1063 (May 16) 1931.

The progress of the general knowledge of etiology will enlarge class A, with the inclusion of other causative agents, while the number of cases ascribed to class B is bound to decrease and ultimately disappear.

CLINICAL AND PATHOLOGIC NOTES

For a long time great importance was attributed to the anemia which almost constantly accompanies Banti's syndrome. It is of moderate degree, normocytic and nonhemolytic and is associated with well marked leukopenia, relative or absolute monocytosis, and frequently with decrease of blood platelets. Its significance decreased considerably when it was generally recognized that this type of anemia, as pointed out by Micheli in 1903,[16] is usually associated with any considerable splenic enlargement, from whatever cause.

Lately attention has been drawn to a condition of splenic and portal congestion of high degree, and it has been noted that, being less considerable or absent in splenomegalies from other causes, this congestion forms a salient and typical feature of Banti splenomegalies. Its presence is inferred from (*1*) the pronounced decrease of splenic volume after injection of epinephrine [17] or after hemorrhage; (*2*) the frequent occurrence of copious hemorrhages from the gastrointestinal tract; (*3*) the frequency of transitory or permanent ascites, and (*4*) the hypertension in the splenic veins, as determined during surgical intervention.[8]

The spleen is invariably greatly enlarged but shows no specific characteristics, and this fact accounts for the long opposition that Banti's idea met with when morphologic criteria were dominating morbid anatomy as well as clinical diagnostics. A certain similarity of lesions, however, was noted, consisting in connective and elastic hyperplasia of the capsule and trabeculae and fibrosis and hyperplasia of the reticular framework of the splenic pulp. The liver is normal in some instances but mostly presents various degrees of Laennec's cirrhosis. Moreover, careful examination showed many definite signs of portal congestion, represented by (*1*) the gross and histologic aspect of the spleen: dilatation of the sinuses, intrasplenic hemorrhages and their residuals and the siderotic nodules [18]; (*2*) the dilatation of small vessels inside the spleen,

15. Minot, G. R.: Anemias, in Christian, H. A.: Oxford Medicine, New York, Oxford University Press, 1932, vol. 2, p. 642.

16. Micheli, F.: Note ematologiche sulla malattia di Banti, Riv. di clin. med. **4**:65 (May); 81 (June); 97 (July) 1903.

17. Greppi.[4a] Villa.[4b]

18. B. de Vecchi, B. Picchi and G. Patrassi (Ricerche sistematiche sulla genesi e sul valore delle lesioni spleniche conosciute col nome di aree di Gamna, Arch. di pat. e clin. med. **8**:17 [Jan.] 1929) and C. Oberling (Le rôle pathogène de *la mycose splénique de Nanta*, Presse méd. **36**:2 [Jan. 4] 1928), examining some of Banti's own slides, observed siderotic nodules also in his original cases.

of the splenic veins and its roots and of portal and mesenteric veins,[19] and (3) the dilatation of collateral portal-general paths of circulation. The aforementioned frequence of gastroesophageal hemorrhages and ascites is, of course, a pathologic as well as a clinical sign of portal congestion.

Pathologists usually evaluate the state of congestion from the anatomic aspect of the spleen removed surgically or at necropsy. This criterion is misleading, as the spleen is larger during life than after death and is subject to shrinkage as an effect of various operative procedures, of anesthetics (both ether and chloroform) and of epinephrine, which is often purposely given. A further amount of blood flows out of the splenic tract of resected veins. That is possibly the reason why the presence of congestion had been so long overlooked by pathologists and by Banti himself. But, once recognized, the importance of splenic and portal hypertension was stressed increasingly.[20] Some authors[21] have used the term congestive splenomegaly as synonymous with Banti's syndrome. Piney[22] wrote: "There seems to be little doubt that Banti's disease is essentially a pathological state of the vascular system of the spleen;" and Greppi[23] noted that the vascular factor was becoming the "Leit-motif" of splenic pathology.

Thrombosis of the splenic and portal veins, their cavernomatous transformation and their stenosis by external compression due to various causes or various stages of hepatic cirrhosis were often noted and referred to as possible or probable causes of the splenic and portal congestion. Experimentally, however, attempts to produce chronic splenomegaly by means of varied derangements in the portal or splenic circulation have been uniformly disappointing.[23a] Only Rousselot and Thomson[23b] have claimed positive results; obviously, their experiments must be confirmed independently before definite conclusions be drawn.

19. McMichael, J.: The Pathology of Hepatolienal Fibrosis, J. Path. & Bact. **39**:481, 1934. Rousselot.[6c]

20. (*a*) Villa, L.: Sulla retrattilità splenica, Rassegna med. **15**:127 (Sept. 30) 1935. (*b*) McNee, J. W.: Croonian Lectures on Liver and Spleen: Their Clinical and Pathological Associations, Brit. M. J. **1**:1017 (June 4); 1068 (June 11); 1111 (June 18) 1932. McMichael.[19]

21. Greppi.[4a] Larrabee.[4c] Rousselot.[4d]

22. Piney, A.: Recent Advances in Haematology, ed. 4, London, J. & A. Churchill, Ltd., 1939, p. 294.

23. Greppi, E.: Morbo di Banti 1938, Riv. di clin. med. **40**:52 (Jan.) 1939.

23a. Castiglioni, G., and Pepere, M.: Ricerche sperimentali intese a modificare il circolo splenico, Arch. ital. di anat. e istol. pat. **11**:14 (Dec.) 1939.

23b. Rousselot, L. M., and Thomson, W. P.: Experimental Production of Congestive Splenomegaly, Proc. Soc. Exper. Biol. & Med. **40**:705 (April) 1939.

A fact of the utmost importance for the proper understanding of this vascular condition was the observation that all these clinical and pathologic signs of congestion could also be found in the absence of any obstructive factor in the portal vessels. Such an event was rarely considered in its real significance, though it clearly resulted from the pathologic records of most of the instances of what was described as Banti's disease in the old and modern literature, and McNee[20b] had already noted that in Banti's disease high portal pressure and changes in the spleen precede the onset of marked fibrotic changes in the liver. Shortly thereafter Klemperer[13b] wrote that chronic portal stasis is not the sole cause of splenic enlargement and that cases have been observed in which the splenomegaly becomes clinically manifest at a period when there is no indication of a hepatic disorder. In other cases, he stated,[13b] the splenomegaly occurs concomitantly with the hepatic alterations and not subsequently; it is not dependent on or secondary to them. Six recent cases of congestive splenomegaly without peripheral obstacle to the venous return from the spleen were cited by me,[7] and 2 others have since come to my attention. Two similar instances were referred to by Larrabee.[4c] Twenty-two others have been collected by Rousselot,[6c] from a total of 55 cases of congestive splenomegaly under his observation in the spleen clinic of the Presbyterian Hospital of New York. If it were borne in mind that often the obstacle to the venous return from the spleen could not logically have accounted for the splenomegaly (frequently old splenomegalies are associated with slight cirrhosis or with recent thrombosis, as observed by Davies[24] and myself[7]), the number of cases of apparently nonsecondary splenomegaly would increase considerably.

Also the observations in cases of schistosomial splenomegaly are rather against the idea of ascribing the splenomegaly to the local deposition of ova and the subsequent fibrosis or to the thrombosis of large portal veins, which is extremely rare in this condition.[25]

MECHANISM OF SPLENIC CONGESTION

The absence of any obstruction in the portal bed is too frequent to be considered an insignificant exception; it forces one to the conclusion that an obstacle to the venous return from the spleen cannot be the first and common cause of the Banti syndrome in all cases and that the

24. Davies, J. C.: Splenic Anaemia and Portal Thrombosis, Lancet **2**:498 (Sept. 8) 1928.

25. Onsy, A. B.: The Pathogenesis of Endemic (Egyptian) Splenomegaly, Tr. Roy. Soc. Trop. Med. & Hyg. **30**:583 (April) 1937. Shafi, A. M.: Historical Review of Egyptian Splenomegaly and Allied Conditions, J. Egyptian M. A. **19**: 561 (Oct.); 631 (Nov.); 652 (Dec.) 1936.

opinion to the contrary, still held by the majority of authors,[26] should be discarded as contrasting with the pathologic evidence at present available.

A few hypotheses have been submitted to explain the congestion independently from an obstruction in the portal bed. Greppi and Cesaris Demel [27] stated the belief that the splenic engorgement was the consequence of the decreased contractility of the capsular and trabecular framework of the spleen. This was based on the opinion that the contraction of the intrinsic muscular framework of the spleen regulated the outflow of splenic blood. But muscle fibers are scarcely distributed in the human spleen, and the efficacy of their contraction is doubtful.[28] Also the rhythmic changes of splenic volume are caused not by a rhythmic contraction and relaxation of the smooth muscular framework of the spleen but by rhythmic variations in the blood flow.[29] By others [30] it has been suggested that the veins of the portal bed have a contractile, arterial-like function which actively helps the blood to overcome the peripheral resistance of the liver. Thus, it was suggested that the insufficiency of this function is the cause of the congestion. But, though portal vessels are rich in muscle fibers and endowed with high contractility, there is no evidence of their arterial-like activity. Nor could it be demonstrated that lesions of the walls of the portal vessels preceded the splenic congestion.

26. Castle, W. B., and Minot, G. R.: Pathological Physiology and Clinical Description of the Anemias, New York, Oxford University Press, 1936, pp. 117-121. Magner, W.: A Textbook of Hematology, Philadelphia, P. Blakiston's Son & Co., 1938, p. 232. Rousselot.[6c]

27. Greppi, E.: Splenomegalie congestizie (da atonia): significato, patogenesi e cura, Boll. Soc. med.-chir., Catania **3**:446, 1935. Cesaris Demel, A.: Considerazioni sull'atonia dell'apparato muscolare contrattile della milza nella patogenesi di alcune splenomegalie, Baglivi **1**:200, 1935.

28. (*a*) Maximow, A. A., and Bloom, W.: A Textbook of Histology, ed. 3, Philadelphia, W. B. Saunders Company, 1938, p. 269. (*b*) Giunti, G.: L'apparato elastico-muscolare dello stroma splenico in diverse condizioni patologiache (considerazioni sulla splenocontrazione e sulla splenoriduzione), Arch. ital. di anat. e istol. pat. **10**:123 (June) 1939.

29. Grindlay, J. H., and Herrick, J. F.: The Blood Resevoir Function and Rhythm of the Spleen: Preliminary Report of an Experimental Study, Proc. Staff Meet., Mayo Clin. **13**:663 (Oct. 19) 1938. Grindlay, J. H.; Herrick, J. F., and Mann, F. C.: Measurement of the Blood Flow of the Spleen, Am. J. Physiol. **127**:106 (Aug.) 1939. Grindlay, J. H.; Herrick, J. F., and Baldes, E. G.: Rhythmicity of the Spleen in Relation to Blood Flow, ibid. **127**:119 (Aug.) 1939. Bariéty, M., and Kohler, D.: Excitations urétérales et changements du volume de la rate chez les chiens normaux, yohimbinisés, atropinsés, cocaïnés et ésérinisés, Compt. rend. Soc. de biol. **127**:972, 1938.

30. Cellina, M.: Splenomegalie da alterato circolo portale e splenomegalie tromboflebitiche, Gior. di clin. med. **15**:615 (July 20) 1934. de Castro and dall'Acqua, G.: Osservazioni sulla splenomegalia tromboflebitica primitiva, Atti Soc. lomb. di chir. **3**:845, 1935.

To explain the genesis of splenic congestion, some other facts must be remembered: 1. The afflux of blood to the splenic pulp is regulated chiefly by the malpighian arteries and by other arteries in the pulp and in the trabeculae, which are rich in muscular tissue. It was noted by Knisely [31] that the contraction of the malpighian arteries is strong enough to obliterate their lumen. There are other vascular systems acting as capillary regulators which determine the afflux and the deflux of blood to and from the sinuses (Knisely [31]), but in the general economy of the splenic circulation, their importance is likely to be a local one, as their insufficiency could be counterbalanced by the muscular system of bigger arteries. 2. The output of splenic blood is limited by the peripheral resistance of the liver, which normally is small, being overcome by a portal pressure of 8 to 10 mm. of mercury. But when the splenic output increases above a definite amount, the blood can overcome the hepatic resistance only if the portal pressure rises adequately. 3. In instances of Banti splenomegalies, lesions of the malpighian and other small arteries—the most evident signs of which are periarteriolar hemorrhages and periarteriolar fibrosis—have constantly been found, even in early stages of the disease.

This last point gives enough evidence, I believe, to warrant the assumption that the small splenic arteries are the seat of early lesions. In consequence, their function of adjusting the intake of blood is altered, and blood enters the spleen in an increased quantity, which cannot be discharged through the hepatic resistance under normal conditions. Thus, the spleen becomes congested and widens; the elastic tension of the supporting framework increases, raising the pressure of the outflowing blood. This condition permits an increased amount of blood to pass through the small hepatic vessels.

The spleno hepatic circulation, altered in consequence of the insufficient regulating function of diseased splenic arterioles, is subject to a compensatory rise of venous pressure, which is a direct result of the splenic dilatation.

Becoming chronic, the splenic engorgement may be directly responsible for some lesions of the splenic pulp (fibrosis or hyperplasia), while the venous hypertension causes dilatation of splenic and portal veins and, eventually, their thrombosis. Further consequences are degenerative changes in the liver cells, which may not be extraneous to the genesis of portal cirrhosis.

Subsequently, either splenic thrombosis or cirrhosis of the liver, or both together, aggravate the portal congestion and may dominate the

31. Knisely, M. H.: Spleen Studies: I. Microscopic Observations of the Circulating System of Living Unstimulated Mammalian Spleens, Anat. Rec. **66**:23 (April 25) 1936; II. Microscopic Observations of the Circulating System of Living Traumatized Spleens and of Dying Spleens, ibid. **66**:131 (April 25) 1936.

further development of the disease. They are complications or associated morbid conditions and not the first cause of the congestion, because —as should always be remembered—splenic congestion may be found independent of either.

Obviously, the favorable effect of splenectomy or of ligation of the splenic artery (Greppi [10a] and Kemp [32]), which often, besides relieving the general and hematologic conditions, diminishes the tendency to gastroesophageal hemorrhages and ascites, is due to the removal of the primary cause of portal congestion. But some failure, often cited in the literature,[33] should have been foreseen, as splenectomy cannot remove the eventual thrombosis or the cirrhosis, nor can it always modify the state of gastroesophageal varices [34] or of the widespread dilatation of submucous and subserous small vessels of the esophagus and the stomach, which is frequently seen in cases of this kind (Ravenna [7] and Fiessinger, Albeaux-Fernet and Varay [35]).

COMMENT

It seems to me particularly significant that the present conception of primary splenic congestion is based on the undisputed presence of lesions in the small splenic arteries. Their fibrosis had been described by Banti [1]; the presence of regressive lesions in their walls and of endoarteritis had been noted by Gamna [13] and by myself.[7] The siderotic nodules themselves are the direct consequence of periarteriolar hemorrhages, as pointed out in 1902 by Marini,[36] the first author who described such lesions, and his interpretation was substantially confirmed by successive observers.[37] The significance of arteriolar lesions in the

32. Kemp, R.: Recurrent Haematemesis in Banti's Disease, Brit. M. J. 1: 222 (Jan. 29) 1938.

33. Pemberton, J. deJ.: Results of Splenectomy in Splenic Anemia, Hemolytic Jaundice and Haemorrhagic Purpura, in Collected Papers of the Mayo Clinic and the Mayo Foundation, Philadelphia, W. B. Saunders Company, 1931, vol. 23, p. 539; Ann. Surg. 94:755 (Oct.) 1931.

34. Hines, L. E., and Fitzgerald, B.: Splenomegaly of the Banti Type: Report of a Case with Postmortem Observations Four Years After Splenectomy, Arch. Path. 26:155 (July) 1938. Kemp,[32] Greenwald, H. M., and Wasch, M. G.: The Roentgenologic Demonstration of Esophageal Varices as a Diagnostic Aid in Chronic Thrombosis of the Splenic Vein, J. Pediat. 14:57 (Jan.) 1939.

35. Fiessinger, N.; Albeaux-Fernet, and Varay, A.: A propos des hémorrhagies persistantes après splénectomie, Bull. et mém. Soc. méd. d. hôp. de Paris 54:494 (March 18) 1938.

36. Marini, G.: Sopra un caso di splenomegalia con cirrosi epatica, Arch. per le sc. med. 26:105, 1902.

37. Gandy, C.: Lésions particulières de la rate en un cas de cirrhose biliaire, Bull. et mém. Soc. anat. de Paris 80:872, 1905. Eppinger,[8d] Gamna.[13] Christeller, E., and Puskeppeleit, M.: Die periarteriellen Eisen- und Kalkinkrustationenx in der Milz, Virchows Arch. f. path. Anat. 250:107, 1924. de Vecchi

mechanism of congestion, however, had never been considered before in human pathology, but recently Greppi [10a] and Lenzi,[38] accepting the arguments discussed in my previous paper, admitted that the first lesion responsible for the splenic congestion might be an arteriolar one. Some experimental attempts to produce active congestion of the spleen were made by Henschen and Howald.[38a] They denervated the spleen of 3 dogs, in 2 of which splenomegaly was obtained. In view of their importance, these experiments should be repeated and enlarged, with the study of the alterations, if any, secondarily produced in the portal circulation and in the liver itself.

Episodes of Gastrocsophageal Hemorrhages and Ascites.—Often this frequent and serious event in the course of the Banti syndrome puzzled the physicians by whom it had been attributed to an organic obstacle in the portal bed, which could not be found at the necropsy.[39] Hemorrhages and ascites may depend on the breakdown of the portal circulation, due to an anatomic obstacle (thrombophlebitis or cirrhosis), as well as to the progress of arteriolar lesions in the spleen and to a transitory increase of hepatic resistance, due to digestive or cardiac exigencies.

In many cases ascites appeared and disappeared quickly (Frugoni [36]), and I think that this fact is rather against the idea of ascribing the condition to a definite anatomic obstacle, such as that represented by thrombosis or cirrhosis. The influence of digestive requirements on splenic circulation is great indeed, as it is proved by the increase of splenic volume during the normal digestive process, and therefore in splenomegalic patients the relation of the hematemeses to digestive phases should be investigated with greater attention.

Splenic Shrinkage After Administration of Epinephrine.—The shrinkage may depend on the stimulation of the splenic arterioles, the

and Zanotti [8b] Fasiani, G. M., and Osellatore, G.: Essai de réproduction expérimentale des nodules de Gandy-Gamna, Presse méd. 37:1136 (Aug. 31) 1929. Jaeger, E.: Ueber Stauungsmilz, Verhandl. d. deutsch. path. Gesellsch. 26:334, 1931; Milzbau und Kreislaufstörung, Virchows Arch. f. path. Anat. 290:531 and 552, 1937. Alexandre, A., and Valducci, E.: Fattori che determinano le incrostazioni siderotiche della milza nei focolai sclerosiderotici, Pathologica 27:321 (May 30) 1935.

38. Lenzi, F.: Sindrome Bantisna-splenomegalia fibroso-congestizia prevalentemente fibrosa-Contributo clinico-Ipotesi patogenetiche, Haematologica 22:47, 1940.

38a. Henschen, C., and Howald, R.: Die anatomischen und klinisch-physiologischen Folgen der operativen Entnervung der Milz. Experimentelle Untersuchungen, Arch. f. klin. Chir. 157:667, 1929.

39. Cellina.[39] de Castro and dall'Acqua.[39] Lucchi, G.: Morbo di Banti a lunghissimo decorso e splenomegalia tromboflebitica con trombosi della vena mesenterica superiore, Riv. di clin. med 36:421 (July 15) 1934.

constriction of which decreases the intake of blood. Thus the shrinkage is due to the elastic retraction of the supporting framework. This conception, suggested by Colombi [40] and Villa,[40a] was adhered to by a detailed study of the musculature in the human spleen by Giunti.[24b] It is supported also by the evidence collected by Grindlay, Herrick and Baldes [28] in their experiments on the blood flow of the spleen. But it has not yet been noted that, if this mechanism be true, epinephrine should decrease the pressure in the splenic vein instead of increasing it. I do not know of any instance in which the pressure in the splenic vein was measured before and after injection of epinephrine, but the fact that the splenic shrinkage due to epinephrine never produced gastrointestinal hemorrhages, even when tried in patients who either previously or subsequently suffered from spontaneous gastrointestinal hemorrhages, speaks rather against the idea of ascribing the splenic reduction to an active contraction of the muscular framework. Obviously, an immediate episode of hemorrhage should have been a frequnet consequence if the epinephrine compressed the spleen and raised the portal pressure.

This mechanism also makes easy to understand why the splenic shrinkage may be of the same degree both when an obstructive factor is present and when it is lacking.[40a] If the epinephrine influenced the regimen of outflow, by actively expressing the blood from the spleen, a difference should have been noted under these two conditions.

A definite proof that in cases of splenic congestion epinephrine does not raise the portal pressure and a further indirect argument on its mechanism of action may be obtained by measuring the splenic venous pressure during surgical interventions. I hope that this will be tried in the near future.

As to the human spleen, the term "contraction" is, I believe, inadequate and probably incorrect; it may advantageously be substituted by "reduction" or "shrinkage," which merely describes the fact of the variation in size, without suggesting any determined mechanism.

Ascoli (Epinephrine) Therapy.—That the size of the spleen could be permanently reduced by intravenous injections of epinephrine was

40. Colombi, C.: La separata funzione del duplice substrato contrattile della milza, Atti Soc. lomb. di med. **2**:615, 1934.

40a. Greppi, E.: La negatività della splenocontrazione adrenalinica non esclude la natura sanguigna del tumore di milza, Policlinico (sez. prat.) **43**:53 (Jan. 13) 1936. Villa.[20a] Grenet, H., in discussion on Weill-Hallé, P.; de Gaudard d'Allaines, and Papaioannou, A.: Hématémèse et mélaena chez un enfant de neuf ans. Splénomégalie ancienne. Arrêt des hémorrhagies après splénectomie, Bull. et mém. Soc. méd. d. hôp. de Paris **53**:1481 (Dec. 6) 1937.

demonstrated by Ascoli, d'Alessandro, Riolo and Pizzillo,[41] who suggested injections of epinephrine hydrochloride as a new method of therapy for chronic malarial splenomegaly. Its favorable effect was confirmed by many authors.[42] The attempt to influence other splenomegalies with the same method is a logical consequence. The best results may be anticipated in cases of the Banti syndrome, in which the vascular factor plays such a great part.

I have tried this treatment on 3 patients, by injecting 0.01 mg. to 0.10 mg. of epinephrine hydrochloride intravenously on each of twenty successive days, as suggested by Ascoli and his associates. Two of these patients were suffering from a cryptogenetic Banti syndrome in an early stage. The spleen reached to about 3 inches (8 cm.) below the costal margin, and the liver was practically normal. A marked decrease of splenic size was obtained, without, however, influencing the general conditions. But the leukocytic count diminished quickly, in 1 case from 2,500 to 650 per cubic millimeter. Therefore, it was believed that further delay might be dangerous, and splenectomy was performed. The postoperative course was uneventful. Both patients were followed up for about a year, and they remained in good general and hematic condition. The third patient had an enormous splenomegaly and hypertrophic hepatic cirrhosis; years before he had suffered from malaria, and the serologic reactions proved that he was syphilitic. His poor condition contraindicated splenectomy. Antisyphilitic treatment together with Ascoli therapy caused permanent decrease of splenic size, a slight decrease of hepatic volume and satisfactory improvement of the general state.

Further experience is required, but I wish to suggest that it may be worth while to try Ascoli's method of treatment in cases in which surgical intervention on the spleen offers few chances of success. If the epinephrine lowers the portal pressure, this treatment might also decrease the danger of serious hematemesis in nonoperable patients.

41. Ascoli, M.: Sulla cura dell'infezione malarica cronica, Riforma med. **52**: 351 (March 14) 1936. d'Alessandro, G.: Sulla cura di M. Ascoli della infezione malarica, Riv. di malariol. (sez. I) **16**:290, 1937. Riolo, P.: Sulla cura di M. Ascoli della infezione malarica, ibid. **16**:34, 1937. Pizzillo, G.: Sulla cura di M. Ascoli della infezione malarica, ibid. **17**:404 and 441, 1938.

42. Gosio, R.: Sondaggio di contrattilità della splenomegalia malarica e trattamento adrenalinico della stato malarico, Riv. di malariol. (sez. I) **16**:123, 1937. Mosna, E.: Sulla cura di M.Ascoli della infezione malarica, ibid. **17**:126, 1938. Nucciotti, L.: Ricerche sulla terapia adrenalinica nella malaria estivo-autunnale primitiva, ibid. **17**:131, 1938. Canova, F.: Associazione chinino-adrenalinica nel trattamento della malaria acuta, ibid. **16**:31, 1937. Froilano de Mello, J.: Experimental Studies on the Treatment of Malarial Splenomegalies by the Method of Ascoli, South African M. J. **12**:835 (Nov. 26) 1938.

SUMMARY AND CONCLUSIONS

Evidence has been accumulating which supports the view that Banti splenomegaly is largely due to splenic congestion and that this congestion is not dependent on an obstructive factor in the portal-venous bed. It is suggested that the congestion may be due to primary lesions of the small splenic arteries which regulate the blood flow into the spleen ("primary active congestion").

The human spleen should be considered as an elastic rather than as a contractile organ. Its variations in size depend on variations in volume of the inflowing blood, rather than on active contractions of the smooth muscle of its supporting framework.

From a mechanical point of view, the spleen might be defined as an automatic controller which regulates the pressure of the splenic venous blood in order to maintain the balance between the volume of inflowing blood and the amount which can be discharged through the hepatic resistance. Normally, and within certain limits, in pathologic conditions, the splenic elasticity guarantees a pressure sufficient to secure the further progress of venous portal blood. Congestive splenic enlargement is therefore a mechanism to counterbalance either increased volume of portal blood or increased peripheral resistance to the discharge of a normal amount of blood.

The Banti syndrome is a symptom complex dominated by chronic fibrocongestive splenomegaly, accompanied by portal hypertension and complicated by, or associated with, hepatic cirrhosis or thrombosis of the splenic and portal veins. It may depend on various causative agents, either infective or toxic. A scheme for its etiologic classification is presented.

The splenic changes of Banti syndrome are probably due to primary lesions of the splenic arterioles, the regulating power of which becomes insufficient to control the inflow of blood. The consequent congestive splenomegaly is the cause of the circulatory disturbance in the portal bed. Secondarily, hepatic cirrhosis and venous thrombosis may aggravate the state of portal circulation.

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Progress in Internal Medicine

GASTROENTEROLOGY

REVIEW OF LITERATURE FROM JULY 1939 TO JULY 1940

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The widespread interest in gastroenterologic problems and their clinical importance is evidenced by the multiplicity of articles appearing in the world literature on all phases of the physiology of the alimentary tract, normal and abnormal, and the therapeutic applications directed thereto. Some new data have been added, particularly to the knowledge of the physiologic response of the digestive tract to various drugs, many of which are actively employed at present. In this review allusion will be made to strictly new discoveries and to new applications of old principles. It will also be my purpose, however, to call attention to many articles of clinical importance for the sake of reemphasizing recognized or partially recognized concepts of gastrointestinal disease.

PHYSIOLOGIC ASPECTS

Interest continues in the various factors influencing gastric secretion. In fact, attempts are still being made to obtain a satisfactory normal gastric secretory curve by varying technics. Wilhelmj and Sachs [1] still pursue their studies of gastric secretion following a test meal consisting of a specially prepared solution of Liebig's meat extract and a standard amount of phenolsulfonphthalein (phenol red). They believe that after such a test meal it is possible to determine what proportion of a given sample is fluid of the test meal remaining in the stomach and what proportion is due to secretions. The total secretions entering the stomach can be separated into acid and nonacid fractions, and the acidity of the total secretions can be determined independent of the acidity of the mixed gastric contents. Multiple curves on given subjects show a rather remarkable agreement, and the amount of acid secretion is usually constant in the same person. The increase in nonacid secretion due to regurgitation from the duodenum varies considerably even in the same

1. Wilhelmj, C. M., and Sachs, A.: The Characteristics of the Normal Human Gastric Secretory Curve Using an Improved Gastric Test Meal, Am. J. Digest. Dis. 6:529, 1939.

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