

# ANGINA IN WOMEN

BY

V. K. SUMMERS

*From the Walton Hospital, Liverpool*

Received December 22, 1947

The relatively infrequent occurrence of angina of effort in women has been noted since Heberden (1772) first gave an account of this disorder. Heberden observed in a lecture before the Royal College of Physicians of London, that he had seen the disease in 20 men and only 1 woman, and in a later publication (1786) wrote: "I have seen nearly a hundred people with the disorder out of which number there have been 3 women." Mackenzie (1923) reported 40 women with angina of effort in a series of 280 cases, which gives a sex incidence of 7 to 1 in favour of men. In more recent years, most investigators have found a sex incidence of 3-4 males to 1 female (White and Bland, 1931; White and Sharber, 1935; Levy and Boas, 1936; Bedford, 1936; Riseman and Brown, 1937; Gallavardin, 1938; and White, 1944) although Bourne and Scott (1938) found a predominance in males of 7 to 1 in 112 cases.

In this paper, a series of 87 cases of angina of effort occurring in women will be analysed in an attempt to discover what aetiological factors are responsible for such a striking sex predominance. The diagnosis of angina of effort, particularly in women, is fraught with many pitfalls; and to avoid these it was decided that only those who complained of substernal pain of constricting quality, with a quantitative relation to exercise and relieved by rest or nitroglycerin, would be included.

TABLE I  
AGE DISTRIBUTION

Age			No. of cases
20-30	..	..	2
30-40	..	..	1
40-50	..	..	18
50-60	..	..	29
60-70	..	..	25
70-80	..	..	12

Although three quarters of all cases of angina of effort occur over the age of 50 (White, 1944), there is a considerable incidence in men under this age.

Only 3 cases occurred under 40 in women in this series; 2 had severe anæmia and the third had aortic regurgitation. Glendy, Levine, and White (1937) in a 100 cases of coronary disease in young people found only 4 women under 40 and 3 of these had severe hypertension. White and Mudd (1927) reported 8 patients with angina under 30; all had aortic incompetence. The age incidence in this series corresponds closely with that given by other observers; Eppinger and Levine (1934) in 141 cases found the usual range of the age at onset to be 36-71 years.

The rather high incidence (14 per cent) in patients over 70 years is unusual. Foti (1937) in 20 cases over 70 found no women and Lian (1932) found only 17 occurring between the ages of 70-75 years in 638 cases of angina.

## THE EFFECT OF PREGNANCY AND THE MENOPAUSE

The effect of pregnancy on the incidence of angina was investigated and the results were as follows:

No child, 12 cases; one child, 16 cases; two children, 22 cases; three children, 14 cases; four children, 9 cases; five children, 4 cases; six children, 6 cases; seven children, 4 cases.

The inference to be drawn from the above data is that no close association between parity and the incidence of angina can be shown. Moreover if pregnancy were of aetiological importance in the production of coronary atheroma, then it might be expected that deaths due to the consequence of this condition would occur with appreciable frequency in multigravida. Sheehan and Sutherland (1940), in an analysis of 813 autopsy records of patients who died during pregnancy, failed to find atheromatous changes in the hearts of any of these.

*Menopause.* The first symptoms of angina of effort in 5 of these patients occurred at the time of the menopause; all had systolic blood pressures over 200 mm. Most patients (76 per cent) experienced their first symptoms many years after the menopause.

## HYPERTENSION

The incidence of hypertension, which for the purpose of this paper was assumed to be present if the systolic pressure was above 150 or the diastolic above 90 is shown in table II; an incidence of 84 per cent was found. The blood-pressure readings recorded here are an average of several readings for each patient.

TABLE II  
PATIENTS WITH HIGH BLOOD PRESSURE

Systolic B.P.	No. of cases	Diastolic B.P.	No. of cases
150-160	4	90-100	14
160-170	6	100-110	26
170-180	4	110-120	18
180-190	12	120-130	8
190-200	7	130-140	2
200-210	12	140-150	4
210-220	10	150-160	4

Davis and Klainer (1940) in 61 cases of angina of effort found that 90 per cent of the women had hypertension compared with 60 per cent of the men. The incidence of hypertension in reported cases of angina of effort varies (Riseman and Brown, 1937, 50 per cent; White and Bland 1931, 36 per cent; Kahn, 1926, 34 per cent).

In women a higher incidence of hypertension is reported (Davis and Klainer, 1940, 90 per cent; Levy and Boas, 1936, 92 per cent; and Eppinger and Levine, 1934, 100 per cent).

The frequent occurrence of hypertension in women suffering from angina of effort suggests a possible aetiological relationship, especially since most investigators record a much lower incidence in men.

## CORONARY ARTERY DISEASE AND CORONARY INFARCTION

There were 34 patients with a history of one or more attacks of coronary infarction and a less certain history was obtained in 14 others. A total of 57 patients showed cardiographic evidence, e.g. changes in the Q and T waves or in the S-T segment, suggestive of coronary artery disease and in 6 of this group necropsy revealed severe coronary atheroma. The highest incidence of coronary disease occurred in the sixth and seventh decades in which 83 per cent of the patients gave, either a history of previous coronary infarction or showed suggestive cardiographic changes. Willius and Smith (1932) reported moderately severe coronary atheroma in all cases in an autopsy study of 381 patients over 70 years and this no doubt is the explanation of the high incidence of coronary disease in the sixth and seventh decades in this series

The incidence of previous coronary infarction varies in reported cases of angina of effort (Bland and White, 1931, 26 per cent; Riseman and Brown, 1937, 37 per cent; Bourne and Scott, 1938, 28 per cent; and Pazzanese and Montenegro, 1945, 72 per cent).

The incidence of evidence of coronary artery disease is high (65 per cent) in this series, but is lower than that reported by Harrison (1944) of 83 per cent.

## OTHER DISEASES OR PATHOLOGICAL STATES

*Syphilis.* One woman of 23 had angina of effort with syphilitic aortic incompetence. Jones and Bedford (1943) reported on 103 patients who had angina of effort of syphilitic aetiology and stated that all their patients under 40 had aortic incompetence. They gave the incidence of aortic incompetence in angina as 5 per cent and this figure closely agrees with those given by Brooks (1927) and Warthin (1930).

*Mitral Stenosis.* No case of mitral stenosis and angina was seen during the course of this investigation. Blackford (1940) reported 2 cases of mitral stenosis and angina of effort and found no coronary lesions post-mortem in either case. Levine and Kauvar (1942) found only 17 cases of mitral stenosis in 2832 cases of angina and coronary thrombosis; the average age of onset of anginal symptoms in these cases was 56 years.

*Myxœdema.* Two patients had myxœdema and angina of effort; both were over 50 and had hypertension. The cardiogram of one showed a left bundle branch block, and of the other a Wilson type of branch block. In both, the symptoms of angina were aggravated by thyroid therapy.

Beaumont and Robertson (1939) suggested that two types of angina occurred in myxœdema; the first occurring during treatment with thyroid extract, whilst the second type occurred prior to treatment and improved following the administration of thyroid extract. Hertoghe (1914) suggested that angina occurring in myxœdema and improving with treatment might be due to involvement of cardiac nerve fibres by myxœdematous infiltration. Cases of this type have been reported by Peel (1943), Benestad (1937), Beach (1935), Ziskin (1930), and Sturgis (1926).

The majority of reported cases of angina of effort occurring in association with myxœdema appear to be due to independent heart disease. Peel (1943) reported 12 cases of myxœdema and angina of effort; 10 had evidence of independent heart disease. Aggravation of anginal pain during thyroid therapy has been noted by d'Abrahami *et al.* (1925), Sturgis and Whiting (1925), Means *et al.* (1926), Fahr (1932),

Mussio-Fournier and Fisher (1940) and Mussio-Fournier (1942).

There is no evidence to suggest that myxœdema is an important ætiological factor in the majority of cases of angina.

*Hyperthyroidism.* No instances of hyperthyroidism and angina were observed in this series and most observers are agreed that there is no direct causal relationship between the two conditions and that there is usually some underlying cause for the angina. Females usually predominate (Lev and Hamburger, 1928 and 1932; Haines and Kepler, 1930).

*Diabetes.* Four patients were suffering from diabetes mellitus; all were over 55 and had hypertension. In two it was known that diabetes had preceded the onset of angina of effort by at least 5 years. Root and Graybiel (1931) noted that on the average diabetes preceded the angina by 9 years and that diabetic angina occurred most often in the seventh decade. They found only 210 cases of angina in 7000 diabetics. Nathanson (1932) who examined the coronary vessels of 100 diabetic patients post-mortem, found the greatest incidence of coronary atheroma occurred over 50, and Hepburn and Graham (1928) found cardiographic changes suggestive of coronary artery disease in 45 per cent of 123 diabetics. Of the four patients observed in the present series, two had a negative T I and one negative T waves in the standard leads and in lead IV F.

It is clear that diabetes mellitus is not an important ætiological factor in the majority of cases of angina occurring in women.

*Obesity.* The state of nutrition was observed in all cases and patients were grouped as thin, normal, and fat. The results were as follows: thin, 27 cases, normal, 37 cases, and fat, 13 cases.

Obesity would not appear to be a significant factor in the ætiology, a finding that confirms those of Eppinger and Levine (1934).

*Anæmia.* Herrick and Nusim (1918), were the first observers to draw attention to the occurrence of angina of effort in severe anæmia, but since this time frequent reports of its occurrence have appeared (Hunter, 1942; Stalker, 1937; Elliot, 1934; and Pickering and Wayne, 1943).

Wilkinson (1933), found only 3 cases of angina in 270 cases of anæmia and Willius and Giffin (1927) found only 43 patients with anginal symptoms in 1560 cases of pernicious anæmia. A higher incidence has been reported by Coombs (1930); Pickering and Wayne (1943); and Hunter (1946);

In the present series 6 patients had anæmia and angina of effort. Two were under 40 and had normal blood pressure; their anginal symptoms

disappeared when their anæmia had been cured. Three of the remaining patients had angina of effort after their blood had been restored to normal; the cardiogram of one showed a left bundle branch block and of the others inversion of T waves in leads I and II: all 3 patients whose anginal symptoms persisted following cure of their anæmia had hypertension. Lewis and Drury (1923) suggested that anginal pain occurring in anæmia was due to anoxæmia, but it has been shown that there is a raised cardiac output in anæmia and a raised venous pressure (Dautebrande, 1925; Stewart, Crane, and Deitrick, 1937; and Sharpey-Schafer, 1944) and this is the more probable explanation of the occurrence of anginal symptoms.

Sometimes no coronary artery lesions have been demonstrated at necropsy in cases of anæmia presenting anginal symptoms (Elliot, 1934) and in spite of this many observers doubt if anæmia alone can cause cardiac pain. It is difficult to avoid the conclusion in the two cases occurring in women under 40, whose cardiac pain was abolished when their anæmias were cured, that their anginal symptoms were solely due to anæmia. There seems little doubt also that the 3 patients who retained symptoms of angina of effort even with normal blood pictures, had coronary artery disease.

*Tobacco and Alcohol.* In this group of patients, smoking was an infrequent habit. Only 17 patients smoked regularly and a careful history in each case failed to reveal any relationship between tobacco smoking and the anginal attacks. White and Sharber (1934-5) in 750 patients found a higher percentage of sufferers amongst teetotallers than amongst those who were not. Pickering and Sanderson (1945) suggested that smoking precipitated an attack of angina only when an attack previously provoked by exertion had just subsided; and they concluded that tobacco did not cause constriction of the coronary vessels. Nevertheless it has been shown by Short and Johnson (1939) that tobacco induces arteriolar constriction and an elevated blood pressure. Bryant and Wood (1947) also demonstrated cardiographic changes of coronary ischæmia that were induced by tobacco smoking.

There is, however, no evidence to suggest in the present investigations that tobacco smoking is of ætiological importance in the production of angina in women, whatever be its relation to the wider problem of this disease in males.

Alcohol did not appear to be an important ætiological factor in the present series of cases.

*Cholecystitis.* The incidence of gall-bladder disease was very low. Two patients had gall stones; 3 gave a history suggestive of chronic

cholecystitis and in 2 of these a Graham's cholecystogram revealed non-functioning gall bladders. Bourne and Scott (1938) found 8 cases of cholecystitis in 112 cases of angina; in only 3 cases, however, was the presence of gall-bladder disease proved beyond doubt.

*Occupation and Environment.* These patients were studied during the past four years; 23 had undertaken factory work in addition to their household duties during the war years, but 7 had carried out such duties for a short time only. All were hospital outpatients, but the incidence of angina amongst the large numbers of patients of this class seen during the period of those observations was very small, and it does not seem likely that there is any relationship between work in addition to household duties and the increased incidence of angina to-day, compared with fifty years ago. It has not been practicable to take into account environmental influences in the earlier years of these patients' lives and to compare them with those obtaining in a woman's life of fifty years ago. Such a comparison might give a clue to the increased frequency with which angina is encountered in women nowadays.

## SUMMARY

A series of 87 cases of angina of effort occurring in women has been analysed. The highest incidence of the disease was in the sixth and seventh decades and the occurrence of the disease below the age of 40 was rare. A high incidence of hypertension (84 per cent) was found and this observation is in accord with those of other observers. Hypertension would appear to be an important factor in the ætiology of angina of effort in women; moreover the importance of hypertension in the diagnosis of this condition in women should be stressed. The frequent occurrence of previous coronary infarction and of evidence of coronary artery disease suggest that coronary sclerosis is the most important factor in the ætiology of angina of effort in women. Other factors, e.g. myxœdema, anæmia, cholecystitis, pregnancy, tobacco, alcohol and occupation appear to be of minor importance only in the ætiology.

I should like to thank Dr. H. Wallace-Jones for his helpful criticism and advice and for permission to include in this series cases seen at the Heart Department of the Liverpool Royal Infirmary. I should like also to thank Dr. E. Noble Chamberlain for his valuable criticism and advice, and Dr. H. H. MacWilliam for permission to include cases seen at Walton Hospital, Liverpool.

## REFERENCES

- d'Abrami, P., Buite, M., and Heitz, J. (1925). *Bull. Mem. Soc. méd. Hôp. Paris*, **47**, 172.
- Beach, C. H. (1935). *J. Amer. med. Ass.*, **105**, 871.
- Beaumont, G. E., and Robertson, J. D. (1939). *Lancet*, **1**, 682.
- Bedford, D. E. (1936). *Brit. Encyclop. med. Pract.*, vol. 1, Lond.
- Benestad, G. (1937). *Nord. med. Tydskr.*, **14**, 1741.
- Bernstein, S. S., and Ginzburg, L. (1942). *J. Mt. Sinai Hosp., N.Y.*, **9**, 142.
- Blackford, L. M. (1940). *Amer. Heart J.*, **20**, 492.
- Bourne, G., and Scott, R. B. (1938). *Brit. med. J.*, **1**, 55.
- Brooks, H. (1927). *Trans. Ass. Amer. Phys.*, **42**, 31.
- Bryant, J. M., and Wood, J. E. (1947). *Amer. Heart J.*, **34**, 20.
- Coombs, C. F. (1930). *Quart. J. Med.*, **23**, 233.
- Dautebrande, L. (1925). *Compt. rend. Soc. Biol.*, **93**, 1029.
- Davis, D., and Klainer, M. J. (1940). *Amer. Heart J.*, **19**, 198.
- Elliot, A. H. (1934). *Amer. J. med. Sci.*, **187**, 185.
- Eppinger, E. C., and Levine, S. A. (1934). *Arch. intern. Med.*, **53**, 120.
- Fahr, G. (1932-3). *Amer. Heart J.*, **8**, 91.
- Foti, A. (1937). *N. Y. St. J. Med.*, **37**, 2018.
- Gallavardin, L. (1938). *J. Méd. Lyon*, **19**, 527.
- Glendy, R. E., Levine, S. A., and White, P. D. (1937). *J. Amer. med. Ass.*, **109**, 1775.
- Haines, S. F., and Kepler, E. J. (1930). *Med. Clin. N. Amer.*, **13**, 1317.
- Harrison, T. (1944). *Amer. J. med. Sci.*, **27**, 322.
- Herberden, W. (1772). *Med. Trans. roy. col. Phys. Lond.*, **2**, 59.
- (1786). *Commentaries on History and Cure of Disease*, p. 366.
- Hepburn, J., and Graham, D. (1928). *Amer. J. med. Sci.*, **176**, 782.
- Herrick, J. B., and Nuzim, F. R. (1918). *J. Amer. med. Ass.*, **70**, 67.
- Hertoghe, E. (1914). *Med. Rec. N.Y.*, **86**, 489.
- Hunter, A. (1946). *Quart. J. Med.*, **15**, n.s., 107.
- Jones, E., and Bedford, D. E. (1943). *Brit. Heart J.*, **5**, 107.
- Kahn, M. H. (1926). *Amer. J. med. Sci.*, **172**, 195.
- Lev, M. W., and Hamburger, W. W. (1928). *Amer. Heart J.*, **3**, 672.
- (1932). *Ibid.*, **8**, 109.
- Levine, S. A. (1930). *Ann. intern. Med.*, **4**, 67.
- , and Kauvar, A. J. (1942). *J. Mt. Sinai Hosp. N.Y.*, **8**, 754.
- Levy, H., and Boas, E. P. (1936). *J. Amer. med. Ass.*, **107**, 97.
- Lewis, T., and Drury, A. N. (1923). *Heart*, **10**, 301.
- Lian, C. (1932). *L'Angine de Poitrine*, Masson, Cie., Paris.
- Mackenzie, J. (1923). *Angina Pectoris*, Oxford Med. Publ., p. 118.
- Means, J. H., White, P. D., and Krantz, C. I. (1926). *Boston med. surg. J.*, **195**, 455.
- Mussio-Fournier, J. C., and Fischer, J. T. (1940). *Presse méd.*, **48**, 364.
- (1942). *Proc. Mayo Clin.*, **17**, 212.

- Nathanson, M. H. (1932). *Amer. J. med. Sci.*, **183**, 495.
- Pazzanese, D., and Montenegro, O. (1945). *Amer. Heart J.*, **30**, 599.
- Peel, A. A. F. (1943). *Brit. Heart J.*, **5**, 89.
- Pickering, G. W., and Wayne, E. J. (1943). *Clin. Sci.*, **1**, 305.
- , and Sanderson, P. H. (1945). *Ibid.*, **5**, 275.
- Riseman, J. E., and Brown, M. G. (1937). *Amer. Heart J.*, **37**, 209.
- Root, H. F., and Graybiel, A. (1931). *J. Amer. med. Ass.*, **86**, 925.
- Sharpey-Schafer, E. P. (1944). *Clin. Sci.*, **5**, 125.
- Sheehan, H. L., and Sutherland, A. M. (1940). *J. Obstet. Gynec. Brit. Emp.*, **47**, 597.
- Short, J. J., and Johnson, H. J. (1939). *J. Lab. clin. Med.*, **24**, 590.
- Stalker, H. (1937). *Ann. intern. Med.*, **10**, 1172.
- Stewart, H. J., Crane, N. F., and Deitrick, J. E. (1937). *J. clin. Invest.*, **16**, 431.
- Sturgis, C. C., and Whiting, W. B. (1925). *J. Amer. med. Ass.*, **85**, 2013.
- (1926). *Boston med. surg. J.*, **195**, 351.
- Warthin, A. S. (1930). *Amer. Heart J.*, **6**, 163.
- White, P. D., and Bland, E. F. (1931). *Amer. Heart J.*, **7**, 1.
- , and Mudd, S. G. (1927). *Ibid.*, **3**, 1.
- , and Sharber, T. (1935). *J. Amer. med. Ass.*, **102**, 655.
- (1944). *Heart Disease*, Macmillan & Co., p. 816.
- Wilkinson, J. F. (1933). *Quart. J. Med.*, **26**, 281.
- Willius, F. A., and Giffin, H. Z. (1927). *Amer. J. med. Sci.*, **174**, 30.
- , and Smith, H. L. (1932-3). *Amer. Heart J.*, **8**, 170.
- Zimmerman, S. L., and Barnett, R. (1944). *Ann. intern. Med.*, **21**, 1045.
- Ziskin, T. (1930). *U.S. Veterans Bur. med. Bull.*, **6**, 24.