Staphylococcal Heart Disease in Children

By

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While staphylococcal infections are in the foreground of medical interest all over the world, staphylococcal diseases of the heart have received less attention, in spite of their incidence showing an upward tendency. Pneumococci, at one time the principal aetiological agents of pericarditis, seem, according to HORAN [17] to cede their hegemony to staphylococci. This has been confirmed by FLAXMANN [12] who found that staphylococci were the pathogen in 79.5 per cent of myocardial abscesses, usually in association with osteomyelitis and bacterial endocarditis. SHELDON and GOLDEN [27], using a special technique, demonstrated cardiac abscess in 12 of 14 patients who had died of bacterial endocarditis. WEISS and WILKINS [33] reported a case of asymptomatic myocardial abscess leading to perforation of the heart. ZETTNER and IRMIERE [36] observed several cases of myocardial abscess. According to HOWE [18], most postoperative infections are of staphylococcal origin. Several authors [5, 15, 16] have described staphylococcal infections following heart operation, especially interventions carried out with extracorporeal circulation. FÜLÖP [13], in a report on 78 post-mortem examinations of children who had died with staphylococcal septicaemia, did not mention cardiac involvement, while DOBSZAY [6] discussed staphylococcal heart disease in some detail.

A few pertinent cases, observed in our Department, have already been described [30, 31]. Some further cases have occurred since then and it is striking how often we have found heart lesions at the autopsy of children who had died of cardiologically symptomless staphylococcal infection. Since animal experiments [20] have changed our original view of the problem at issue, we feel justified in discussing at anew.

Our present study deals with 36 cases. These may be divided into three categories.

[i] Acute septicaemic peri-myocarditis (9 cases, of which 4 with fatal outcome).

[ii] Subacute bacterial endocarditis (2 cases).

[iii] Cases in which only the post-mortem examination revealed cardiac involvement (25 cases).

(Thus, out of the total of 36 cases, 29 ended fatally).

History

[i] In the peri-myocarditis group, a primary febrile disease (osteomyelitis, bronchopneumonia and — especially in infants — pyoderma) had preceded by 1 to 3 weeks the appearance of cardiac symptoms. The original focus of infection could not always be ascertained. The localisation is determined less by the actual site of invasion than the immune-biological condition and the susceptibility of the affected organ [20,26]).

[ii] The two children suffering from subacute bacterial endocarditis had congenital defects; they had been subjected to heart catheterization 11 and 12 months, respectively, prior to their present admission.

Diagnosis

[i] Members of the peri-myocarditis group were in a severe condition at admission, with septic temperatures, elevated ESR (mean, 50 mm per hr), leucocytosis (mean, 18,000); the smears invariably revealed toxic granulation. Pericardial rubs and the fading of heart sounds were present in all members of this group. The dullness of the heart increased from day to day. The ECG showed ST and T changes characteristic of pericarditis. In 5 cases, 4 of which subsequently died, the ST interval was elevated in several chest leads; the sign therefore seems to be indicative of a bad prognosis.

[ii] The diagnosis of bacterial endocarditis has been based on the following symptoms: intermittent fever; splenomegaly; haematuria; skin

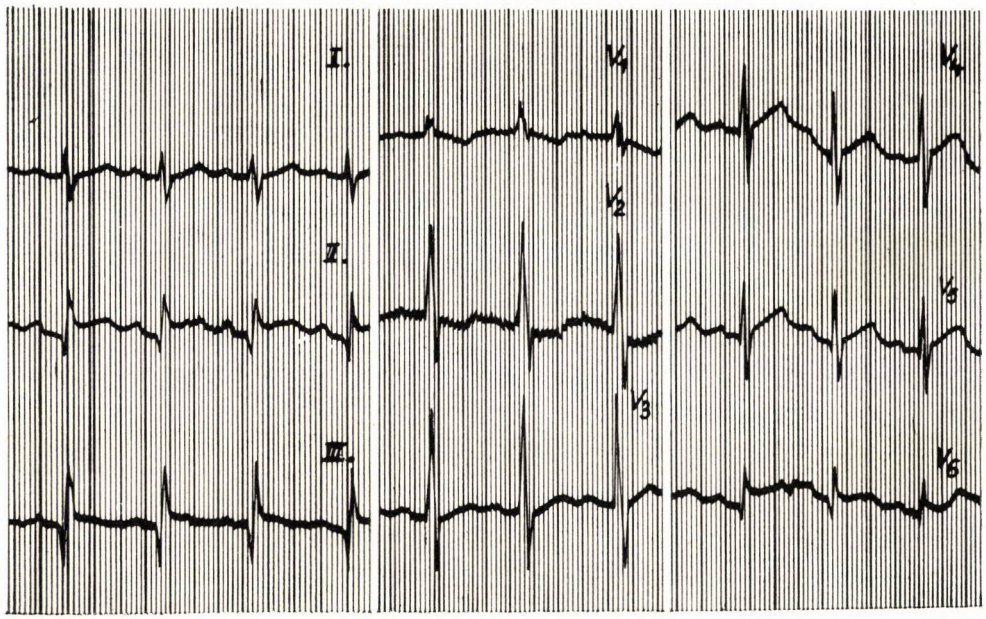

Fig. 1. ECG of M. K., a child 18 months of age suffering from peri-myocarditis (Standard I—II—III and V_1—V_6 leads)

lesions pointing to embolism; repeated isolation of pathogens from blood.

[iii] No such symptoms as the above were present in the cases in which heart disease had not been diagnosed during life; it is, of course, possible that the cardiac symptoms were obscured by those of the septicaemia. The patients in this group were treated in other departments of our hospital.

Pathogens

Bacteriological details are outside the scope of the present report, and we refer in this respect to the monographs of Elek [8] and Dobszay [6]. It should be noted that coagulase-negative strains of *St. albus* may be pathogenic [5, 10, 12, 15, 34]. Levinson, Griffith and Pearson [22] claim that bacterial endocarditis is as often due to strains of *St. albus* as to those of *St. aureus*. According to Flaxmann [12], *Micrococcus pyogenes var. albus* is commonly recovered from myocardial abscesses.

In the course of post-mortem examinations we isolated staphylococci in 29 cases (of which 4 had been diagnosed during life), from the blood, throat, the pericardial pus and the bone marrow, generally from several parts of one and the same cadaver. There were two apparently typical cases in which we failed to recover the pathogen.

Treatment

[i] The fundamental principles governing the treatment of children suffering from peri-myocarditis have been described previously [30]. It is essential that the pericardium should be drained and adequate antibiotic treatment started at an early stage, although it occurred several times that the patient died during treatment with an antibiotic to which the pathogens had shown a high degree of sensitivity *in vitro*.

[ii] Although the strains of staphylococci, isolated from patients with subacute endocarditis, had proved resistant or only moderately sensitive to penicillin and streptomycin *in vitro*, cure was achieved by combined treatment with penicillin (several million units daily) and streptomycin (0.5 to 1.0 g daily) to which polymyxin was added in one case. Sensitivity to antibiotics *in vitro* is frequently misleading in cases of endocarditis [11, 14, 19, 24].

[iii] The autopsy findings revealed that grave cardiac lesions of staphylococcal origin may be present in spite of the absence of clinical symptoms. We had 37 cases of bacteriologically verified fatal cases of staphylococcal septicaemia during the last 2½ years and it was in 29 that we succeeded in demonstrating cardiac complications (out of which there were 25 cases where the involvement of the heart was discovered post mortem only).

It is seen from Table I that a gross lesion was observed in 12 cases. These lesions were [i] myocardial abscess and rupture of the heart; [ii] pericarditis invariably associated with myocarditis; [iii] ulcerative thrombo-

Table 1

Age distribution of autopsied cases of staphylococcal infection accompanied by cardiac complication

Age	History	Clinical diagnosis	Diagnosis anatomical	Cardiac diagnosis	Diagnosis
days	—	intracranial haemorrhage	umbilical infection	myocarditis, haemorrhage	Histologic
10 days	—	spina bifida	meningitis	myocarditis, haemorrhage	Histologic
11 days	—	Empyema	bronchopneumonia, abscess	pericarditis	Gross
3 weeks	pyoderma	phlegmone of neck	dermatogenous septicaemia	myocarditis	Histologic
3 weeks	operation	sacrolumbal teratoma	meningitis	pericarditis	Gross
3 weeks	pyoderma	umbilical infection	bronchopneumonia, abscess, umbilical infection	myocarditis	Histologic
3 weeks	pyoderma	bronchopneumonia	bronchopneumonia, abscess	myocarditis	Histologic
4 weeks	—	spina bifida	nephritis, suppurative meningitis	pericarditis, myocardial abscess	Gross
5 weeks	pyoderma	abscess at occipital region	bronchopneumonia, abscess	pericarditis, myocardial abscess	Gross
6 weeks	pyoderma	bronchopneumonia, hygroma of neck	bronchopneumonia, abscess	pericarditis	Gross
6 weeks	pyoderma	bronchopneumonia, empyema	bronchopneumonia, abscess	myocarditis	Histologic
2 months	—	bronchopneumonia, empyema	bronchopneumonia, abscess	myocarditis	Histologic
2 months	enteritis	spina bifida	meningitis	myocarditis	Histologic

3 months	pyoderma	dermatitis broncho-pneumonia	bronchopneumonia	myocarditis	Histologic
3 months	pyoderma asthma	bronchopneumonia, pneumothorax	bronchopneumonia, abscess	myocarditis	Histologic
3 months	—	spina bifida	empyema	myocarditis	Histologic
3 months	pyoderma	intestinal occlusion	peritonitis	myocarditis	Histologic
4. months	pyoderma enteritis	bronchopneumonia, septicaemia	nephritis, bronchopneumonia	pericarditis	Gross
4 months	pyoderma	Leiner's erythrodermia	Leiner's erythrodermia	myocarditis	Histologic
5 months	pyoderma	bronchopneumonia, furunculosis	dermatogenous septicaemia	myocarditis	Histologic
5 months	pyoderma	bronchopneumonia	bronchopneumonia, abscess	myocarditis	Histologic
6 months	enteritis	bronchopneumonia	bronchopneumonia, abscess	pericarditis	Gross
8 months	—	bronchopneumonia	lung abscess	subepicardial abscess	Gross
$1^1/_2$ years	pyoderma	suppurative peri-myocarditis	myocardial abscess, heart rupture	pericarditis, myocardial abscess	Gross
2 years	scarlet fever gluteal abscess	Waterhouse Friderichsen's syndrome	suprarenal apoplexy	myocarditis	Histologic
3 years	pyoderma	bronchopneumonia, abscess	bronchopneumonia, abscess	pericarditis, myocardial abscess	Histologic
5 years	operation	congenital rectovaginal fistula	peritonitis	myocardial abscess, subepicardial abscess, myocarditis	Gross
7 years	pyoderma	suppurative peri-myocarditis	peri-myocarditis	pericarditis, myocardial abscess	Gross
8 years	pyoderma	osteomyelitis, bronchopneumonia	lung abscess osteomyelitis	ulcerative thromboendocarditis	Gross

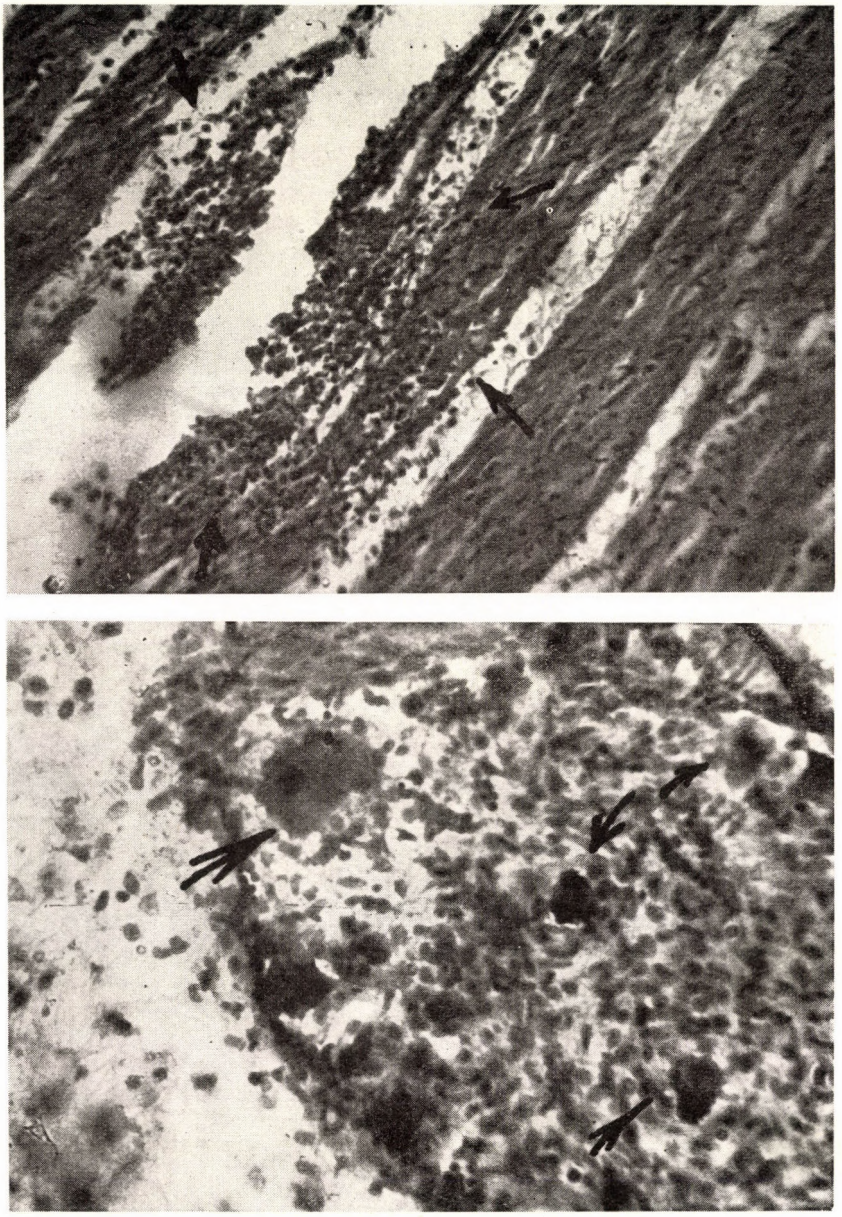

FIG. 2. *a)* Incipient inflammatory infiltration (↑), and lymphatic congestion in hypoxic myocardium.
b) Spread of pericarditis to the right atrial ganglion; note advanced degeneration of ganglion cell (↑) adjacent to inflammatory infiltration

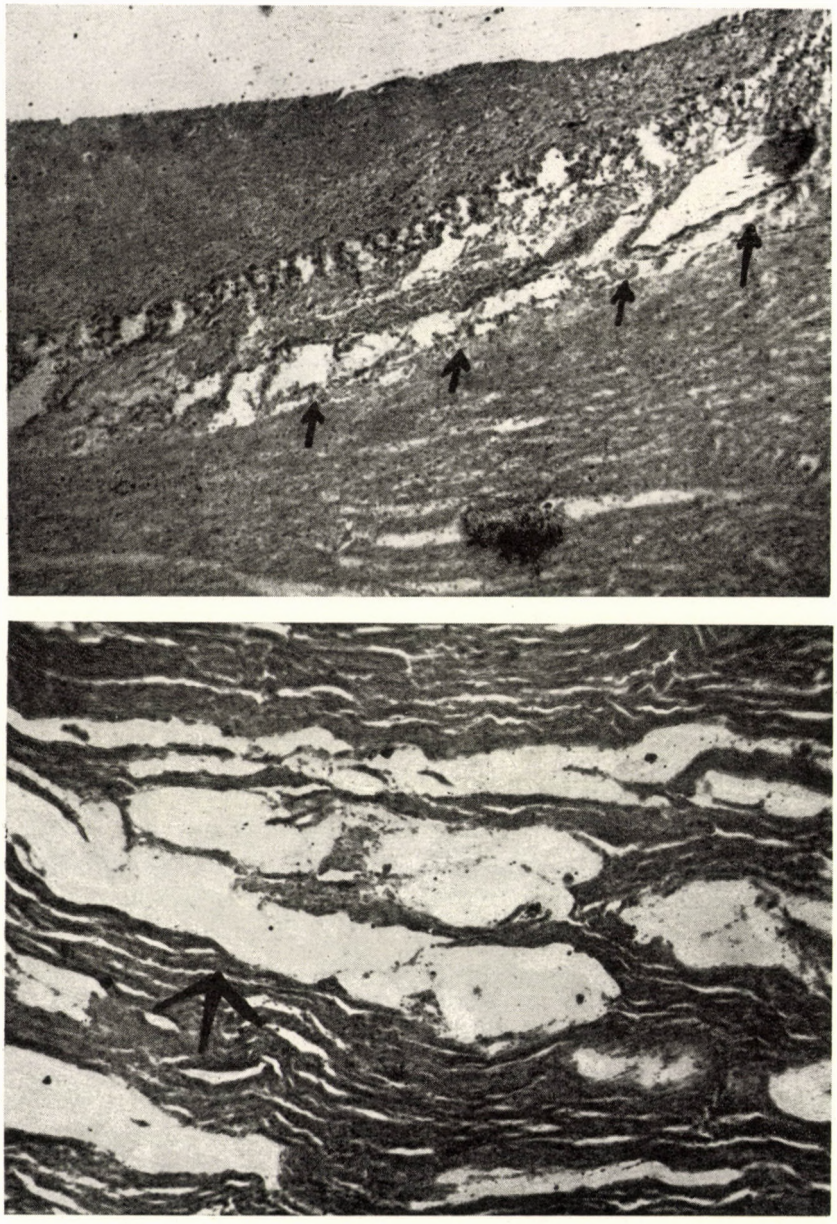

FIG. 3. *a)* Dilatation of the uppermost subepicardial lymphatic plexus in connection with staphylococcic suppurative pericarditis.
b) Excessive dilatation of lymph spaces in the myocardium of the left ventricle, indicative of dynamic insufficiency of cardiac lymph circulation

endocarditis (in a single case). Exclusively microscopic changes were observed in 17 cases. They consisted of interstitial perivascular and adventitial infiltration of inflammatory cells associated with myocardial oedema; microscopic abscesses; necrobiosis; extravasation of blood.

The lesions occurred in the muscles of the left ventricle, less frequently in the atria. Careful histological analysis revealed hardly any changes in the right ventricle. Pronounced dilatation of the lymphatics was frequent; this presumably has an important pathomechanical role and indicates dynamic insufficiency of the cardiac lymph circulation. While pulmonary and cardiac manifestations of staphylococcal infection are frequently associated, we have never observed cardiac involvement (not even histological changes) in cases of staphylococcal enteritis. The pathomechanism of staphylococcal heart disease (insufficiency of cardiac blood and lymph circulation, allergy, previous diseases, surgical stress) will form the subject of a subsequent communication.

It is remarkable that the overwhelming majority of our autopsy material consisted of infants. In the age group under one year the involvement of the heart was discovered post mortem only, so that these cases of staphylococcal septicaemia seem to be especially asymptomatic or at least poor in heart symptoms.

Results

[i] Five out of the 9 children suffering from peri-myocarditis survived. In the 4 fatal cases there were extensive pericardial adhesions. Such adhesions seem to impair recovery very considerably.

[ii] Both cases of subacute endocarditis recovered: they are being followed up, and no relapses have occurred so far. One of them has undergone a cardiac operation in the meantime.

Discussion

Heart diseases of staphylococcal origin are, according to our observations, not infrequent. We saw them mostly as a partial manifestation of septicaemia; yet, in some cases, heart disease appeared as an isolated phenomenon.

Both children with subacute endocarditis had an interventricular septal defect. Catheterization of the right heart had occurred in the history of both cases, but we do not suggest that it was instrumental in the production of the disease. It may, according to some authors [2, 3], play a certain role in the development of right-sided endocarditis. We have never observed a phenomenon of this nature, although we catheterized the right heart of approximately 200 children during the last 5 years.

Only a single case of peri-myocarditis (diagnosed post mortem) was accompanied by unmistakable symptoms of endocarditis. This shows that acute ulcerative staphylococcal endocarditis, so often referred to in literature, is no common occurrence in children.

Although developmental abnormalities make their bearers susceptible

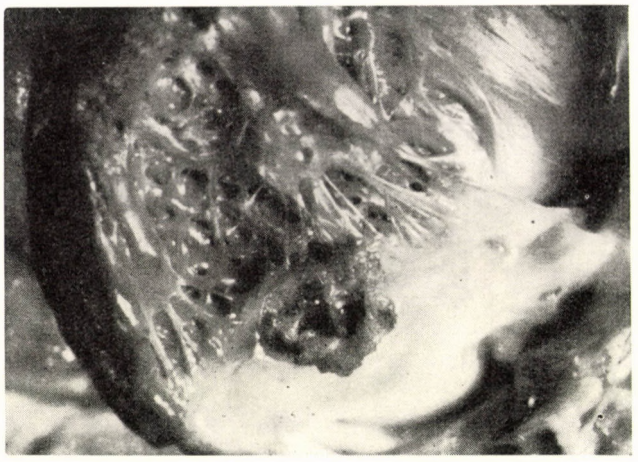

FIG. 4. Anatomical preparation of our case of ulcerative staphylococcal endocarditis. Abscess at left venous orifice

to staphylococcal infection, our observations did not support the generally accepted view that a congenital or acquired defect is a prerequisite of septic acute myocarditis. No member of our corresponding group had such a defect. On the other hand, we, too, found the existence of defects to be a factor predisposing to endocarditis. Although both patients with

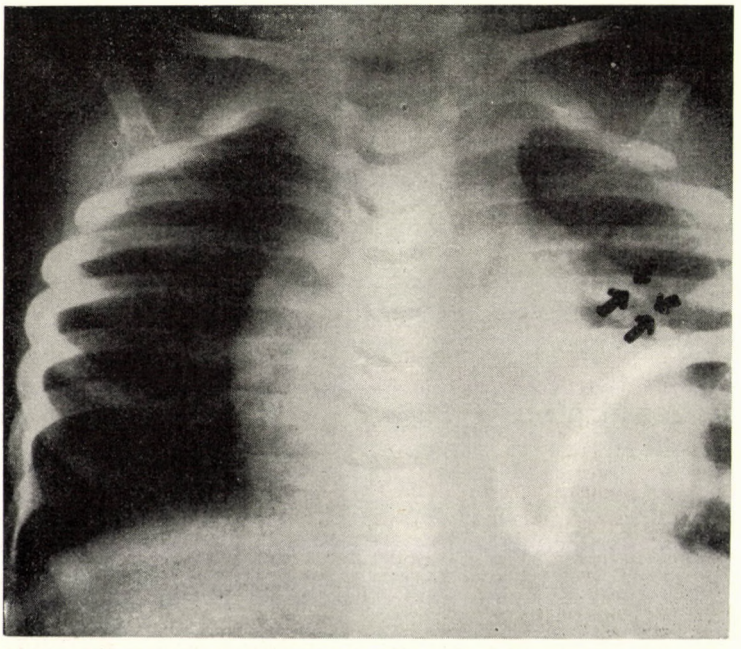

FIG. 5. X-ray of the child in Fig. 1. Thickened pericardium with introduced tube is indicated by arrows

FIG. 6. Heart of the child in Figs. 1 and 5. Immediate cause of death was heart perforation. Arrows point to myocardial abscess. The rubber tube lies in the ruptured abscess

subacute endocarditis recovered, two cases do not suffice for definite prognostic conclusions to be drawn.

It was remarkable that 4 out of 9 cases of peri-myocarditis should have ended fatally, although the same treatment had been applied in all of them. The much-discussed increase in antibiotic resistance does not fully explain the phenomenon. Extensive pericardial adhesions have been revealed post mortem in all of the four fatal cases. Notwithstanding the fact that these children had developed evidence of pericarditis only during the last days, the adhesions pointed to inveterate processes.

Diseases of staphylococcal origin, and so also their cardiac complications, seem to remain a grave problem, especially since beside that of the other antibiotics, a decrease in the potency of erythromycin has also been noted [24, 25, 35]. It is from the discovery of new antibiotics that some authors expect an improvement of the situation. Of recent, synthetic penicillin [BRL 1241] has ensured satisfactory results in cases of staphylococci resistant to the usual preparations [7, 29, 32]; this drug therefore seems to exert its effect in spite of the presence of bacterial penicillinase [21, 23, 28].

The problem of staphylococcal disease is, however, not merely, and not even in the first place, one of antibiotics. Improvement can only be expected from prophylactic measures. Fundamentally important as the given factors of constitution and general condition undoubtedly are, the observation of the rules of general hygiene is likewise of decisive importance. It is noteworthy that the overwhelming majority of our cases consisted of country children living under unfavourable social and hygienic conditions. To ascertain the occurrence of infections acquired during hospitalization or during examinations; to become acquainted with previous diseases; to discover latent or subclinical staphylococcal infections preceding the actual grave disease: these are important tasks in any given case.

SUMMARY

Thirtysix cases of staphylococcal heart disease have been reported, among them 9 of acute septic pericarditis-myocarditis, of which 4 with fatal outcome; 2 cases of subacute

endocarditis; finally, 25 cases in which cardiac lesions were revealed only post-mortem. Of 37 children who had died of staphylococcal septicaemia in recent years, it was in 29 that serious carditis could be demonstrated. Most of the victims were infants. Pancarditis was observed in one case only. Acute ulcerative staphylococcal endocarditis is rare in children. Important as early diagnosis and vigorous antibiotic treatment are, prevention is nevertheless of the highest significance. Although cardiac complications mostly constitute but part of the disease, they are frequently the immediate cause of death.

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