This may be contrasted with the slow recovery in the other patients in the series and in the three controls shown in the table. There are two reasons, however, for caution in interpreting these results: (1) Final rod threshold is not a very satisfactory measurement to apply to small groups because of the range of individual variation, though it is believed that the differences shown here are too great to appear by chance. Again, it cannot be excluded that as a result of the greater frequency of testing in these men facilitation of response may have contributed to the improvement. (2) The plasma vitamin A was estimated chemically in three subjects, and in two of them the rise produced by 96,000 units of vitamin A was so slight that it is difficult to see how it could have improved their dark-adaptation.

Discussion

Vitamin A abnormality in infective hepatitis is associated with a rise of the final rod threshold and only slight alteration in the rod-cone transition time. This is the type of change that has been found in most experiments on simple acute dietary avitaminosis A. In contrast Haig, Hecht, and Patek (1938) found that in chronic liver disease the lengthening of the rod-cone transition time was as marked as the impairment of the final rod threshold. Similarly in the recent Sheffield experiments (Med. Res. Cncl., 1945), in which volunteers were kept on a vitamin-A-free diet for long periods, the rod-cone transition time was affected as well as the final rod threshold. These differences may be explained by the suggestion made by Hecht and Mandelbaum (1939) that "it may well be that this difference in behaviour of the rod-cone break is purely a matter of short-period avitaminosis versus prolonged deprivation."

It has previously been pointed out that dark-adaptation is less satisfactory as a measure of vitamin A abnormality than chemical estimation. In this trial, for instance, there was no diagnostic impairment in individual patients, and statistical analysis was necessary to show the effect, whereas using chemical estimation of the plasma vitamin A as an index a definitely abnormal result was obtained in most patients. The insensitivity in measurement of dark-adaptation arises from two factors: the range of normal variation from individual to individual and the wide margin of error in the same individual found by repeated testing on the same day.

A second disadvantage is that dark-adaptation may be affected by other factors than vitamin A lack. Malingering can generally be detected with the Craik adaptometer, since a self-inconsistent record is produced, but some psychoneurosis can cause poor dark-adaptation (Wittkower, Rodger, Scott, and Semeonoff, 1941). Pyrexia is a cause which can be disregarded in the present series, since most of the cases had no significant fever. It has been suggested that raised blood bile salts might play a part, as bile salt is a solvent for visual purple *in vitro*. No evidence was obtained for this when one of us (K.J.W.C.), after dark-adaptation was complete, was given an intravenous injection of bile salts. The injection was given by a dim light while the subject wore dark goggles and the record continued immediately. No alteration in threshold resulted either from bile salts or from the control injection of sterile water.

Summary

The course of dark-adaptation was investigated by means of the Craik adaptometer in patients with infective hepatitis.

The mean final rod threshold for 37 men tested within one week of admission to hospital was significantly impaired in comparison with that of 20 normal adults of comparable age.

In 14 men retested after an interval of one month or more the mean final rod threshold was significantly improved.

No alteration was apparent in cone threshold, and the rod-cone transition time was only slightly prolonged.

Dark-adaptation under the conditions of this experiment was a less sensitive measure of vitamin abnormality than chemical estimation of plasma vitamin A.

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TUBERCULOUS PERICARDITIS

BY

HARRY KOPELMAN, M.D., M.R.C.P.

Pericardial effusion caused by tuberculosis has always been considered a rare condition, carrying with it a high mortality. Of recent years, however, more cases have been diagnosed as being due to tuberculosis, and doubt has been cast upon other cases which had previously been labelled rheumatic. Some of the many cases published have been proved to be tuberculous either during life or at necropsy, but in many a diagnosis has been presumed only by the presence of other tuberculous manifestations or by the absence of signs which have been taken to be rheumatic in origin. Thus in Harvey and Whitehill's (1937) collection of 95 cases taken from 45 years of records of the Johns Hopkins Hospital there are 37 proved cases, 34 unproved, and 24 proved in which the pericardial lesion was of no clinical importance. The mortality varied greatly in this series; in proved cases it was 83%, whereas in the unproved cases it was only 6%. There was little difference in the characteristic signs and symptoms in the unproved group from those in the proved group, and it was on these signs that the clinical diagnosis was achieved. These groups were further subdivided into those with large pericardial effusion and those without effusion, and while in the proved group of 37 cases 20 had effusion, in the unproved group 31 of the 34 cases had large effusions. In Ellman's (1945) excellent paper on this subject he quotes six cases, and, again, although the clinical picture and progress are strongly suggestive of tuberculous pericarditis, in three cases the diagnosis was not proved.

In all these series of cases in which the diagnosis has been tuberculous pericarditis with effusion the following features have been taken to be characteristic of the clinical picture: (1) no enlargement of the heart; (2) no gross murmurs or murmurs indicative of valvular involvement; (3) no rheumatic manifestation; and (4) no past or family history of rheumatism. In addition, there was no marked anaemia, an insidious onset, no leucocytosis, and, although the effusion might be large, the symptoms, especially precordial pain, were not marked.

Massie and Levine (1939) investigated 135 cases of rheumatic pericardial disease diagnosed by the presence of pericardial rub or pericardial effusion. They found that 110 cases had definite arthritis or arthralgia, one case had chorea, and 17 of the others had a past history of one or more attacks of rheumatic fever, sore throat, or a family history of rheumatism. On the other hand, of the 82 cases followed up for a period of seven years one-third had no evidence of any organic heart disease. Although Sheldon (1946) has recently published six cases demonstrating tuberculous arthralgia, acute rheumatism with serositis, and chronic rheumatism, this should not confuse the diagnosis with that of rheumatism if the criteria of the small heart, etc., are taken into consideration. While dealing with the differential diagnosis of tuberculous and rheumatic pericardial effusion it is also of interest to note that in Harvey and Whitehill's (1937) series several cases developed auricular fibrillation when the effusion was maximal, and that there was no evidence of myocardial involvement clinically or in those cases which came to post-mortem examination. In addition, these cases appeared particularly susceptible to digitalis, heart-block occurring with relatively small doses.

Pathology

Primary tuberculous pericarditis in the strictly pathological sense of the word is a very rare condition, and in the previously quoted series only one case at necropsy appeared to have the pericardium as the sole site of infection. On the other hand a pericardial effusion as a first clinical manifestation of active tuberculosis is not so uncommon. Although Blatt and Greengard (1928), after an extensive search of the literature, claimed their case of a child of 9 years as the youngest in which this condition had been diagnosed during life, one of the cases described below occurred in an infant of only 18 months.

Reisman (1901) described four means by which the pericardium might be affected: it may form part of a general miliary process, or part of a serous membrane tuberculosis, or be an extension from neighbouring structures, or, finally, develop independently. It seems generally agreed that the pericardial sac is relatively immune in a general miliary spread, and it appears that if miliary spread is present it is probably subsequent to the pericardial lesion. In most cases of tuberculous pericarditis involvement of the mediastinal glands has been demonstrated and it is probable that the pericardial lesion followed as a result of lymphatic spread. In one case described by Seligman and Lederer (1940) the pericardium was involved as a result of rupture of a caseous lymph node draining a Ghon lesion. This must, however, be as uncommon as pericardial involvement from the lung or the pleura.

Once the pericardium becomes infected the subsequent progress may follow the course taken by a case described by Barrett and Cole (1944). In this case there was increasing effusion with cardiac embarrassment lasting four months, followed by a phase of decreasing effusion with temporary recovery lasting three months, and, finally, increasing thickening and fibrosis of pericardium leading to congestive failure and death in three months. Although this may be the usual course in fatal cases, those that recover may have an effusion which is far more transient and which, with absorption of the fluid, gives rise to no residual signs or symptoms of pericardial involvement. It is in this type of case that the diagnosis is so difficult to prove, and most of the described cases have not been completely proved. In Barrett and Cole's case a guinea-pig inoculated with pericardial fluid lived from April 28 until Oct. 8 (over five months) and appeared ill only a short time before death.

The age incidence of tuberculous pericarditis varies in the many cases reported. In Ellman's (1945) cases with effusion the ages ranged mainly between 20 and 35 years. In Heimann and Binder's (1940) 31 cases among Bantu patients the ages of those with large pericardial effusions ranged between 20 and 40 years. Another series, however, collected as primary tuberculosis of the pericardium, as judged by post-mortem examination, with the pericardium having the main or oldest tuberculous lesion (Thompson, 1933), the average age was 69.5 years (the range was 49 to 84) in the 28 cases described. These cases showed a pathological picture of adhesive caseous tuberculosis and a clinical picture of an insidious onset, cardiac enlargement, accompanied by a rapidly progressive and unexplained condition of cardiac insufficiency, together with pyrexia and wasting.

In the four cases described below only one is proved to be tuberculous, in two there is strong circumstantial evidence which makes the diagnosis probable, while in the fourth case there is a clinical picture which strongly suggests a tuberculous aetiology.

Case 1

A male child aged 18 months was admitted to hospital, into an adult female ward, on Aug. 25, 1945, with an impetiginous

rash over most of his body and two abscesses on his skull. Apart from a haemangioma the size of a shilling on the right side of the forehead nothing abnormal was found on clinical examination. The impetigo was treated with penicillin cream; the abscess was incised, and a penicillin-sensitive haemolytic streptococcus was grown. Sulphamezathine—in all 11 g.—was given. Under this treatment the condition soon subsided, and he became a great favourite in the ward. This unfortunate child, who had been in a very neglected and dirty condition on admission, was not wanted by his parents, and, with their consent, arrangements were made for his admission to a suitable home. As is usual in these affairs, coupled with the fact that he had become a great favourite with the patients and the nursing and medical staff, the matter was not treated urgently and some weeks passed before the necessary arrangements were completed. By the first week of November, 1945, some 11 weeks after admission, he began to get irritable, the temperature ranging between 99° and 100° F. (37.2° and 37.8° C.), with a pulse of 110–120. Finally, on Nov. 10, 1945, his temperature rose to 104° F. (40° C.) and his pulse to 140–150.

On examination both drums were injected, especially the right, which showed some bulging, and myringotomy was performed. A course of sulphathiazole was started. Next day the patient looked much better, but subsequently he continued to run a swinging temperature of 100°–101° F. (37.8°–38.3° C.) and a tachycardia of 150–160; there was no evidence of bronchopneumonia, and his drum now showed a dry perforation. On Nov. 15 his condition was unchanged, but during the day there was a steady rise in the respiration rate to 50, and examination showed an area of dullness over the front of the chest. The liver was enlarged and tender, and the tip of the spleen was palpable. The heart sounds were somewhat diminished in intensity. A radiograph of the chest confirmed the presence of a large pericardial effusion. Full doses of parenteral penicillin were started; it was thought that this was an infective condition secondary to that of his ears.

Pericardial paracentesis was performed under paraldehyde and local anaesthesia, the needle being inserted between the apex beat, which was normal in position, and the outer border of the area of cardiac dullness. With some ease 130 ml. of fluid were withdrawn and a little air replaced. The fluid was clear and pale amber green. Examination showed practically 100% small lymphocytes; no organisms were seen on direct smear and ordinary culture was negative. A guinea-pig was inoculated with the fluid on Nov. 20. After aspiration there was a dramatic improvement in his general condition, his pulse dropped to 120 and his respirations from 60 to 35. This was not maintained; there was a gradual deterioration in his condition and aspiration was repeated on Nov. 22. This time 160 ml. of fluid were removed and 10,000 units of penicillin instilled. There was little improvement after this and his condition remained unchanged except that both clinically and radiographically the effusion appeared to be getting smaller. Penicillin therapy was discontinued on Nov. 26. His condition deteriorated further, and on Nov. 30 pericardial aspiration was again attempted. This time it was obvious that the effusion was much smaller and that the pericardium was much more resistant to penetration, and it was only with difficulty that 60 ml. of blood-stained fluid were aspirated. In both these pericardial fluids no organisms were found and the cells were practically 100% lymphocytes. The white blood cell counts were as follows:

Date	White Cells	Polymorphs	Lymphocytes	Mononuclears
Nov. 12 ..	13,200	49%	40%	6%
" 21 ..	22,400	41%	56%	3%
" 29 ..	45,280	53%	38%	7%

The haemoglobin was 55%, the red cells numbered 4,940,000 per c.mm., and the colour index was 0.56. On Nov. 24 the Mantoux test (1: 100,000) was negative, and on Nov. 29 it was doubtful positive (1: 10,000).

The patient's condition remained unchanged, the pulse was still around 130, respirations 40, and temperature normal. By Dec. 18 there was considerable oedema of the face and eyes and puffy swelling of the legs, which did not pit on pressure; there was also some distension of the abdomen. By Dec. 23

this oedema had improved and a radiograph of the chest on Dec. 27 showed a bilateral pleural effusion, with a marked diminution in the pericardial effusion. His condition remained unchanged and oedema recurred. He became much worse on Jan. 2, 1946, and died the next day.

Post-mortem examination showed a grossly thickened pericardium loosely adherent to a normal-sized heart. The pericardium was 1 cm. thick and appeared fibrous. Sections showed tubercles in this tissue. There was an area the size of a shilling of a breaking-down caseous lesion in the lingula of the left lung and caseation of the mediastinal glands immediately adjacent to the pericardium. There was a recent miliary spread in the lungs, liver, and spleen.

The guinea-pig was killed on Feb. 5. It had appeared relatively well until this time, but there was evidence of tuberculous infection when it was examined post mortem.

Case 2

A soldier in the Royal Pioneer Corps aged 20 was admitted to hospital on March 6, 1945, complaining of breathlessness, pain in the chest, and cough. These symptoms gradually developed during the past four weeks while undergoing training in the Army. During the past two weeks he noticed that he was becoming increasingly breathless and that he had a pain below the right nipple which was worse at night and on coughing. He had also had a cough for some three weeks which was non-productive. He had no pain in any limb, but had an ache across the left shoulder for the last two or three days, which was worse on movement. There was no history of rheumatic disease.

On examination the temperature was normal, pulse 115, and respirations 25. He was sweating, with no obvious joint involvement, and the left shoulder movements were full. *Cardio-vascular system:* Pulse was of poor volume, blood pressure 110/85. The apex beat was not palpable; it was 4 in. (10 cm.) from the midline in the fifth intercostal space. The area of cardiac dullness was greatly increased and extended to the right two fingerbreadths from the edge of the sternum and approximately 5 in. (12.5 cm.) from the midline, although the left border was difficult to determine owing to dullness on percussion at the base of the left lung. The heart sounds were very distant and best heard just within the nipple line, where they were accompanied by a soft systolic murmur. Pericardial friction rub was audible over most of the praecordium, with maximum intensity around the left fourth costal cartilage. *Chest:* There was dullness to percussion below the sixth rib on both sides, with marked diminution of air entry; some rales were present. *Abdomen:* The liver was enlarged three fingerbreadths below the costal margin. The spleen was not palpable. There was no ascites or oedema. After resting in bed for some hours the pulse improved in volume and marked pulsus paradoxus became apparent.

Progress.—The pulse became irregular and the pericardial rub disappeared but returned again on March 12. On March 14 the blood sedimentation rate was 27 mm. in 1 hour, cell volume 45%, corrected to 27 mm. The Mantoux reaction was negative 1: 10,000. The patient continued to improve but had some dysuria, and on March 25 the temperature rose to 102.8° F. (39.3° C.). A radiograph of the chest showed collapse of the left base as well as a large pericardial effusion. On April 6 the Mantoux reaction was positive 1: 10,000. On April 20 pleural friction rub appeared in the right axilla and lasted five days. His condition remained unaltered; he still showed pulsus paradoxus and appeared very depressed mentally. During this time he had occasional pain in the chest, but by May 23 this had disappeared and he was then feeling much better. On May 29 a radiograph of the chest showed the pericardial shadow to be much smaller, and there was marked improvement in his pulse rate and general condition. The improvement continued until June 13, when he again did not feel so well, the pulse volume was poor, and pulsus paradoxus recurred. A radiograph showed that the pericardial shadow was much larger. The blood pressure was 100/70. His condition continued unchanged until July 1, when there was obvious absorption of the pericardial effusion. He improved until July 25, when he was discharged to a convalescent home, with only a very small pericardial effusion. He finally made a complete and uninterrupted recovery with no residual pericardial lesion.

Case 3

An unmarried woman aged 39 attended hospital on Aug. 8, 1945, complaining of pain in the left shoulder and right chest for three weeks. There was no cough but some dyspnoea on exertion. She had had a hysterectomy in 1944 for fibroids. There was no history of pleurisy or rheumatic fever, and no family history of tuberculosis. Pain in the right lower chest had developed three weeks previously; it had been worse on deep breathing and had lasted about two days. It was replaced by aching pain in both shoulders diagnosed as fibrositis, and she was feeling out of sorts.

On examination the apex beat was 3½ in. (8.75 cm.) from the midline in the fifth intercostal space. There was impairment of the percussion note at the left base, with diminution of breath sounds. The heart sounds were normal and there were no murmurs, but at the base to the left of the sternum a to-and-fro pericardial rub could be heard. The blood pressure was 120/80 and the pulse of good volume. The temperature on admission was 101° F. (38.3° C.), pulse 90, and respirations 20. A radiograph of the chest on Aug. 8 showed an enlargement of the heart shadow on both sides. The liver and spleen were not palpable. There was no oedema.

Progress.—Next day it became clinically obvious that the area of cardiac dullness had extended considerably beyond the apex beat, and a radiograph of the chest showed a large pericardial effusion with some pneumonic consolidation of the lingula of the left lung. For the next three days, until Aug. 12, the pericardial effusion increased in size, the temperature remained around 101° F. (38.3° C.) and the pulse at 90, and she had pain over the praecordium. The area of cardiac dullness extended to the mid-axillary line and upwards to the second rib. The pulse was of poor volume, the apex beat was not palpable, and the heart sounds were diminished in intensity. A Mantoux test on Aug. 10 was positive 1: 1,000 old tuberculin. After Aug. 13 the temperature settled to normal, the pulse to 72, and there was daily improvement in her general condition. It became clinically obvious that the area of cardiac dullness was rapidly diminishing, and by Aug. 28 it was practically back to normal heart outline. A radiograph on Aug. 22 showed the heart shadow to be normal in size, shape, and position. The patient's general condition improved considerably, and a heart examination on Sept. 7 showed the apex beat 3½ in. (8.75 cm.) from the midline in the fifth space; the sounds were clearly heard, and there were no murmurs. When last seen on Oct. 12, 1945, in the out-patient department her pulse was 84 and regular, there was no enlargement of the heart, and no murmurs.

Subsequent Progress.—She was readmitted to the County Hospital, Farnborough, in November, 1945, with left pleural effusion. Aspiration showed this to be typically straw-coloured tuberculous effusion, although no tubercle bacilli were actually seen in the fluid.

Case 4

A boy aged 11 was admitted on Nov. 18, 1941, with pain in the epigastrium and right hypochondrium of two days' duration. This had been accompanied by vomiting and diarrhoea on the day of admission. During the previous five days there had been an unproductive cough accompanied by some mild headache, but he had been relatively well until the onset of abdominal pain. The previous medical history revealed nothing relevant.

On examination he looked pale and ill, his temperature was 102° F. (38.9° C.), pulse 120, and respirations 32. The heart sounds were muffled, with dullness at both bases, especially the left, where there was marked diminution of air entry. The abdomen was tender in the right epigastrium and there was marked guarding of the right upper rectus. X-ray examination confirmed a diagnosis of a large pericardial effusion. On Nov. 20 the heart sounds were more muffled, dullness extended from the right nipple to 1 in. (2.5 cm.) outside the normal left border of the heart, and there was rigidity over the whole of the epigastrium.

Full doses of sodium salicylate were given with no effect. Sulphapyridine was substituted. An enema relieved the abdominal distension, and the liver was palpable three fingerbreadths below the costal margin. On Nov. 24 a pleuro-pericardial rub developed and his white cell count was then

6,560 (54% polymorphs). After four days on sulphapyridine there was no response and the temperature still ranged between 101° and 102.8° F. (38.3° and 39.3° C.). It was stopped after 13 g. had been given. By Dec. 4 the general condition was obviously better and there was decreasing cardiac dullness on the left; by the 12th the apex beat became palpable and showed no enlargement, the heart sounds were clearly audible, and there were no murmurs. There was still some tenderness of the liver, which was palpable, and a radiograph of the chest showed marked diminution in the size of the pericardial effusion. The patient was discharged to a convalescent home on Jan. 17, 1942. In a radiograph of the chest taken before his discharge from the home the heart shadow appeared to be normal.

When seen subsequently as an out-patient there was no enlargement of the heart, no murmurs, the sounds were clear and normal, and there was no tachycardia. There were, however, a fixed apex beat, dilated veins in the neck, and a palpable liver. Constrictive pericarditis was diagnosed. He was afterwards seen several times as an out-patient, when it was apparent that the engorgement of the neck veins and the liver enlargement were becoming less, and on April 11, 1946, when he was admitted to hospital for dental extraction, there was no evidence of cardiac involvement, his pulse was regular, the apex beat was 3½ in. (8.75 cm.) from the midline in the fifth space, the sounds were normal, and the blood pressure was 130/80. A radiograph of the chest showed a normal heart in shape and position, and no pulmonary lesion was seen.

This boy showed no rheumatic manifestations, no response to salicylates or sulphonamides, no cardiac enlargement, and no subsequent cardiac manifestations.

Discussion

Case 1 shows the development of a large pericardial effusion in a child of 18 months. The rapidity with which the pericardium contracted down and became thickened was very marked. This was almost certainly a primary infection, as the child had been in the ward for some weeks previously and during this time a case of open tuberculosis had been admitted for a short period. As has been noted by others the guinea-pig test may take several months to develop—five months in Barrett and Cole's (1944) case—and in some cases it may be negative and yet at necropsy or operation the aetiology be proved (Suzman, 1943; Sellors, 1946). In this case the guinea-pig survived for three months after inoculation. The patient had died before this.

In Case 2 the clinical picture is typical of this condition without rheumatic manifestations of cardiac involvement. The Mantoux reaction changed from negative to positive during the course of the illness. In Case 3 the subsequent development of a typical tuberculous pleural effusion makes it likely that this was the cause of the pericardial effusion. In this case there was great rapidity in the development and absorption of the effusion, the whole process taking little over two weeks. The fourth case shows no real evidence of a tuberculous aetiology, but there was marked absence of any rheumatic or cardiac manifestations and there was no response to salicylate treatment. Boas and Ellenburg (1940) claim that in rheumatic pericardial effusion salicylates in large doses produce a prompt relief in the general condition of the patient and a more rapid absorption of the effusion, although the actual endocardial involvement is not affected.

It is suggested that tuberculous pericardial effusion may be a commoner condition than previously diagnosed and that its prognosis is not nearly as bad as has been apparent. It may be argued that in many of the cases which have been quoted, including three of the four cases described, the actual causation has not been proved, and it is these improved cases which carry the best prognosis. This is similar to the position with regard to the so-called idio-

pathic pleural effusion in which the direct evidence of infection by the tubercle bacillus may be extremely difficult to prove, and yet follow-up of cases indicates that most of these are tuberculous in aetiology. The difficulty in proving an effusion to be tuberculous may further be stressed by the duration for which guinea-pigs survive. In Case 1 the guinea-pig survived long after the patient was dead, and in other cases (Suzman, 1943; Sellors, 1946) the guinea-pig test was negative, although subsequently at necropsy or operation the lesion was shown to be tuberculous. Again, in Harvey and Whitehill's (1937) series of 13 proved cases in which paracentesis was performed five showed no evidence of tubercle bacillus by examination or guinea-pig inoculation.

The analogy between pericardial and pleural effusion may be taken further; thus a large pericardial effusion may be a late primary tuberculous manifestation occurring in younger subjects secondary to mediastinal gland involvement. In these cases the tubercle bacilli would be scanty and difficult to demonstrate. The pericarditis may, however, progress to caseation and death, producing a condition similar to that which occurs in later life but terminates in an adhesive caseation. This would account for the higher age incidence in this latter type of case and for the higher mortality of those cases which prove easy to establish as tuberculous.

All cases of pericardial effusion without joint or other rheumatic manifestations should be considered as potentially tuberculous. Especially is this so when the heart itself remains small, though this may be difficult to determine with a large and radio-opaque effusion. In these cases paracentesis and air replacement is of great value in allowing the heart outline to be visualized. The value of pneumopericardium as a therapeutic measure in preventing pericardial adhesion and fibrosis is considered by some, however, to be slight. The fluid aspirated is usually similar to that of the pleural effusion, but may be blood-stained, the usual predominating cell being the lymphocyte. There are of course many other causes of pericardial effusion, and Smith and Willius (1932) in sorting 373 cases of pericarditis into adherent pericarditis, calcification of the pericardium, and pericarditis with effusion found that there were 113 in the latter group—77 were acute purulent and 30 were fibrinous, and only three were tuberculous and three of non-inflammatory origin. The fibrinous pericardial effusions were mainly secondary to intrathoracic infection, but even then nine of these cases might very well belong to the group now under discussion.

With regard to the development of Pick's disease it has been suggested that in the healing of such a pericardial effusion constrictive symptoms may develop and that as the process is one of healing there may be no pathological lesion resembling a tubercle left in the fibrous pericardium. Thus Norris (1911) collected 1,780 cases of tuberculosis of which 82 showed tuberculous pericarditis, but in only 32 were actual tubercles seen, while in the others no tubercles or any other demonstrable aetiology could be found. If this was so it would account for Smith and Willius finding tuberculosis present in only 2.1% of the 373 cases of Pick's disease examined.

Summary

Four cases are described. Only one case is bacteriologically proved tuberculous, although the others strongly suggest a similar aetiology.

The proved case was that of an infant of 18 months in whom the pericardial effusion was the presenting clinical feature; the condition was diagnosed, although not proved, during life.

It is suggested that tuberculous pericardial effusion may be a commoner condition than has been previously recognized and

that it may be insidious in its onset, transient in its course, and complete in its resolution. It is also suggested that in some cases it may be a late primary tuberculous manifestation and analogous to pleural effusion.

The difficulty in proving the aetiology is stressed and the value of pneumopericardium in allowing the heart outline to be visualized is noted.

Guinea-pigs inoculated with pericardial fluid may survive for many months before showing signs of disease, and much longer than the conventional six weeks is required before passing judgment.

Gross pericardial thickening may develop in a relatively short space of time, and this relationship with Pick's disease is considered.

All cases of pericardial effusion with a small heart and absence of rheumatic manifestations should be considered as potentially tuberculous unless proved otherwise.

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MEDULLARY SUPRARENAL CHROMAFFINOMA PRODUCING MALIGNANT HYPERTENSION

BY

DAVID GUTMANN, M.D.

Assistant Physician, Lister Emergency Hospital, Hitchin, Herts

The following case of medullary suprarenal chromaffinoma (phaeochromocytoma), with presenting features of intermittent attacks of paroxysmal hypertension and vasomotor crises, ending in malignant hypertension with uraemia as the cause of death, seems worthy of record.

Case History

A married woman aged 38 was admitted to hospital on Oct. 13, 1944. She complained of cough with sputum of several years' duration, and attacks of dyspnoea, chiefly at night. These usually started with a feeling of discomfort in the lower abdomen, followed by nausea and shivering, severe palpitation, sensation of constriction in the chest, profuse perspiration, pain behind the eyes, and marked tremor of the hands. The patient was kept under close observation and was examined during and between attacks, which occurred about every third day. The following is a brief description of a typical one.

The attack was induced by the patient's turning on the right side whilst lying in bed. She became restless, trembled, was very excited and talkative, and sweated so profusely that her underclothing was drenched with perspiration. There was pronounced tachypnoea and some dyspnoea and pallor, with cyanosis of the lips, ears, cheeks, hands, and forearms. The forearms and legs were cold and white and the fingers and toes cyanotic. Pulsation of the brachial and radial arteries was palpable, but in both dorsalis pedis and the popliteal and femoral arteries it was feeble. The pulse rate was rapid—approximately 130—but regular. The blood pressure was

300/170. The pupils were much dilated; the temperature was in the region of 100° F. (37.8° C.) and the urine contained albumin and sugar. *Neck*: The thyroid was not enlarged; there was no lymphadenitis; the trachea was central; there was no venous pulsation or engorgement. *Chest*: Signs of disease were absent save for a few scattered rales and rhonchi at both bases. *Heart*: This was slightly enlarged to the left. The cardiac impulse was forcible and diffuse and the sounds were normal. *Abdomen*: There was some fullness and marked tenderness below the right costal margin, but no rigidity in the right hypochondrium. Dullness to percussion was present over an area of about 2½ in. (6.3 cm.) in this region. The liver and spleen were not palpable. *C.N.S.*: Some oedema was observed round the eyes, which watered profusely. The pupils were dilated, but reacted promptly to light and accommodation. The retinae showed bilateral papilloedema, greater on the left side than on the right, and multiple haemorrhages and discrete exudates. The reflexes were brisk. There were marked dermographism and tremor of the fingers, tongue, and upper lids. There were no other abnormalities.

The urine passed during an attack was copious, clear, and almost watery in colour, with a specific gravity varying between 1004 and 1010. It contained a slight trace of albumin and sugar (0.1 and 0.2%). The average duration of an attack was about half an hour.

After the attack the patient, though exhausted, was calm and placid, talking slowly and normally. The cyanosis and pallor soon disappeared, the skin became dry and the pulse slow (approximately 72), and the blood pressure fell below normal, varying between 90 and 100 systolic and 70 and 80 diastolic, only to rise slowly to about 200/120, which was her usual blood pressure between attacks. It remained fairly constant at that level until a further attack occurred, when it abruptly rose again to 300/170.

From the history and from physical examination during and after attacks a preliminary diagnosis of medullary suprarenal chromaffinoma was made. That it was on the right side was suggested by the fullness present below the right costal margin and by the fact that the attacks were precipitated by turning on to that side. There were no symptoms or signs indicating involvement of the cortex in the way either of hyperfunction resulting in "adreno-cortical syndrome" or of hypofunction resulting in Addison's syndrome.

Ancillary investigations were carried out with the following results.

A catheter specimen of urine after an attack showed: specific gravity, 1008; albumin, slight trace; sugar, 0.2%; deposit, occasional leucocytes, epithelial cells, a fair number of erythrocytes, hyaline and cellular casts; culture, sterile. Blood urea was 54 mg. per 100 ml. From a urea-clearance test the renal function appeared to be 34% of the average normal maximum clearance and 24% of the average standard clearance. The glucose-tolerance test showed diminished tolerance, as the fasting blood sugar was 150 mg. per 100 ml.; 3/4 hr. after 50 g. of glucose, 270 mg.; and in another 3/4 hour, 260 mg. Lumbar puncture revealed cerebrospinal fluid under normal pressure. This was clear and colourless and contained 1 lymphocyte per c.mm.; protein, 30 mg. per 100 ml.; sugar, 130 mg. per 100 ml.; and chlorides, 740 mg. per 100 ml. The Queckenstedt test was positive.

Radiological examination of the skull showed no evidence of abnormality. The pituitary fossa was rather small, but the clinoid processes appeared normal. Radiographs of the chest revealed some fibrosis in both lungs probably due to old healed tuberculous infiltration. Bronchial thickening was present at both bases.

X-ray examination showed that the heart was globular in shape, suggestive of concentric hypertrophy of heart muscle without dilatation. An electrocardiogram revealed depression of S-T intervals in all leads, but otherwise it was within normal limits. Intravenous pyelograms showed that the kidneys were normal in size and position. Both excreted well. There was no evidence of any organic lesion in the urinary tract. No suprarenal calcification was found, but there was a depression in one calix of the right kidney, probably due to external pressure and suggesting that the tumour was on the right side.