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CARDIOVASCULAR MANIFESTATIONS OF RHEUMATOID ARTHRITIS*

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RHEUMATOID ARTHRITIS is a chronic inflammatory disease of unknown etiology, the principal manifestations of which are polyarthritis and subcutaneous nodules. Rheumatoid disease of the cardiovascular system is known to occur but is rare by contrast with rheumatic heart disease.[1, 2] The pathological changes which may occur in the heart in rheumatoid disease are distinct from those caused by rheumatic fever. The object of this paper is to record three examples of fatal rheumatoid cardiovascular disease.

MATERIAL

CASE 1.—A 16-year-old white girl was admitted to hospital in 1957 because of fever and pain in multiple joints. These symptoms had been present for two weeks and followed a mild sore throat for which she had not sought treatment.

A maternal uncle had died at the age of 48 after having rheumatoid arthritis for 11 years. The cause of his death is unknown.

In 1951, at the age of 10, the patient had had pain and swelling of multiple joints lasting for three months. During this illness her heart was apparently normal and she had no residual joint deformities afterwards. In 1954, at the age of 13, she had a further attack of polyarticular pain and swelling associated with fever and anorexia. There had been some preceding lassitude but no apparent respiratory infection. She became bedridden and remained in bed for about nine months, during which time her weight fell to 66 lb. The wrists, cervical spine, hips and knees were the most prominently affected joints. Flexion deformities developed in her hips and knees (Fig. 1).

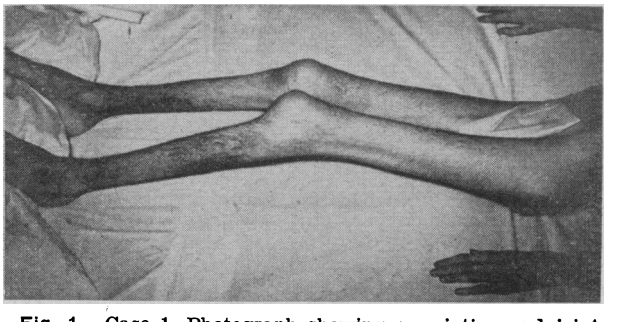

Fig. 1.—Case 1. Photograph showing emaciation and joint deformities.

There was no enlargement of the spleen or superficial lymph nodes, no psoriasis and no clinical evidence of heart disease. Radiography showed partial fusion of the sacroiliac joints, narowing of the joint spaces of the hips and skeletal rarefaction. She was treated in hospital for one year with an active physiotherapeutic regimen and some cortisone. When she returned home she weighed 80 lb. She was able to walk with the aid of canes but her wrist movements were limited to a few degrees.

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During the next two years she had recurrent small effusions in her knee joints and developed bony ankylosis of her left hip.

In 1957, she had a mild upper respiratory infection followed by the abrupt onset of fever, anorexia and joint pain. On admission to hospital two weeks later she looked very ill and was pale and in considerable pain. She weighed 96 lb. Her temperature was 104° F., pulse rate regular at 140, and blood pressure 120/60 mm. Hg. There was multiple arthritis affecting particularly her shoulders, elbows and left ankle. Her heart

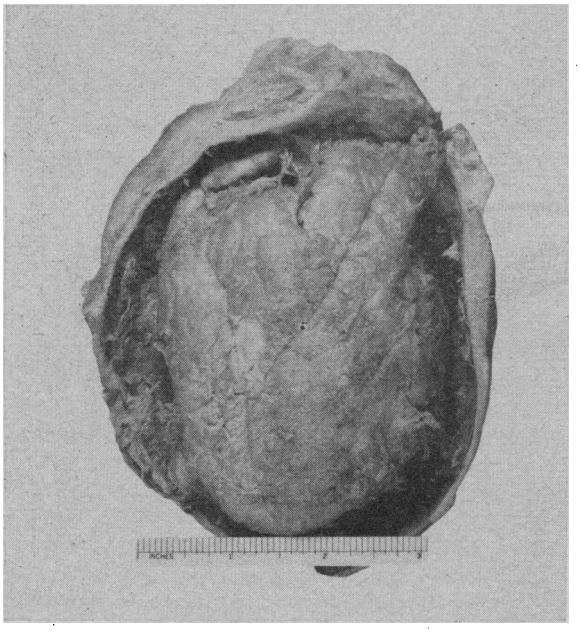

Fig. 2.—Heart and pericardium showing the ragged pericardial exudate.

was not clinically enlarged, no cardiac murmur was heard and there was no evidence of cardiac failure. Her hæmoglobin level was 9 g. %, and white blood cell count 40,000 per c.mm., of which 84% were neutrophils. Repeated blood cultures were negative. Agglutination tests against Salmonella and Brucella organisms were negative. The antistreptolysin titre was over 1000 units and the C-reactive protein test positive. Plasma fibrinogen determined chemically was

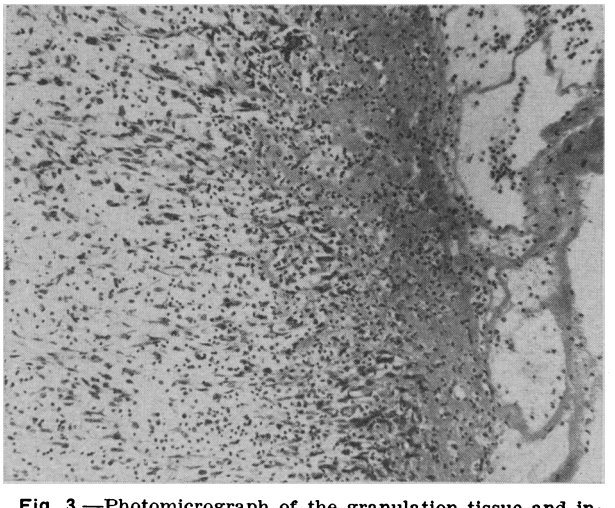

Fig. 3.—Photomicrograph of the granulation tissue and inflammatory exudate on the pericardium. × 150.

1.04 g. %. Serum albumin determined electrophoretically was 1.45 g. %, alpha$_1$ globulin 0.35 g. %, alpha$_2$ globulin 1.12 g. %, beta globulin 0.74 g. % and gamma globulin 1.40 g. %. Radiographs on admission showed some enlargement of the cardiac shadow.

Treatment with sodium salicylate for one week and then with cortisone produced no significant improvement. Two weeks after admission she became dyspnœic and was found to have pulsus paradoxicus. A chest radiograph showed a left pleural effusion and further enlargement of the cardiac shadow. One hundred and ten ml. of bloodstained fluid was aspirated from the pericardial cavity, with marked improvement of the patient's condition. The aspirated fluid contained numerous neutrophils but no bacteria and was sterile on routine media. The dyspnœa subsequently returned and the patient died suddenly while preparations were being made to repeat the aspiration of the pericardial fluid.

Autopsy

The presence of joint deformities was confirmed. The spleen weighed 170 g. and was soft, and there was no enlargement of lymph nodes. Effusions were present in the peritoneal and both pleural cavities and there was centrilobular congestion of the liver. The pericardial cavity was distended with 350 ml. of turbid bloodstained fluid. Both layers of the pericardium were thick and ragged and covered with plaques of fibrino-purulent exudate (Fig. 2). The heart was not enlarged but the combined weight of the heart and thickened pericardium after releasing of the fluid was 480 g. Apart from the pericarditis there was no gross abnormality of the heart or great vessels. The valves and chordæ tendineæ were normal. Microscopically the pericardium was thickened by granulation tissue and fibrino-purulent exudate (Fig. 3). No Aschoff bodies were seen in the myocardium. The endocardium and heart valves were normal. There was no microscopic evidence of lupus erythematosus.

Diagnosis

1. Rheumatoid arthritis associated with pericarditis.
2. Death caused by cardiac tamponade.

CASE 2.—A 68-year-old white woman was admitted to hospital in 1956 because of transient loss of consciousness. During the preceding three years she had suffered from rheumatoid arthritis and had been treated with cortisone. She had no past history of acute rheumatic fever and no family history of rheumatoid arthritis.

Twelve hours before the patient died, she lost consciousness for a short time while sitting in bed eating supper. She had no pain before or after the loss of consciousness and on recovery had no motor or sensory disorder. In hospital she was found to have deformities of her wrists and fingers and limitation of movement of her shoulders and knees but no subcutaneous nodules. Her pulse was irregular, its rate 110. Her blood pressure was 130/60 mm. Hg. Heart rhythm was irregular but otherwise the heart sounds were normal and there were no cardiac murmurs. There was no evidence of cardiac failure. An electrocardiogram showed complete A-V block and multiple ventricular extrasystoles (Fig. 4). The serum V.D.R.L.

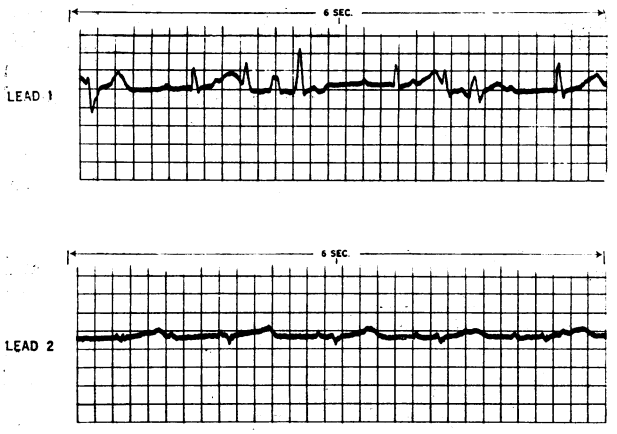

Fig. 4.—Case 2. Electrocardiogram. There is complete A-V block and multiple ventricular extrasystoles.

test for syphilis was negative. The patient died suddenly before further investigations could be performed.

Autopsy

The only significant changes were in the heart and skeletal system. The presence of rheumatoid arthritis was confirmed. The pericardial cavity was normal and the heart weighed 380 g. At the upper end of the interventricular septum below the anterior cusp of the aortic valve there was a V-shaped fibrous thickening (Fig. 5). Otherwise the heart was normal.

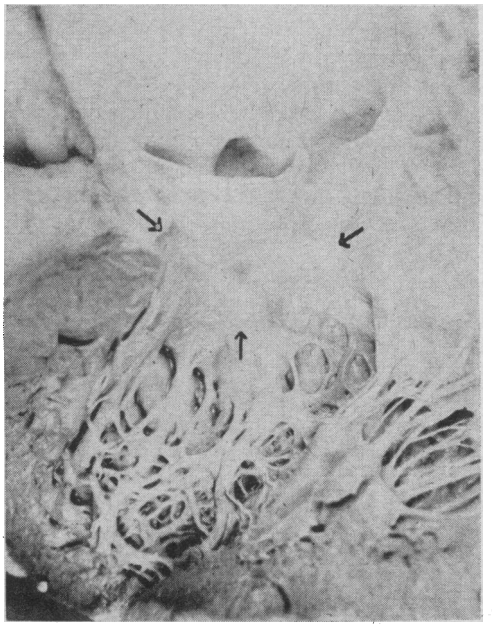

Fig. 5.—Photograph of the heart. The position of the V-shaped fibrous thickening is indicated by the arrows.

Microscopically the thickened area in the interventricular septum was composed of granulation and fibrous tissue resembling a subcutaneous rheumatoid nodule. The centre of this structure was composed of dense hyaline fibrous tissue around which there were focal areas of necrosis and poorly formed palisades of fibroblasts. Numerous plasma cells and occasional multinucleate giant cells were present (Fig. 6).

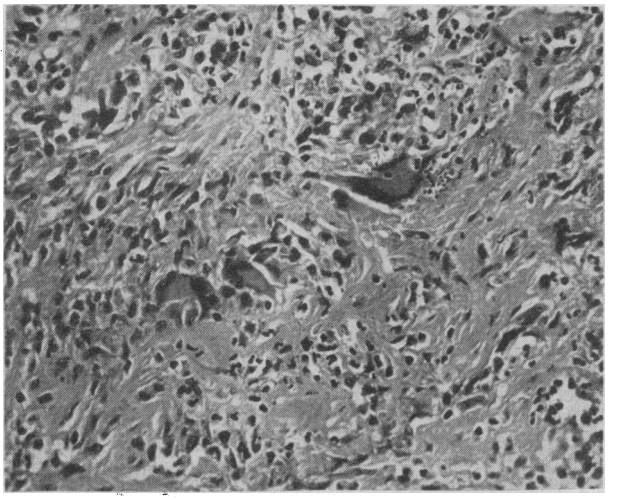

Fig. 6.—Photomicrograph of the nodule in the heart showing collagenous fibrous tissue, plasma cells and multinucleate giant cells. × 250.

Diagnosis

1. Rheumatoid arthritis.
2. Rheumatoid granuloma in the heart causing A-V block and multiple ventricular extrasystoles.
3. Death probably due to ventricular fibrillation.

CASE 3.—A 66-year-old white man was admitted to hospital in 1957 with swelling of his feet and legs which had been present for one month, and severe aching pain in both legs for two weeks.

Since 1942 he had suffered from recurrent afebrile attacks of pain and swelling in his ankles, knees, wrists and elbows. Treatment with cortisone commenced in 1951 and continued almost without interruption until after his final admission to hospital. In 1951 there was no clinical evidence of cardiovascular disease. In 1955 subcutaneous nodules were noted and there were deformities of his fingers and feet. Radiographs showed narrowing of the joint spaces of his hips and knees.

In 1957, on final admission to hospital, the patient complained that for one month he had had swelling of his feet and ankles. On direct questioning he admitted that he had also experienced dyspnœa on exertion, but denied any pain or sensation of constriction in his chest. His legs were found to be œdematous, the liver edge was palpable below the right costal margin and was tender, and there were crepitant rales at the bases of both lungs posteriorly. His blood pressure was 140/80 mm. Hg, and previous records confirmed the absence of hypertension.

In addition, the patient complained of severe continuous pain in both legs which was worse in the recumbent posture and was relieved by hanging his legs over the side of the bed. The pain was not related to exertion and was not relieved by rest. There was no loss of pulsation in the dorsalis pedis or posterior tibial arteries. While in hospital the skin over the back of the right calf and over the outer border of the right foot became indurated and ulcerated (Fig. 7).

The serum V.D.R.L. test for syphilis was negative. The hæmoglobin value was 12.5 g. %, hæmatocrit 41%, corrected sedimentation rate (Wintrobe) 49 mm., in one hour, and white blood cell count 3200 per c.mm., of which 70% were neutrophils. The sheep cell agglu-

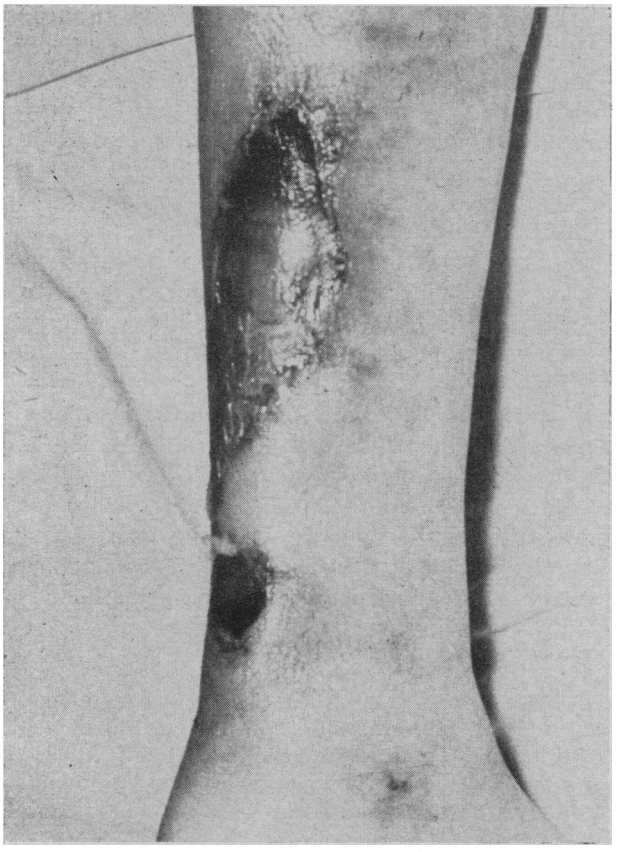

Fig. 7.—Case 3. Ulceration of the skin over the back of the right calf.

tination test for rheumatoid disease was positive to a titre of 1 in 1024; the difference in titre between normal and sensitized cells was 256. The serum albumin determined by the electrophoretic method was 1.71 g. %, alpha$_1$ globulin 0.62 g. %, alpha$_2$ globulin 1.22 g. %, beta globulin 0.99 g. % and gamma globulin 1.16 g. %. Tests for the L.E. phenomenon were negative.

Electrocardiograms initially showed non-specific changes but two days before death there was heart block and lowering of the S-T segments in the three standard leads. The cardiac failure progressed and caused the patient's death.

Autopsy

Autopsy was performed by Dr. M. Saiphoo. The presence of cardiac failure, joint deformities and ulcers of the right leg and foot was confirmed. The spleen weighed 190 g. and was soft, and there was no enlargement of lymph nodes. The heart weighed 320 g. No recent area of infarction was seen, but the right coronary artery was occluded by firm grey tissue at a point 2½ cm. from its origin. No other occlusion of the coronary arteries was present. There was moderate atheroma of the left coronary artery and its branches. The cut surfaces of the myocardium and papillary muscles of the left ventricle showed fine strands of fibrous connective tissue. The valves and chordæ tendineæ were normal.

Microscopically, tissue from the bases of the leg ulcers showed non-specific necrosis and infiltration with neutrophils. There was diffuse ischæmic fibrosis of the myocardium of the left ventricle and papillary muscles. The small arteries in the papillary muscles

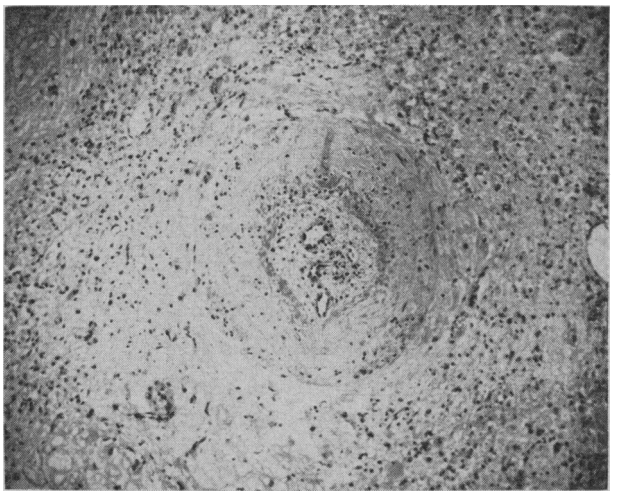

Fig. 8.—Photomicrograph of an artery in a papillary muscle showing recanalization of the previously occluded lumen. × 150.

were thick-walled and showed inflammatory changes (Fig. 8). In some of these arteries there was evidence of past occlusion with subsequent recanalization. Similar inflammatory changes were present in arteries in the pancreas and in uninflamed skeletal muscle at a distance from the leg ulcers (Fig. 9). The structural

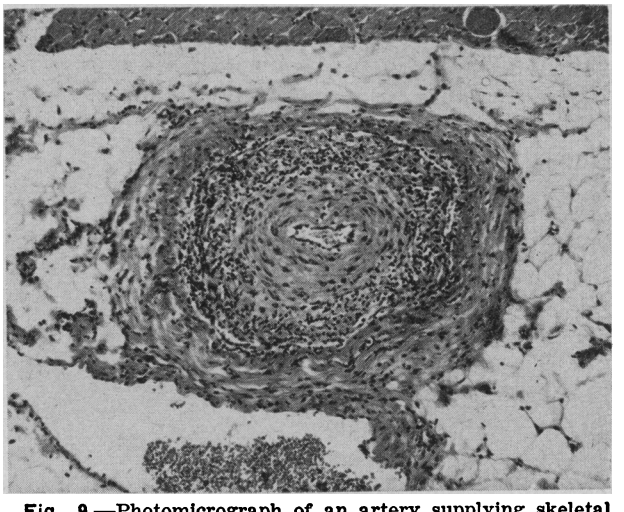

Fig. 9.—Photomicrograph of an artery supplying skeletal muscle. There is proliferation of intimal fibroblasts and infiltration with inflammatory cells. × 150.

pattern of the arterial walls was preserved in all the affected vessels and there was no evidence of fibrinoid change.

Diagnosis

1. Rheumatoid arthritis.
2. Rheumatoid arteritis, affecting the myocardial branches of the coronary arteries and arteries in the pancreas and skeletal muscle.
3. Death due to cardiac failure.

DISCUSSION

There are three circumstances in which cardiovascular disease and chronic polyarthritis are known to occur together. Firstly, rheumatoid arthritis may develop by coincidence in a patient with cardiovascular disease due to some other

cause such as acute rheumatic fever. Secondly, rare patients who have suffered repeated attacks of acute rheumatic fever may have persistent joint deformity of the type known as the chronic fibrous rheumatism of Jaccoud. Lastly, rheumatoid arthritis may be associated with specific rheumatoid disease of the cardiovascular system.[1, 3] The patients described above illustrate three different ways in which the heart may be affected by rheumatoid disease.

Rheumatoid Pericarditis

In 1897, Still described the occurrence of pericarditis in association with chronic joint disease in children and compared the features of this disease with those of rheumatoid arthritis. He observed 19 children with chronic joint disease. Three of these subsequently died, and at autopsy "in each case the pericardium was universally adherent". In two others there were signs (unspecified) of adherent pericardium.[4] Subsequent reviews of autopsies on patients with rheumatoid arthritis have confirmed the occasional occurrence of pericarditis.

Case 1 described above is an example of pericarditis associated with rheumatoid arthritis during adolescence. Pyogenic and tuberculous infections of the pericardium were excluded by direct examination and culture of the pericardial fluid.

Acute rheumatic fever occurring during the terminal illness and causing pericarditis is more difficult to exclude, because the absence of demonstrable myocarditis in such a short illness is of little significance. It is considered that the similarity between the joint disease in the terminal and preceding illnesses, the lack of response to salicylates, and the severity of the pericarditis suggest that the patient had rheumatoid rather than rheumatic pericarditis.

Rheumatoid Granuloma in the Heart

Foci of granulomatous inflammation resembling subcutaneous nodules have been described in the heart by several authors.[1, 7, 8] These nodules are usually incidental findings at autopsy and contribute little to the patient's illness. Similar lesions may occur in other viscera. In Case 2 described above, the situation of the granuloma at the upper end of the interventricular septum caused heart block. This site is one where gummata are known to occur and produce similar effects on the conduction of the cardiac impulse. In this patient the V.D.R.L. test for syphilis was negative and the microscopic appearance of the lesion was unlike that of a gumma. The inflammatory cells were not distributed perivascularly and there was no endarteritis.

Rheumatoid Arteritis

Inflammatory changes in small arteries supplying skeletal and cardiac muscle and other viscera are known to occur in rheumatoid arthritis.[2, 9]

The size of the vessels affected varies from 75 to 400 microns and the changes affect principally the intima. Concentric thickening of the intimal fibrous tissue occurs and there may be thrombosis and subsequent recanalization. Inflammatory cells may be found throughout the wall of the vessel but there is little change in the elastic lamina and no fibrinoid necrosis in the media.

These changes are distinct from those of polyarteritis nodosa, cortisone-induced arteritis, thromboangiitis obliterans, and giant-cell arteritis of the type commonly occurring in the temporal arteries.

In Case 3, described above, arteritis caused gangrene of the right calf. The patient died of cardiac failure due to myocardial ischæmia. This ischæmia may have been due to atheroma, but the distribution of the fibrosis in the myocardium suggests that it was caused by arteritis of the myocardial branches of the left coronary artery.

SUMMARY

A description is given of three patients with rheumatoid arthritis who died as a result of rheumatoid disease of the cardiovascular system. These three patients illustrate the occurrence of rheumatoid pericarditis, rheumatoid nodules in the heart and rheumatoid arteritis. These lesions are known to occur in rheumatoid arthritis and are not rheumatic in origin.

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TOO BUSY TO KEEP UP

"Undoubtedly it is becoming increasingly difficult to keep up with the 400 new drugs, something like 20,000 detail men, and the thousands of direct mail pieces that physicians receive every year. There are 6000 medical journals, hundreds of bulletins, reports, and meetings of societies and associations where new techniques are described. Attempts have been made by pharmaceutical houses and the editors of throw-away journals to print digest articles for our consumption. It is tough, but to keep up we have no recourse except to limit our practice or take several weeks off each year to be posted on what is happening. Otherwise it means giving up home life and recreation. Let's not get to the stage of the nattily attired heart expert who told Mr. Wood, 'The best G.P. nowadays is the one who knows what kind of specialist to send his patients to.' Let's stop playing God and be a little more humble."—Editorial: *Illinois M. J.*, 114: 72, 1958.