PARASITES of the HUMAN HEART

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Parasites of the Human Heart

Dedicated to

MAJ. GEN. MORRISON CLAY STAYER, M.C.U.S.A. (RET.)

for

INSPIRATION *and* OPPORTUNITY

Introduction

WE HAVE attempted to summarize in this monograph our knowledge concerning parasites of the human heart. The purpose is to improve the antemortem diagnosis of parasitic cardiopathies by systematizing available information about these diseases. More precisely, the work deals entirely with protozoan and metazoan parasites, excluding other classes of organisms which are also in the strictest sense parasitic upon man, *i.e.*, the viruses, bacteria, rickettsiae, and fungi.*

Stoll[1] in his now classic paper, "This Wormy World," concluded that in 1947 there were 2.26 billion cases of parasitic infection in the world. The fact that this represented 104.2 per cent of the total population at that time may be accounted for by multiple infections in a single individual. There is little reason to believe that the percentage has been significantly reduced in the past two decades. With the increase in the world's population, it seems safe to estimate that at least 2.5 billion individuals are currently parasitized.

Levy[2] has stated that practically all of the known parasites of man have been reported at one time or another to involve the heart. More recently, Luckey[3] has discussed the importance of parasitic heart disease, such as Chagas' disease, and has raised the question as to whether some of the cardiopathies of unknown cause may be due to parasites.

Until World War II, many parasitic diseases were considered merely as medical curiosities in the United States. Their infrequency in temperate climates, and the varied and confusing symptoms presented by some of them did not encourage their ready recognition by the average clinician. Although most of these conditions prevail in geographic areas where modern sanitation is unknown or inadequate, a number of parasitic infections, such as hookworm and malaria, have nevertheless always represented very important public health problems in this country. The

*Indexing difficulties well-known to medical bibliographers and now being explored by such agencies as the National Medical Library make it virtually impossible to collect every reported case of a particular parasitic infection. For example, if an author discusses primarily cysticercosis of the nervous system and only incidentally mentions an occurrence in the heart, the cardiac lesion will not be indexed as such. If readers will inform us of authenticated cases of parasitic infection of the heart which we have overlooked, we will record this information in a later (hopefully) edition.

presence of suitable vectors and intermediate hosts in the United States makes still other "tropical" diseases potential public health menaces of considerable proportions. The deployment of troops to endemic areas in remote corners of the world and the frequency of intercontinental air travel have resulted in the appearance of numerous cases of hitherto rare conditions in this country as well as in other temperate areas. The Advisory Committee to the Division of Medical Sciences of the National Academy of Sciences, headed by Dr. Albert B. Sabin, has systematized the tropical disease problems currently facing this country and the world.[4]

A prime example of these problems is South American trypanosomiasis, or Chagas' disease, in which the infecting organism, *Trypanosoma cruzi*, exhibits an extraordinary cardiotropism unmatched by any other animal parasite of man. The ubiquitous *Trichinella spiralis*, constituting perhaps the major parasitic public health menace in the United States, also causes cardiac damage in a significant proportion of cases.

In lands where sheep-raising is an important industry, Uruguay and New Zealand among others, the hydatid cyst of *Echinococcus granulosus* localizes in the heart with sufficient frequency to create a strong impetus for clinicians to consider it routinely in diagnostic studies. In recent years, the importance of this entity has increased in direct proportion to advances in cardiac surgical techniques, since of all the diseases to be discussed here, echinococcus invasion of the heart is the only one in which full cure through surgery may be expected if diagnosis is made early enough. The importance of the latter requirement cannot be overstressed, since the usual outcome of untreated cardiac echinococcosis is catastrophic.

Pathologically, lesions of the heart resulting from parasitic infection may be specific, by virtue of the presence of the parasitic agent itself or its ova within the tissues of the heart or pericardium;[4a] or non-specific, the changes being secondary to the presence of the parasite in an adjacent or even distant site. An enormous body of literature purports to prove that many parasites which do not directly invade cardiac tissue nevertheless exert clinically significant effects by virtue of their "toxicity" or "antigenicity." The evaluation of these data is immensely difficult, and we have preferred, with but few exceptions, to limit our consideration to those diseases in which the parasite directly invades the substance of the heart, its orifices, or its coverings. Notable among these exceptions is the discussion of the influence of malaria upon the heart, since the effects which this disease exerts by virtue of its toxicity, and those which stem from the actual presence of the parasite within the nutritive vasculature

of the heart, are not clearly distinguishable by current methods of study. Another such exception is hookworm disease, in which the development of cardiac lesions is constant enough to demand consideration, despite the fact that neither the adult parasite nor its visible products have ever been found in the cardiac tissues proper.

We have not included the large body of literature dealing with experimental infection in animals, except where we felt that an evaluation of the experimental findings would materially aid in understanding the nature of the lesion in man.

Since we have been primarily concerned in this work with the parasitic cardiopathies, the reader is referred to any of the standard reference works in tropical medicine, parasitology, or helminthology for more detailed descriptions of any of the disorders mentioned. We hope, however, that we have made evident the fact that recent studies of epidemiology and incidence have increased our awareness of the important cardiologic characteristics of each infection.

Many of the illustrations in this book are reproductions from original articles and, despite the photoengraver's skill, are not totally satisfactory. However, we feel that they should be published mainly because of their historic importance.

Lastly, lest we be tempted to dismiss the parasitic cardiopathies too lightly because of their present status as curiosities, we would do well to note the advice given by a most eminent clinician and parasitologist over 50 years ago:[5] "It should be remembered that findings which appear anomalous and inexplicable at present may eventually be found to be natural and logical phases of the parasitic existence of these animals, and be classed actually as commonplace in the future."

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Section A

Protozoan Diseases

Chapter I

Amebic Pericarditis

THREE DECADES AGO, few North American clinicians considered parasitic diseases in the differential diagnosis of their problem cases, except perhaps automatically to order that a casual stool specimen be examined for "ova and parasites." Today, owing primarily to the influence of global warfare on the epidemiology of parasitic diseases, the majority of practitioners recognize the fact that amebiasis, at least, is a cosmopolitan and often occult infection which may first present rather unorthodox symptoms. As far as the heart is concerned, however, though the cardiologist may occasionally be requested to evaluate patients about to be given emetine for the treatment of hepatic amebiasis,[1-3] this is generally the limit of common experience.

On a number of occasions, nevertheless, the association of suppurative pericarditis and amebic involvement of the liver (the latter not infrequently being occult) has produced a puzzling clinical situation of considerable gravity. Both clinician and pathologist have shown tremendous interest in this entity despite the fact that only some 66 proven cases of suppurative amebic pericarditis have been mentioned in the recent world literature. The majority of these have been summarized.[2-5]

PATHOGENESIS

By amebiasis is meant infection with *Endamoeba histolytica*. None of the other amebas are known to have invaded the heart.

Hematogenous involvement of the heart muscle proper with either diffuse myocarditis or abscesses has never been reported as a complication of amebiasis. The only manner in which this parasite is known to involve the heart is by secondary extension of a suppurative process in the liver across the diaphragmatic barrier into the cardiac envelope. The infective process tends readily to spread from below the diaphragm upwards, but rarely if ever in the reverse direction.[6] Ochsner and DeBakey,[7] as well as others,[8-11] have noted that pericardiac complications are more likely to result from amebic abscesses located in the left lobe of the

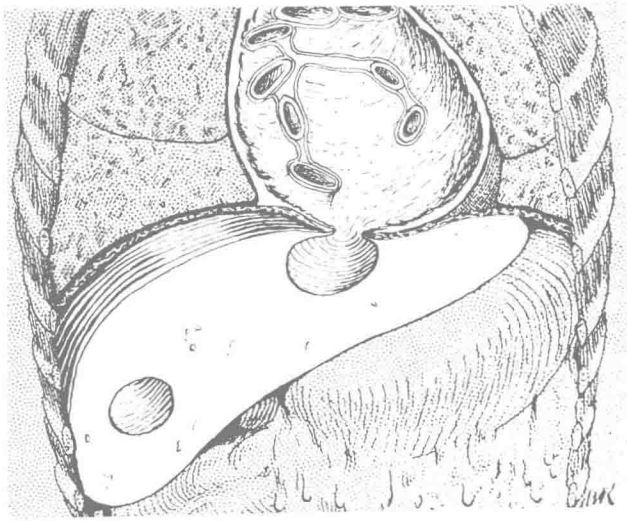

Fig. 1.—Note the communication between the pericardial sac and the amebic abscess in the left lobe of the liver. Artist's sketch of gross findings at autopsy (after Carter and Korones[4]).

liver, not only because of the favorable anatomic relationships in such instances but because the rarity of left-sided hepatic abscesses as compared to those on the right, and their relative clinical silence, combine to make their correct diagnosis prior to rupture notoriously difficult.

An amebic abscess localized at either hepatic dome may eventually involve the heart if it grows large enough, (1) by penetrating into the pleural space, and thence into the pericardium; (2) by creating a secondary abscess of the lung which then ruptures into the pericardial sac; or (3) by penetrating the central portion of the diaphragm directly into the pericardium. Examples of each mechanism may be found in the case material described in the literature. These catastrophic complications generally occur in those neglected patients having massive involvement of both liver and lung, and pericardial extension is simply then a preterminal feature of overwhelming infection. Occasionally, however, the pericarditis alone may completely dominate the clinical picture,[5,11,12] but true suppurative pericarditis must be distinguished from those instances of non-specific pericardial effusion occurring in patients moribund by reason of debilitating infection, anemia, malnutrition, and general cachexia.

INCIDENCE

Since amebic pericarditis has never been observed unassociated with amebic liver abscess, it is pertinent to inquire first into the incidence of the latter. Amebic liver abscess was reported by Ochsner and DeBakey[7] to have been diagnosed in only 4.88 per cent of 10,000 collected clinical cases of amebiasis, but was found to be present in 36.6 per cent of 5200 collected autopsy cases of persons infected with *E. histolytica*. These authors, however, found only one instance of true amebic pericarditis in their own series of 181 patients with amebic liver involvement, and concluded that less than 2 per cent of such individuals could be expected to have cardiac complications. This agrees roughly with the observation of Vergoz and Hermanjat-Gerin,[12] who reported that only 2.8 per cent of 889 ruptured amebic liver abscesses entered the pericardium. In contrast to these figures, Craig[13] stated that of 192 cases of rupture of amebic abscess of the liver, 70 extended into the pleura, 47 into the lung and 38 into the pericardium. In any event, the great rarity of suppurative pericarditis as a complication of amebic infection is apparent.

In Clark's[14] extensive review of 186 postmortem examinations of persons with amebic lesions of various types, no instances of pericardial involvement were encountered. In a more recent survey covering a 35-year period, Kean and his associates[15] analyzed 148 cases of fatal amebiasis, and found that four of these had died in heart failure, but only two with amebic pericarditis, the other two having had myocarditis attributed to emetine toxicity. In a later series, Gordon[10] recorded eight cases of suppurative amebic pericarditis among 2000 autopsied subjects (representing less than 10 per cent of all deaths) between 1950 and 1955 in Durban, South Africa. He also described an additional case in an African who recovered fully.

In one instance, a case of "amebic aortitis" was reported from South America,[16] but unfortunately, the original article describing this unique entity was unavailable during preparation of this review.

Table 1 summarizes certain information about 65 cases of suppurative amebic pericarditis.

SPECIFIC VERSUS NON-SPECIFIC INVOLVEMENT

In numerous instances, prominent cardiac symptoms and signs have been observed in patients with intestinal amebiasis, as well as in those with hepatic and pulmonary abscesses; however, causal relationship between the amebic process and the cardiac disturbance can rarely be established. Positive proof of specific etiology demands the identification

Table 1.—*Summary of Cases of Suppurative Amebic Pericarditis*
(Modified after Carter and Korones[4])

Authors	Year	No. of Proven Cases	Diagnosed during Life	Survival
Howard and Hoover[17]	1897	1	no	no
Craig[18]	1904	2	no	no
Justi[19]	1923	19	—	—
Surbek[20]	1930	1	no	no
Kataropulo[21]	1932	1	no	no
Vergoz and Hermanjat-Gerin[12]	1932	13	no	no
Huard and Meyer-May[22]	1936	3	*yes*	*yes*
Ochsner and DeBakey[7]	1943	1	no	no
Herrlich[8]	1943	1	no	no
Kern[11]	1945	1	no	no
Singh[23]	1946	1	*yes*	no
Carter and Korones[4]	1950	1	*yes*	*yes*
Hartz[9]	1950	1	no	no
Coiralt et al.[24a]	1955	1	*yes*	*yes*
Kean et al.[15]	1956	2	no	no
Norris and Beemer[5]	1956	2	no	no
Gordon[10]	1956	9	*yes*	*yes*
Michon et al.[31]	1959	1	yes	*yes*
Felix et al.[32]	1960	3	yes (2)	*yes* (2)
Polani et al.[33]	1963	1	yes	no
Totals		65	10	7

of *E. histolytica,* either in the purulent exudate obtained from the pericardial cavity, or in histologic sections of the tissues lining the abscess.

One of the earliest instances of proven parasitic pericarditis was reported in 1897 by Howard and Hoover.[17] They identified degenerate forms of *E. histolytica* in the fibrino-purulent exudate obtained from their patient at autopsy, but could not demonstrate a direct communication between the underlying amebic liver abscess and the pericardial cavity, despite partial destruction of the right diaphragmatic leaf by the suppurative process.

Examples of both specific and non-specific pericardial involvement were recorded by Craig in 1904,[18] in an analysis of 80 fatal cases of amebiasis. In 12 of these, Craig found marked "oedema of the pericardium," and stated: "This condition I have found to be one of the most characteristic complications observed in the fatal cases." The pericardial cavity in each case was filled with clear, straw-colored effusion, although in a few cases small shreds of fibrin were observed. Both layers of the pericardium appeared normal as far as could be judged. In two of the cases, however, a true suppurative pericarditis was found, in both in-

stances being secondary to "perforation of an amebic abscess of the liver into the pericardial cavity," with resultant distention of the sac by purulent exudate.

Huard and Meyer-May[22] noted the presence of serous pericardial effusion in six of 150 patients with amebic liver abscess whom they studied; one of the three cases of suppurative pericarditis also described in this series was correctly diagnosed during life by aspiration of the pericardium through the underlying liver abscess. Purcell,[24] and also Laigret,[25] reported single cases of amebic abscess of the liver, associated with prominent signs of pericarditis. Both patients recovered following treatment with emetine, without the nature of the fluid having been ascertained. It is probable that in these two instances only a serous effusion had been present. Laha[26] reported a supposed case of specific pericarditis in a 17-year-old girl in whom there developed postpartum fever, tender enlargement of the liver, and a pericardial friction rub. Quinine and sulfonamides were administered without benefit, but the rub disappeared 6 days after a course of emetine was begun. The diagnosis of amebic pericarditis was based solely upon the latter observation. Laha felt that a non-specific effusion would not have produced the dry friction rub, which he took to be indicative of fibrinous deposits accompanying suppuration.

Edwards[27] reported in great detail the clinical history of a similar case which progressed to rupture of an hepatic abscess into the right lung, and eventual recovery following discharge of its contents in the sputum. The chief interest of this case, however, lies in the fact that fully 10 weeks before the earliest suggestion of the correct diagnosis (i.e., the appearance of a rounded elevation of the right diaphragmatic leaf on x-ray), a persistent pericardial friction rub had been heard over a period of 12 days, in the total absence of any other physical sign. The rub was described as "coarse and creaking," but there was no cardiac enlargement, and the blood pressure was well maintained within normal limits. It is interesting to note that "activation" of the liver abscess was heralded so far in advance by the persistent pericardial friction rub, which, in turn, was probably only a non-specific reaction to the underlying focus of infection. Understandably, the attending physicians discerned no plausible relationship between the rub and the symptom of right subcostal pain which first brought the patient to the hospital over 3 months before the abscess ruptured.

CLINICAL AND DIAGNOSTIC FEATURES

Symptoms in amebic pericarditis may be entirely lacking until the terminal collapse of the patient, or may be protracted but extremely ill-

defined. In other cases, evidence of pericardial involvement may be quite florid, but the proper diagnosis is not made because the associated liver abscess is unrecognized. The failure of diagnosis in such cases is due, no doubt, to the relative rarity of left-sided amebic liver abscesses, as well as to their tendency to be clinically "silent." For example, in the case described by Norris and Beemer,[5] the patient had been entirely well until the onset of massive left-sided empyema, followed in 2 weeks by the fatal episode of cardiac tamponade. (It was of interest that in this case there was a 10-day delay between death and permission for autopsy.) In an earlier unpublished case of theirs, the sole symptom in a middle-aged woman had been progressive weight loss so marked as to suggest disseminated malignancy. Death occurred suddenly, and was found to have been due to rupture of an unsuspected hepatic abscess into the pericardium. Until recently, few[4,10,22,24,24a,31,32] authenticated cases had been correctly diagnosed prior to autopsy.

Lack of suspicion has been responsible for failure to make several diagnoses. Hartz[9] described a particularly unusual case in which the electrocardiographic changes following the patient's collapse had been quite characteristic of pericarditis; nevertheless, this diagnosis was rejected because of the confusing clinical picture dominated by embolic processes. The clinical diagnosis was aortic thromboembolism with left femoral involvement, but necropsy examination unexpectedly revealed a left-sided hepatic abscess communicating with the pericardial cavity, plus typical amebic ulceration of the cecum and ascending colon. The cause of the left femoral embolism was not ascertained.

Changes in the roentgen ray heart shadow suggested involvement of pericardium to Norris and Beemer,[5] but because of the absence of physical signs or electrocardiographic abnormalities, they erroneously assumed that the pericardium had become involved by extension from the adjacent chronic empyema, and did not suspect suppuration within the pericardium until the final episode of tamponade.

Kern's patient,[11] on the other hand, had a clinical picture dominated by pericarditis, with a globular cardiac shadow, loud friction rub, neck vein distention, a strikingly paradoxic pulse, and an almost vanishing pulse pressure. Because of this, however, little attention was paid to the abdominal pain present on entry or to the history of pain in the right shoulder 3 months earlier; similarly, the important x-ray finding of bilateral diaphragmatic elevation was not given proper consideration. Kern frankly pointed out that these factors should have directed suspicion toward a possible hepatic abscess. Furthermore, he felt, at least in retrospect, that the typically "amebic character" of the chocolate-colored material aspirated from the pericardium should have cast some

doubt on the rather intuitive clinical impression of tuberculous pericarditis.

A harsh pericardial friction rub is generally the most constant and reliable physical sign of intra-pericardiac suppuration, but even this sign may be absent despite advanced exudative and proliferative changes, as in Norris and Beemer's case.[5] In other instances, the rub may be transient, disappearing as sufficient fluid accumulates to separate the inflamed surfaces; or sometimes it is simply not recognized because of the louder and more diffuse pleural friction rub which may accompany it.

Fluoroscopy may be quite helpful in revealing diminished or virtually absent cardiac pulsations,[11] even in the absence of enlargement of the cardiac shadow. Contrary to expectations, the electrocardiogram is of much less diagnostic help. In Edwards' patient,[27] the electrocardiogram remained normal except for left axis deviation throughout the prolonged illness. In Norris and Beemer's case,[5] the electrocardiogram, although abnormal, did not contribute to the diagnosis, since it showed only nonspecific T-wave changes. In Kern's case,[11] several electrocardiograms taken even after the pericarditis had become advanced showed only iso-electric T-waves in leads I and II.

Examination of the stool for cysts and trophozoites of *E. histolytica* is not a dependable aid to diagnosis, as Elsom[28] pointed out, because a past history of amebic dysentery or even simple diarrhea is unobtainable in up to two-thirds of patients with hepatic complications. Ochsner and DeBakey[7] found that only 11–36 per cent of the patients with liver abscess collected from various series passed amebic trophozoites and/or cysts in their stools. This is not surprising when it is remembered that even many autopsied cases showed no signs of either active or healed intestinal ulceration.[4,7,11]

Probably the most valuable diagnostic procedure in agnogenic suppurative pericarditis, short of microscopic examination and culture of fluid aspirated from the pericardium, is the amebic complement-fixation test devised by Craig, which is claimed to be positive in up to 90 per cent of patients with hepatic or intrathoracic amebiasis.[29] Unfortunately, this technique is not readily available in most laboratories, and is trustworthy only in the most expert hands, owing to the extreme difficulty of preparing and maintaining an antigen of reliable potency.[29]

A most unusual event leading to correct diagnosis, and one that has occurred probably only once, was described by Carter and Korones.[4] In their patient, open pericardiotomy with marsupialization of the abscess lining to the anterior chest wall was performed because of the impracticability of continuing daily paracenteses indefinitely. On the 8th