accompanied by marked reticulocytosis of thirty-four and forty-four days' duration, respectively, were observed. This phase was followed by more rapid increase in hemoglobin and maturation of the red cells.

2. Coincident with the evidence of stimulation of the bone marrow, marked subjective improvement was noted.

3. In the light of our limited experience, it seems probable that a product can be obtained from the gastric contents of swine of such potency that a single intramuscular injection may be sufficient to bring about a complete remission in pernicious anemia. Should this prove to be true, it seems not unreasonable to predict that one injection of potent material at intervals of two or more months may be all that is required in this disease to maintain the blood count and the hemoglobin at normal levels.

TWO MECHANISMS IN THE PRODUCTION OF DUROZIEZ'S SIGN

THEIR DIAGNOSTIC SIGNIFICANCE AND A CLINICAL TEST FOR DIFFERENTIATING BETWEEN THEM

HERRMAN L. BLUMGART, M.D.
AND
A. CARLTON ERNSTENE, M.D.
BOSTON

The combination of an aortic diastolic murmur and peripheral signs, such as capillary pulse, wide pulse pressure, and Duroziez's sign, readily establishes the diagnosis of aortic insufficiency. In certain instances, however, the diagnosis is beset with difficulties. A diastolic murmur may be heard along the left border of the sternum in a patient with mitral stenosis, and the possibility of this murmur being due to the Graham Steell phenomenon presents itself. Under such conditions the presence or absence of the peripheral signs of aortic regurgitation assumes considerable importance. In other patients the peripheral signs of aortic regurgitation may be clearly evident, but the presence of the diastolic murmur may be doubtful.

Our purpose in this communication is to present the results of a study which permit a clearer understanding of the meaning of peripheral vascular signs and so help to resolve the clinical difficulties mentioned. Duroziez's sign has been the particular focus of this study, but the various peripheral signs tend to be present concomitantly, and so the accurate evaluation of one sign leads to a clearer understanding of the others.

Corrigan,[1] in his classic description of aortic insufficiency, was the first observer to note the presence of a diastolic murmur over the larger vessels. "In the cases where insufficiency is considerable and permits a large quantity of blood to flow back into the ventricle, one hears a double bruit in the ascending aorta." This sign, according to Corrigan, was one of the three vascular signs of aortic insufficiency. The presence of a double murmur heard over the peripheral vessels by pressure of the stethoscope was first described by Bouillaud.[2] It remained for Duroziez,[3] however, to study the phenomenon more closely and correlate its occurrence with the postmortem observations of aortic insufficiency.

In 1861, Duroziez[3] emphasized the diagnostic significance of the phenomenon and said: "The double intermittent crural murmur always accompanies aortic insufficiency; it reveals it in difficult and complicated cases; it is its pathognomonic sign. Now this has not been said by any author—I am going to prove it." In the course of his communication, Duroziez modified this somewhat dogmatic statement by mention of patients with enteric fever, saturnism and chlorosis, in whom the sign was present even in the absence of aortic regurgitation. In the years since, clinical observations have made it increasingly evident that, while Duroziez's sign usually can be elicited in patients with the intracardiac signs of aortic insufficiency, these phenomena are mutually independent—one may be present without the other. The diagnostic significance of Duroziez's sign consequently has occasioned considerable discussion and investigation.

Tice,[4] in 1911, made a valuable clinical contribution on the significance of the peripheral signs of aortic insufficiency. In a series of 124 cases of aortic insufficiency, the presence of Corrigan's pulse was observed in 95 per cent of the cases; capillary pulsation, 90 per cent; Duroziez's sign, 88 per cent; visible arterial pulsation, 76 per cent; pistol shot sound, 45 per cent, and femoral tones, 24 per cent. He stated that Duroziez's sign is not pathognomonic of aortic insufficiency but that it is also observed in other diseases with perfectly normal and competent valves. His concept of the mechanism whereby the double murmur is produced is not clear. "The essential portion of the phenomenon, the cardiodiastolic or arteriodiastolic, results from the backward flow of blood, produced chiefly by the vasomotor dilatation."

More recently, Laubry, Brosse and van Bogaert[5] have reported an extensive study of Duroziez's sign.

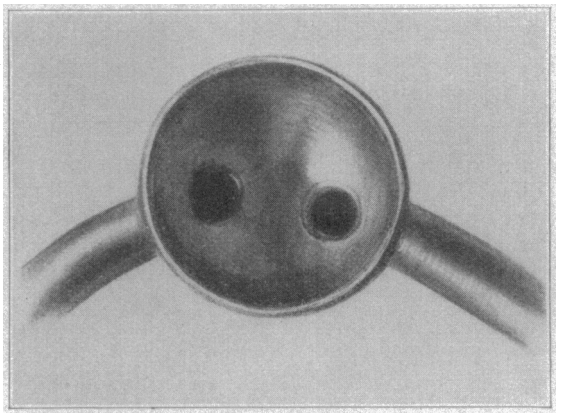

Fig. 1.—The Peabody bell stethoscope. The well defined edges and the absence of a diaphragm facilitate the production of diastolic arterial murmurs.

They state that perception of Duroziez's sign on simple auscultation over the femoral artery by compressing it only with the aid of the stethoscope and without resorting to any other technic is pathognomonic of aortic insufficiency. They corroborated Duroziez's original observations that in certain other conditions the sign may be produced by digital compression of

From the Medical Research Laboratories of the Beth Israel Hospital and the Department of Medicine, Harvard University Medical School.
This investigation was aided in part by a grant from the DeLamar Mobile Research Fund of Harvard University.

1. Corrigan, D. J.: On Permanent Patency of the Mouth of the Aorta, or Inadequacy of the Aortic Valves, Edinburgh M. & S. J. **37**: 225, 1832.
2. Bouillaud, J. B.: Maladies du coeur, ed. 2, 1841; cited by Duroziez.[3]
3. Duroziez, P. L.: Du souffle intermittent crural, comme signe de l'insuffisance aortique, Arch. gén. de méd. **17**: 417, 588, 1861.
4. Tice, Frederick: The Clinical Determination and Significance of Some of the Peripheral Signs of Aortic Insufficiency, Illinois M. J. **20**: 271, 1911.
5. Laubry, C.; Brosse, Mlle. T., and Bogaert, van A.: Doubles tons et doubles souffles vasculaires au cours de l'insuffisance aortique, Ann. de méd. **30**: 193 (Oct.) 1931.

the artery peripheral to the site of auscultation. They also report that compression of the artery below the point auscultated by means of a pneumatic cuff inflated to arterial systolic pressure may elicit the sign in conditions other than aortic insufficiency. The mechanism of the sign, according to these authors, is the same in all conditions, the diastolic murmur being due to a diastolic reflux of blood backward toward the heart. They regard local conditions, particularly "hypotonicity of the arterial wall," indispensable to its production.

Duroziez's original description referred to observations over the femoral artery, but clinical usage has sanctioned the wider application of this sign to a diastolic murmur heard over any of the larger peripheral vessels when pressure is exerted on the artery by means of the stethoscope.[6] In the present communication the term "Duroziez's sign" is used in this wider sense. In some of our subjects, observations were made over both the brachial and the femoral arteries; in others, observations were confined either to the brachial or to the femoral blood vessels. We have used the Peabody bell stethoscope[7] (fig. 1) during the course of this investigation because it seemed most suited to the elucidation of the phenomena under investigation. The standard mercury sphygmomanometer was used in all the observations. For application of pressure to the forearm, a cuff 14 cm. wide was used. A special cuff 20 cm. in width was used in applying pressure to the thigh. All the observations recorded in this communication were checked by two observers.

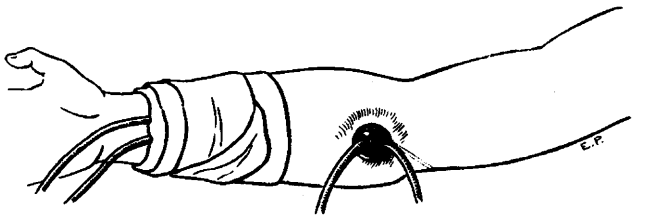

Fig. 2.—The manner of applying pressure to the forearm distal to the point of auscultation. This procedure accentuates the diastolic arterial murmur of aortic insufficiency but diminishes or abolishes the diastolic arterial murmur of other conditions.

OBSERVATIONS

Our observations demonstrate, we believe, that Duroziez's sign, a diastolic murmur heard over the larger arteries on pressure with the stethoscope, is heard in two entirely different types of conditions. The mechanisms by which the sign is produced in these two conditions are opposite in nature and can be differentiated with ease at the bedside by certain simple clinical tests.

Patients with Marked Peripheral Vasodilatation.—In twelve of twenty consecutive patients with thyrotoxicosis (table 1), a definite diastolic murmur was heard over the brachial or femoral arteries by pressing on the vessel with a stethoscope. In other patients with arterial hypertension and with generalized arteriosclerosis and in patients with fever, the sign also was elicited. We believe that in these patients the diastolic arterial murmur was due to an increased forward flow of blood toward the periphery during diastole. Normally, the rate of blood flow through the arteries, arterioles and capillaries is greatest during systole and less during diastole. In patients with increased local blood flow associated with peripheral vasodilatation, blood flow during diastole may be greatly increased and give rise to the diastolic murmur when the artery is stenosed by the stethoscope. The evidence for this concept is as follows:

1. If a stethoscope is placed over the brachial artery in the antecubital space and a blood pressure cuff is wrapped about the middle of the forearm above the wrist (fig. 2), inflation of the cuff to a pressure definitely below the diastolic level will completely abolish the diastolic murmur. Inflation of the cuff raises the pressure of the blood in the veins almost to the level of diastolic arterial pressure and so substitutes an artificial increase in the peripheral resistance for the low peripheral resistance of vasodilatation. The diastolic forward flow of blood is evidently more affected than the systolic forward flow of blood, for the diastolic murmur disappears and the systolic murmur diminishes somewhat in intensity. In conformity with these considerations, we have observed on numerous occasions that with the cuff inflated at a low pressure the diastolic murmur would disappear gradually in from ten to fifteen beats, while with pressures close to arterial diastolic the murmur would vanish in from one to three beats.

2. Simple immersion of the arm of the patient in cold water abolishes the diastolic murmur over the brachial artery quite as effectively as application of the blood pressure cuff. Immersion in hot water accentuates the diastolic murmur. Immersion of the arm up to a level some 15 to 20 cm. below the area auscultated is sufficient to bring about these changes. The importance of local changes in the wall of the artery is, contrary to the opinion of others,[5] therefore negligible. The appearance and disappearance of the murmur under such circumstances is evidently related to the degree of peripheral vasodilatation, vasodilatation permitting a marked increase in diastolic blood flow, and vasoconstriction resulting in a marked decrease in diastolic blood flow. The close relation between the state of the smaller peripheral vessels and the presence of the diastolic murmur is further shown by the fact that in certain subjects, in whom the vasomotor system was irritable (flushing, sweating), the murmur showed considerable variation.

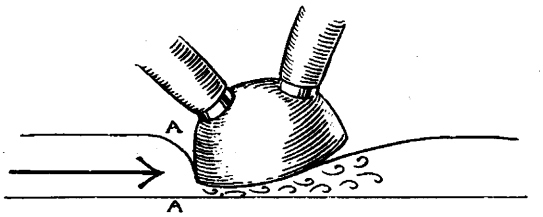

Fig. 3.—The production of Duroziez's sign in subjects with predominant vasodilatation. The arrow indicates the direction of blood flow toward the hand or foot during diastole. Pressure with the upper edge of the stethoscope is the most effective means of producing the eddy currents that give rise to the diastolic arterial murmur.

3. Immersion of the arms of normal subjects in hot water at 114 F. or exposure to high room temperature causes peripheral vasodilatation and results in the appearance of a diastolic murmur over the brachial arteries similar in all respects to that heard in patients with spontaneous vasodilatation (table 1). As in the case of spontaneous vasodilatation, this murmur is readily diminished or abolished by application of subdiastolic pressure to the forearm.

4. That the diastolic murmur is produced by a diastolic flow of blood forward toward the periphery is further shown by the fact that pressure on the artery

6. White, P. D.: Heart Disease, New York, Macmillan Company, 1931.
7. Manufactured by George P. Pilling and Son Company, Philadelphia.

predominantly with the upper edge of the stethoscope is far more effective in eliciting the sign than pressure with the lower edge of the stethoscope (fig. 3). This is in accord with the widely accepted concept that murmurs are produced mainly by eddies in the current when the cross sectional diameter of the stream is suddenly increased. The eddy currents are produced mainly at *A* in figure 3 and give rise to a murmur immediately beneath the stethoscope. If the flow of blood were in the reverse direction, the situation would be as shown in figure 4. The eddy currents would be produced mainly at *B*, beyond the area included by the bell of the stethoscope, and the murmur would be

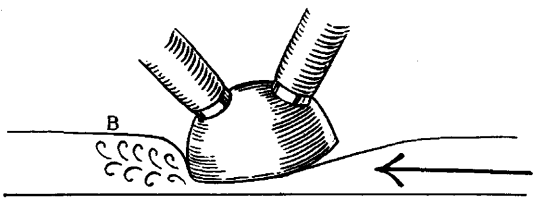

Fig. 4.—Production of the diastolic arterial murmur in peripheral vasodilatation by pressure with the upper edge of the stethoscope is inconsistent with a backward flow of blood during diastole. With pressure applied in this manner, a backward flow of blood would give rise to eddy currents beyond the area included under the bell of the stethoscope, and a diastolic murmur would be faint or inaudible.

fainter or inaudible. Actual observations substantiate these considerations.

5. In congenital phlebarteriectasis the blood flow of the affected extremity is greatly increased because of free artery to vein communications, and a diastolic murmur may be elicited by pressure with a stethoscope over the principal arteries. We recently studied a patient with this condition [8] and concluded that (*a*) there was a greatly increased blood supply to the extremity and (*b*) the diastolic murmur was due to an increased forward flow of blood during diastole.

6. The diastolic murmur tends to be transmitted toward the periphery rather than centrally. While the sign was produced in the antecubital fossa by one observer, the murmur was sometimes heard by a second observer over the radial, but not over the brachial, artery. This is in accord with our concept, for arterial murmurs tend to be transmitted in the direction of blood flow.

Patients with Aortic Regurgitation.—In patients with aortic regurgitation, the diastolic arterial murmur produced by pressure on the artery with the stethoscope sounds like that heard in other conditions. The mechanism of Duroziez's sign in patients with aortic regurgitation is directly opposite, however, to that of Duroziez's sign in subjects with other conditions. This is shown by the following tests:

1. If subdiastolic pressure is applied to the forearm or thigh while one listens over the brachial or femoral arteries, the murmur, instead of disappearing, is strikingly accentuated (table 2). The rise in peripheral resistance resulting from the application of pressure favors the backward flow of blood.

2. The diastolic murmur is brought out or accentuated not by pressure with the upper edge but by pressure with the lower edge of the stethoscope (fig. 5). In aortic insufficiency, the direction of arterial blood flow in diastole is the reverse of that present in other subjects with Duroziez's sign, and the technic of accentuating the murmur is the opposite.

8. Blumgart, H. L., and Ernstene, A. C.: Hemangiectatic Hypertrophy and Congenital Phlebarteriectasis, with Particular Reference to the Diagnostic Importance of the Peripheral Vascular Phenomena, Arch. Int. Med. **49**: 599 (April) 1932.

3. In aortic regurgitation, simple immersion of the arm in cold water tends to accentuate the diastolic murmur. The peripheral resistance is increased and reflux of blood toward the heart during diastole is favored. This reflux [9] may be a result of structural changes in the semilunar valves or a result of relative insufficiency of the valves due to dilatation of the aortic ring.

4. Application of the blood pressure cuff inflated to subdiastolic pressure not only accentuates Duroziez's sign when already present in aortic insufficiency but in certain patients it will even cause the diastolic murmur to appear. In subjects in whom the arterial diastolic pressure is only 0 to 20 mm. of mercury, a pressure of 20 to 30 mm. may be applied instead of subdiastolic pressure.

COMMENT

The divergent views in regard to the significance of Duroziez's sign and the mechanism of its production are more easily understood on the basis of the foregoing observations. Duroziez's sign denotes a flow of blood in the artery beneath the stethoscope during diastole. By itself the sign does not tell whether the diastolic flow of blood is toward the periphery, as in subjects with peripheral vasodilatation and competent aortic valves, or backward toward the heart, as in aortic insufficiency. The direction of the diastolic flow, and hence the diagnostic significance of the sign, must be decided by application of subdiastolic pressure distal to the point of auscultation.

As might be expected, in patients with aortic insufficiency the effect of immersing the arm in hot water varies. In some subjects the diastolic murmur is accentuated, in others diminished, according to whether there is a predominance of the one factor, aortic insufficiency, favoring a reflux of blood, or a predominance of the other factor, vasodilatation, favoring a forward diastolic flow of blood.

Much of the discussion in regard to the clinical significance of capillary pulsation and Duroziez's sign has been due to the lack of knowledge concerning the physiologic mechanisms involved in the production of these signs. It has become increasingly apparent that

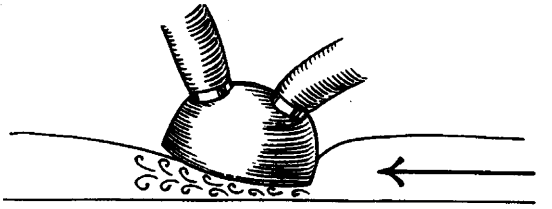

Fig. 5.—The production of Duroziez's sign in subjects with aortic insufficiency. The arrow indicates backward flow of blood toward the heart during diastole. Pressure with the lower edge of the stethoscope is the most effective means of producing the eddy currents which give rise to the diastolic arterial murmur beneath the bell of the stethoscope.

capillary pulsation is not necessarily associated with aortic reflux but is an expression of the local dilatation of the peripheral minute vessels.[10] As Lewis [11] states,

9. Wiggers, C. J.; Theisen, Harold, and Williams, H. A.: Further Observations on Experimental Aortic Insufficiency: II. Cinematographic Studies of Changes in Ventricular Size and in Left Ventricular Discharge, J. Clin. Investigation **9**: 215 (Oct.) 1930.

10. Quincke, H. I.: Ueber Capillarpuls und centripetal Venenpuls, Berl. klin. Wchnschr. **27**: 265, 1890. Glaessner, K.: Klinische Untersuchungen über den Kapillarpuls, Deutsch. Arch. f. klin. Med. **97**: 83, 1909. Herz, M.: Der Puls der kleinsten Gefässe, Wien. Klin. **22**: 165, 1896. Lewis, Thomas: Studies of Capillary Pulsation, with Special Reference to Vasodilatation in Aortic Regurgitation and Including Observations on the Effects of Heating the Human Skin, Heart **11**: 151 (April) 1924.

11. Lewis, Thomas: The Blood Vessels of the Human Skin and Their Responses, London, Shaw & Sons, Ltd., 1927.

"even in disease of the aortic valves the pulsation is much more dependent upon a strictly local condition of the blood vessels than upon change in the general arterial blood pressures arising out of the valve injury." The presence of capillary pulsation must therefore be regarded as indicating peripheral vasodilatation in the part studied; but whether this vasodilatation is the result solely of local conditions (increased skin temperature) or whether it is a secondary consequence of aortic insufficiency cannot be ascertained on the basis of the sign alone. Similarly, Duroziez's sign as usually elicited simply denotes an increased blood flow in the artery beneath the stethoscope during diastole but does not indicate whether blood flow occurs in a forward direction because of preponderant vasodilatation or backward toward the heart because of aortic reflux. The tests we have outlined enable one to decide these questions and are of value in differentiating aortic insufficiency from other conditions. They permit one to attach greater diagnostic significance to peripheral diastolic arterial murmurs than is at present possible in the case of capillary pulsation.

SUMMARY AND CONCLUSIONS

1. Duroziez's sign, one of the so-called peripheral signs of aortic regurgitation, may be present in patients with competent aortic valves.

2. A study of Duroziez's sign has shown that it occurs in two entirely different conditions and that the two mechanisms producing the sign are opposite in nature and can be differentiated with ease at the bedside by certain simple clinical tests.

3. In patients with preponderant peripheral vasodilatation (thyrotoxicosis, anemia, fever, normal subjects with increased local blood flow due to immersion of the limb in hot water), the diastolic arterial murmur is due to an increased forward flow of blood toward the periphery during diastole.

4. In patients with aortic regurgitation, the diastolic arterial murmur elicited by pressure on the artery with

TABLE 1.—*Observations on Duroziez's Sign in Subjects Without Aortic Insufficiency*

Subject	Sex*	Age, Years	Diagnosis	Pulse Rate per Minute	Arterial Pressure: Systolic, Mm. Hg	Arterial Pressure: Diastolic, Mm. Hg	Capillary Pulsation	Duroziez's Sign: Present	Brought Out by Hot Water	Subdiastolic Pressure Test: Pressure Applied, Mm. Hg	Subdiastolic Pressure Test: Effect on Diastolic Murmur	Comment†
H. D.	♂	36	Thyrotoxicosis	94	124	68	+	+	..	40	Abolished	Basal metabolic rate +30%
F. J.	♂	45	Thyrotoxicosis	112	116	74	+	+	..	60	Abolished	Basal metabolic rate +68%
M. R.	♀	43	Thyrotoxicosis	90	128	82	+	0	+	80	Abolished	Basal metabolic rate + 8%
S. C.	♀	30	Thyrotoxicosis	120	134	88	+	+	+	60	Abolished	Basal metabolic rate +39%
C. E.	♀	25	Thyrotoxicosis	124	108	72	+	+	+	40	Abolished	Basal metabolic rate +35%
E. S.	♀	63	Thyrotoxicosis	100	150	86	+	0	..	..	.....	Basal metabolic rate +51%
A. B.	♀	53	Thyrotoxicosis	128	134	70	0	0	..	..	.....	Basal metabolic rate +34%
M. B.	♀	42	Thyrotoxicosis	128	126	62	+	+	..	60	Abolished	Basal metabolic rate +26%
M. V.	♀	46	Thyrotoxicosis	120	112	56	+	0	..	..	.....	Basal metabolic rate +31%
A. C.	♂	45	Thyrotoxicosis	100	118	68	+	+	..	60	Abolished	Basal metabolic rate + 9%
E. P.	♀	19	Thyrotoxicosis	84	110	56	+	+	..	40	Abolished	Basal metabolic rate +16%
R. G.	♀	14	Thyrotoxicosis	96	128	56	+	+	..	..	.....	Basal metabolic rate +13%
D. M.	♀	32	Thyrotoxicosis	80	116	64	+	+	..	60	Abolished	Basal metabolic rate +13%
A. D.	♀	16	Thyrotoxicosis	134	126	74	+	0	..	..	.....	Basal metabolic rate +40%
M. C.	♀	41	Thyrotoxicosis	82	136	72	0	0	..	..	.....	Basal metabolic rate +11%
I. L.	♀	40	Thyrotoxicosis	82	130	74	0	0	..	..	.....	Basal metabolic rate +13%
H. B.	♂	40	Thyrotoxicosis	110	162	82	+	+	+	60	Abolished	Basal metabolic rate +39%
J. K.	♀	30	Thyrotoxicosis	100	138	72	+	+	..	60	Abolished	Basal metabolic rate +38%
M. S.	♀	48	Thyrotoxicosis	112	128	68	+	+	..	50	Abolished	Basal metabolic rate +41%
S. R.	♀	50	Thyrotoxicosis	108	126	70	+	0	..	..	.....	Basal metabolic rate +20%
S. T.	♂	51	Chronic nephritis; hypertension	64	190	102	+	+	+			
L. B.	♀	32	Chronic nephritis; hypertension	96	256	154	0	0	+			
N. F.	♂	59	Generalized arteriosclerosis; secondary anemia	92	98	42	+	+	..	40	Abolished	Oral temperature 100.2 F.
I. R.	♀	48	Carcinoma of the colon	120	110	70	+	+	..	40	Abolished	Oral temperature 102.6 F.
B. M.	♂	20	Normal	92	108	76	0	0	+	70	Abolished	
A. F.	♂	30	Normal	126	70	80	+	+	..	40	Abolished	Room temperature 80 F.
B. A.	♂	23	Normal	76	120	84	+	+	+	80	Abolished	Room temperature 86 F.
J. R.	♂	29	Normal	80	120	90	+	+	+	60	Abolished	Room temperature 86 F.
D. G.	♀	30	Normal	100	110	70	..	+	+	..	.....	Room temperature 86 F.
B. S.	♀	23	Normal	76	120	82	0	0	+	60	Abolished	Room temperature 85 F.
J. M.	♂	18	Normal	68	122	78	+	+	+	70	Diminished	Room temperature 85 F.

* In the tables, ♂ denotes male; ♀, female.

† The basal metabolic rates recorded were obtained, except in two instances, within one day of the time of making the observations on Duroziez's sign.

TABLE 2.—*Observations on Duroziez's Sign in Subjects With Aortic Insufficiency*

Subject	Sex	Age, Years	Diagnosis	Pulse Rate per Minute	Arterial Pressure: Systolic, Mm. Hg	Arterial Pressure: Diastolic, Mm. Hg	Capillary Pulsation	Duroziez's Sign: Present	Subdiastolic Pressure Test: Pressure Applied, Mm. Hg	Subdiastolic Pressure Test: Effect on Diastolic Murmur
H. G.	♂	27	Rheumatic heart disease	80	170	0	+	+	30	Increased
B. A.	♂	26	Rheumatic heart disease; subacute bacterial endocarditis	88	128	42	+	+	30	Increased
I. S.	♂	18	Rheumatic heart disease	84	122	30	+	+	60	Increased
L. C.	♂	20	Rheumatic heart disease	72	136	0	+	+	40	Increased
S. N.	♂	11	Rheumatic heart disease	126	122	0	+	0	60	Produced
M. S.	♀	44	Rheumatic heart disease	76	142	70	+	0	70	Not produced
P. A.	♂	29	Rheumatic heart disease	80	124	44	+	+	40	Increased
R. C.	♂	65	Syphilitic aortitis	92	168	90	+	+	70	Increased
G. R.	♂	52	Syphilitic aortitis	96	184	64	+	+	54	Increased
D. M.	♂	58	Syphilitic aortitis	76	174	36	+	+	30	Increased

the stethoscope is similar to that heard in other conditions, but it is due not to a forward flow of blood but to a backward flow of blood during diastole toward the heart.

5. In patients with aortic regurgitation the diastolic murmur may be strikingly accentuated by pressing predominantly with the lower edge of the stethoscope bell, by immersing the arm in cold water, or by applying a cuff inflated to subdiastolic pressure to the limb below the site of auscultation.

6. In patients with preponderant peripheral vasodilatation the diastolic murmur is increased by pressure with the upper edge of the stethoscope, while the murmur is abolished by immersion of the limb in cold water or by application of subdiastolic pressure distal to the site of auscultation.

7. Duroziez's sign as classically elicited simply denotes, therefore, an increased flow of blood in the artery beneath the stethoscope during diastole but does not indicate whether blood flow occurs in a forward direction toward the periphery because of preponderant vasodilatation or backward toward the heart because of aortic reflux. The tests we have outlined enable one to decide these questions and are of value in differentiating aortic insufficiency from other conditions.

330 Brookline Avenue.

DIABETIC OR MYCOTIC VULVOVAGINITIS

PRELIMINARY REPORT

H. C. HESSELTINE, M.D.
CHICAGO

According to gynecologic textbooks, monographs and articles,[1] diabetic genital pruritus and vulvovaginitis are produced by dextrose or other substances in abnormal amounts in the urine. However, the following observations indicate that Eumycetes (fungi) are in most instances the etiologic agent, which is in accord with the statement by Plass, Hesseltine and Borts [2] that "pregnancy and diabetes are predisposing factors" for such infection. Although the reasons for this predilection are not completely known, it is obvious that with the constant spill of excessive dextrose over the vulva a satisfactory medium is created, especially since students [3] in this field have shown that the pathogenic yeasts thrive on dextrose and levulose in the presence of acid.

While the proponents of urinary irritants are supported in their view by local improvement simultaneously with control of the diabetic state, I believe that the fungi cease producing symptoms because of an inadequate medium (cessation of glycosuria). Genital mycoses explain more readily why pruritus and vulvitis continue in some individuals in spite of diet and insulin, or why fungicidal therapy alone completely cures the genital disease.

The clinical appearance of yeast infections of the vulva have been described by Plass and his co-workers.[2] Briefly, the tissues are reddened and are usually edematous, sometimes covered with thrush patches, caseous material or again only with an excessive discharge. The leukorrhea not infrequently contains minute flakes and sometimes bubbles. If the disease is of long duration, the skin of the labia and groin may be reddened, or thickened, roughened and "bronzed." Not infrequently, excoriations or localized desquamation are observed; the former may be the result of local tissue sensitization or toxic necrosis, while the latter is caused by the extensive scratching. With such pathologic tissue changes, an ample portal of entry is available for staphylococci, streptococci, certain diplococci, or other bacteria which may grow in the presence of these yeasts. The symptoms of itching and local discomfort may vary from a mild to a most distracting and sleep disturbing complication.

TABLE 1.—*New Diabetic Patients with Pruritus*

	Fungi		
	Present	Absent	Total
With glycosuria	15	0	15
With no glycosuria	3	3	6
Total	18	3	21

Since typical thrush patches are less often present and direct smear of the vulvovaginal discharge and lesions may not reveal the presence of mycelia (hyphae) and conidia, cultures are without question the most reliable diagnostic procedure.[4] The treatment consists of semiweekly vulvovaginal application of 1 per cent gentian violet (in an aqueous or glycerin vehicle) or of diluted iodine solution, and daily 1 per cent sodium bicarbonate vaginal douches.[2]

OBSERVATIONS, EXPERIMENTS AND COMMENT [5]

This study included only those diabetes mellitus patients who had genital itching or infection. The age incidence varies from 12 to the late seventies. Two of the younger patients had not menstruated, yet their development was such that menstruation could be expected at any time. Table 1 shows that in eighteen of the twenty-one cases fungi were present. In one of the three negative cases, the patient had applied a heavy ointment which interfered with the obtaining of a satisfactory culture, and unfortunately she has not

TABLE 2.—*Yeast—Classified* *

Saccharomyces	1
Cryptococcus	1
Endomyces	6
Monilia	1
Yet undetermined	3
Lost	2

* This includes only those cultures collected at the University of Chicago.

From the Department of Obstetrics and Gynecology, the University of Chicago.
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