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The classification of staphylococci from colonized ventriculo-atrial shunts

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SYNOPSIS Micrococcaceae isolated from the shunt, ventricles, and bloodstream of children with colonized ventriculo-venous shunts were classified within the scheme of Baird-Parker (1963). With one exception, all belonged to subgroup II of the genus Staphylococcus; tests were therefore devised for division within this subgroup, and results are reported in 30 cases from this and other hospitals.

Skin and nasal staphylococci isolated from many of these patients were compared with those recovered from their shunts and blood. Evidence is offered for the occasional coexistence of more than one strain of staphylococcus in colonized shunts and in the bloodstream. Successive recolonization of replaced shunts was apparently not necessarily caused by the same type of staphylococcus.

Nasal and skin micrococcaceae from many other babies, both in hospital and in parental care, from hospital staff and from adults selected at random from non-hospital sources, were similarly classified.

The validity and significance of the findings are discussed.

Ventriculo-atrial shunt procedures for the alleviation of hydrocephalus have been in use for a decade, and it is now generally recognized that bacterial colonization of the valve and catheters is a common and serious complication. A frequent accompaniment of such infection is a persistent bacteraemia. Occasionally coagulase-positive staphylococci or other organisms are responsible for a fulminating septicaemia, but by far the greater proportion of cases present as a chronic, indolent bacteraemia caused by coagulase-negative staphylococci.

Estimates of the incidence of generalized infection associated with colonized shunts vary from perhaps 6% (Carrington, 1959; Bruce, Lorber, Shedden, and Zachary, 1963) up to 20% (Matson, 1964) during the whole time that the shunt is in position; Eckstein and Cooper (1968) reported recently that 12% of patients in their series subsequently had bacteraemia. It is not always clear how much time had elapsed between the initial insertion of the shunt and the clinical recognition of bacteraemia; in some cases the valve had functioned successfully for several years before evidence of infection appeared (Perrin and McLaurin, 1967). There is, however, general agreement that intensive chemotherapy is unlikely to eradicate the infection as long as the colonized shunt remains within the body. The bacteraemia may be controlled by antibiotics, but it has repeatedly been found that such therapy almost invariably fails to sterilize the valve, although the bactericidal concentration *in vitro* of the antibiotic for the colonizing organism may be greatly exceeded in the cerebrospinal fluid. Early revision of the shunt, under the cover of adequate chemotherapy, appears to be obligatory and is usually carried out in this hospital on clinical evidence of bacteraemia combined with two or three positive blood cultures in close succession. The entire shunt system thus removed is subjected to bacteriological examination, each component being cultured separately. Whenever available, specimens of cerebrospinal fluid obtained by ventricular tap are similarly cultured.

Interest in the classification of the micrococcaceae (Gram-positive, catalase-positive cocci) isolated from clinical sources has been greatly stimulated by the reports published by Baird-Parker (1962, 1963, 1965), and following a wide survey of such organisms on various skin sites and in the anterior nares of babies, children, and adult staff in this hospital, it was decided to apply his classifying procedures to the coagulase-negative cocci recovered from the shunt, bloodstream, and, occasionally, the cerebra ventricles of hydrocephalic infants.

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CLINICAL MATERIAL AND METHODS

Specimens of venous blood were taken by aseptic technique and 2 to 3 ml was diluted in 40 ml glucose broth. After mixing, the bottles were incubated aerobically at 37° for 17 days. The broths were subcultured with extreme care on days 1, 2, 3, 10, and 17, two subcultures being made on to individual blood agar plates to minimize the risk of errors from casual plate contaminants.

Fluid aspirated from the ventricles was cultured directly on to blood agar plates and also diluted about 1 : 100 into large volumes of infusion broth subsequently incubated. This procedure serves to dilute antibiotics that may be present in the fluid, thus minimizing their inhibitory action. The broth culture was subcultured on to blood agar plates after one and two days.

Colonized shunts were sent to the laboratory immediately after removal; there they were dismantled under aseptic conditions and fluid was withdrawn from within the proximal and distal catheters and from the lumen of the valve. Cultures were made on to blood agar plates and into large volumes of infusion broth. The interior surfaces of the valve and catheters were examined by low-power magnification for evidence of micro-colonies being formed.

Skin cultures were taken from the patient by the pad technique (Holt, 1966), in most cases from the axilla and the interscapular region; the latter area was selected as one not readily accessible to oral, faecal, or manual contamination, and therefore likely to reveal the 'resident' flora (Price, 1938). A swab moistened in sterile broth was inserted into both anterior nares in turn.

Towards the end of the series reported below, a search for staphylococci in the faeces was begun; faeces were plated on to MacConkey agar (Oxoid) and inoculated into 7% salt broth; organisms were subcultured after incubation on to infusion agar plates.

As this investigation proceeded, the need to examine several discrete colonies from each primary culture plate was realized. Consequently 10 widely scattered colonies were selected, and each was subcultured on to infusion agar and subsequently examined more fully. If more than one colonial type was observed on any plate, representative colonies of each were subcultured. Such colonial differentiation was sometimes enhanced by the use of special media; 10% milk agar and MacConkey agar were particularly valuable for this purpose, the latter being used increasingly.

METHODS FOR IDENTIFYING STAPHYLOCOCCI AND MICROCOCCI

The classification of Gram-positive, catalase-positive cocci has long presented many difficulties. The position was considerably clarified by the proposal by Evans, Bradford, and Niven (1955) that the family Micrococcacae be divided into two genera, Staphylococcus and Micrococcus. The former should contain the mainly parasitic, facultative-anaerobic cocci producing acid from glucose under aerobic and anaerobic conditions; the genus Micrococcus should contain the mainly saprophytic cocci capable only of aerobic oxidation of glucose. This division has since been embodied in the Recommendations of the International Subcommittee on Staphylococci and Micrococci (1965). It is perhaps arguable on practical grounds that Sarcina, found frequently in skin cultures during the survey here, might be assigned to a third parallel genus, since it appears unable to hydrolyse glucose with acid end products.

SEPARATION OF MEMBERS OF THE GENUS STAPHYLOCOCCUS FROM MEMBERS OF THE GENUS MICROCOCCUS The methods and media used throughout this part of the investigation were those proposed by the International Subcommittee. Care was taken to deaerate the medium for the detection of anaerobic fermentation by heating it at 100°C for a few minutes immediately before use; it was inoculated as soon as it had cooled to 37°C. Small batches of eight to 10 cultures were inoculated at a time, to minimize the delay before sterile Vaseline was overlaid.

On the basis of six other tests, Baird-Parker (1963) was able to subdivide the genus Staphylococcus into six groups SI to SVI, and Micrococcus into seven groups M1 to M7. These tests are for coagulase, phosphatase, and acetoin production and the aerobic production of acid from mannitol, lactose, and 1-arabinose.

Coagulase production This was tested by the slide procedure (Cadness-Graves, Williams, Harper, and Miles, 1943) and organisms which gave equivocal results were examined again by incubation in plasma broth, the tubes being examined after two, four, and 18 hours' incubation at 37°C (Gillespie, 1943).

Phosphatase production This was first tested by the plate procedure reported by Barber and Kupfer (1951). Despite many attempts in these laboratories since 1951 to make the results of this test more decisive, some difficulty has always been experienced in differentiating between those organisms producing pale pink or deep pink on exposure to ammonia vapour. The use of a liquid medium was therefore tried and found to be much more decisive in result. One ml of infusion broth, adjusted to *p*H 7·5 and containing 0·01% phenolphthalein diphosphate, was inoculated fairly heavily with the organism under test, and incubated at 37°C for seven days. One drop of N NaOH was then added; the production of a deep mauve colour indicated a phosphatase-producing organism. Very few organisms produced a pale pink, equivocal colour. The test must be read within 20 to 30 seconds of the addition of alkali, since the bright colour fades irreversibly after this. A similar medium was tested and subsequently used routinely by Brown, Sandvik, Scherer, and Rose (1967). Baird-Parker (1966) recommends testing for phosphatase production at 30°C; at his suggestion, therefore, about 100 of these strains of cocci were retested in exactly the same way excepting that they were incubated at 30°C for seven days and no difference in results was noted.

Acetoin production This was tested in the way described by Baird-Parker (1963) but incubation was again at 37°C for three days; the presence of acetoin was demonstrated by Barritt's modification of the Voges-Proskauer test (Barritt, 1936).

The production of acid under aerobic conditions from carbohydrates was tested by growth in peptone water sugars for seven days at 37°C.

SUBDIVISION OF STAPHYLOCOCCUS GROUP II When the need for further subdivision of this group became apparent, a wide range of further characteristics was investigated. Ultimately it was decided that five further characteristics were sufficient to give adequate subdivision. These were the ability to produce acid aerobically from three hexoses—galactose, fructose, and mannose—hydrolysis of gelatin and urease production. The carbohydrate media were prepared by adding 10% of a 10% aqueous solution of the hexose, sterilized by membrane filtration, to sterile peptone water with indicator. A large volume of each medium was prepared at the same time, to ensure comparability of results throughout the investigation.

Gelatin hydrolysis was demonstrated by the charcoal gelatin disc method described by Kohn (1953). Infusion broth tubes were inoculated and the disc was introduced, followed by incubation for 14 days at 37°C.

Urease production was tested by growth in Maslen's liquid modification of Christensen's medium (Maslen, 1952) for seven days at 37°C.

The scheme revealed 15 patterns of characteristics among those staphylococci of group II tested.

Subdivision	*Galactose*	*Frı ctose*	*Mannose*	*Gelatin Hydrolysis*	*Urease*
IIA	+	+	+	+	+
IIB	+	+	+	+	0
IIC	+	+	+	0	+
IID	+	+	+	0	0
IIE	+	+	0	0	+
IIF	+	+	0	0	0
IIG	+	+	0	+	+
IIH	+	+	0	+	0
IIJ	+	c	+	+	+
IIK	+	0	0	0	+
IIL	+	0	0	0	0
IIM	0	0	0	+	+
IIN	0	0	0	0	+
IIP	0	+	+	0	+
IIQ	0	+	0	+	+

To ensure that this series of tests gave consistently reproducible results, cultures of IIA, IIB, IIC, and IIE were tested again at weekly intervals for seven weeks; the same results for fermentation and hydrolysis were found throughout.

Individual colonies of several of these subtypes were plated out on nutrient agar, and several colonies from each plate were subsequently retested to detect any variation of the five characteristics on subculture; in no case was there any such change.

Staphylococci isolated from the skin, nose, blood, and a colonized valve of 12 patients were kindly examined by Professor R. E. O. Williams, using a set of phages active on coagulase-negative staphylococci.

RESULTS

QUEEN MARY'S HOSPITAL, CARSHALTON In this hospital, approximately 100 ventriculo-atrial shunts have been inserted annually for the past three to four years. During the period January 1967 to June 1968, 17 children showed clinical evidence of indolent bacteraemia and some of deficient shunt performance. Each child had repeatedly positive blood cultures accompanied by colonized Spitz-Holter shunts. Coagulase-negative, catalase-positive, Gram-positive cocci were cultured from both sites in each of these cases; on complete classification the following results were obtained.

No. of Cases	*Subgroup and Type of Organism Isolated from*	
	Blood	*Valve*
5	Staphylococcus IIA	SIIA
1	IIB	IIB
2	IIE	IIE
1	IIE	IIE and IIC
3	IIG	IIG
1	IIH	IIH
2	IIJ	IIJ
1	IIM	IIM
1	IIM	IIF

Two other infants had repeatedly positive blood cultures, but the valves on removal and culture proved to be sterile. Staphylococcus IID was recovered from the blood of one and Micrococcus M5 from the other.

OTHER HOSPITALS IN BRITAIN Through the kindness of laboratory staff at other hospitals dealing with similar cases, strains of cocci recovered from the blood, valve, or ventricles of children with infected shunts were classified.

CLASSIFICATION OF ORGANISMS FROM OTHER BODY SITES

Cultures were taken from the skin surface and anterior nares of the last 10 of the children with colonized valves investigated in this hospital.

In each case the subtype or subtypes found in the blood and colonized shunt were also found in heavy, often predominant, numbers on at least one site examined. In all 10 children the subtype was present in the nose, often accompanied by other members of the genera Staphylococci and Micrococci. In six of the cases, the subtype was present in the inter-scapular region. Cultures from the axilla of six also revealed the presence of the same subtype as that in the bloodstream and shunt.

Following a suggestion by Dr M. T. Parker, the faeces of the last child of this series were examined, resulting in the recovery of a Staphylococcus of the same subtype (SIID) as that in the bloodstream.

MIXED INFECTIONS

The possibility of more than one subtype of Staphy-

TABLE I

CLASSIFICATION OF ORGANISMS FROM INFECTED SHUNTS IN CASES FROM OTHER HOSPITALS IN BRITAIN

No. of Cases	*Subgroup and Type of Organism Isolated from*		
	Blood	*Shunt*	*Ventricular Cerebrospinal Fluid*
Hospital A			
1	Staphylococcus IIC	SIIA & SIIC	
1	IIC	SIIC	
1	IIC	IIC & IIF	
1	IIA & IIC	IIA	
1	IIP	IIP	
1	IIC & IID	IIC	SIIC
Hospital B			
1		IIE	
1		IIL	
1		M.6	
Hospital C			
1	IIH	IIH	IIH
Hospital D			
1		IIA	
1			IIA
Hospital E			
1	IIC	IIC	

lococcus, group II, being present in the bloodstream or shunt at the same time was realized when subtypes SIIA and SIIC were found in cultures received from hospital A; the predominant strain in this culture was SIIC, the only strain found in blood cultured three days before removal and examination of the shunt. Careful examination of the primary culture plate revealed two colonial types, although the difference was not very obvious and was only apparent after several days' incubation. This finding seemed so significant that henceforward 10 individual colonies from each plate were fully examined, with the result that two other shunt cultures were found to be mixed, as were two blood cultures. On no occasion were both blood and shunt found to contain mixed subtypes at the same time. It was possible to examine skin and nasal cultures from only one of the children showing mixed cultures in a shunt. This was a Carshalton child with SIIE in his blood and SIIE and SIIC in the shunt removed six days after the blood culture. The axilla culture revealed only SIIE but that both SIIC and SIIE were present in the nose and interscapular skin cultures.

SUCCESSIVE SHUNT INFECTIONS

One child (Carshalton) had three shunts in succession colonized and changed within a period of seven weeks. The detailed history of this child (P.W., born 4 May 1967), in whom a Spitz-Holter shunt was first inserted on 11 May 1967, is as set out in Table II.

A second child (hospital A) had one subtype (SIIC) in a colonized valve; 13 days after revision a blood culture again revealed one subtype (SIIC only), but the valve, revised three days later (16 days after the earlier revision) then contained subtypes SIIA and SIIC.

A third child (hospital A) had SIIC in his blood culture; the shunt, removed some 10 days later, also yielded subtype SIIC alone; a week after revision

TABLE II

SOURCES AND RESULTS OF CULTURES FROM ONE CASE

Date	*Source of Culture*	*Result of Culture*
24.11.67	Blood	SIIJ only
26.11.67	Blood	SIIJ only
27.11.67	Blood	SIIJ only
30.11.67	Shunt revised, old valve contained	SIIJ only
4.12.67		Sterile
19.12.67	Blood	Sterile
20.12.67		Sterile
22.12.67	Blood	SIIE only
24.12.67		SIIE
23.12.67	Nose and interscapular cultures	SIIE (negative for SIIJ)
4.1.68	Shunt revised, old valve contained	SIIE only
12.1.68		SIIE only
15.1.68	Blood	SIIE only
16.1.68		SIIE only
18.1.68	Shunt revised, old valve contained	SIIE only
22.1.68	Blood	Sterile
5.2.68	Child died, valve removed at necropsy	Overgrown with proteus, no staphylococci isolated

the blood culture again grew only SIIC, but the shunt, again revised 14 days later, gave two subtypes, SIIC and SIIF, in approximately equal proportions.

The cultures from hospital C showed that this patient had SIIH in the shunt and ventricular fluid, followed eight and 10 days later by positive blood cultures also containing SIIH alone. Fluid aspirated from the valve 20 days later then showed an apparently pure growth of SIIE.

The results of these investigations had clearly to be viewed against a background of information on the skin and nasal flora of other children, both in this hospital and in parental care; the last category was selected on a random basis. Skin cultures from hospital staff and from adults outside this hospital were also examined. The results from these additional surveys are presented in Tables III, IV, and V.

DISCUSSION

The ability of some coagulase-negative members of the family Micrococcaceae to behave as opportunist pathogens has long been recognized (Cunliffe, Gillam, and Williams, 1943; Smith, Beals, Kingsbury, and Hasenclever, 1958; Quinn, Cox, and Fisher, 1965, and many others); such pathogenic activity is nearly always relatively feeble and associated with preexisting tissue damage, as in bacterial endocarditis, or where a foreign body has been deliberately implanted. In recent years the increasing use of ventriculo-venous shunts has offered a situation *in vivo* apparently well suited to colonization by these bacteria, almost always accompanied by indolent bacteraemia. The application of Baird-Parker's

TABLE V

50 SUCCESSIVE ISOLATES SUBTYPES OF SII TYPES FROM DIFFERENT BABIES IN FIRST TWO CATEGORIES OF TABLE III

Subtype	*No. Isolated*
A	12
B	5
C	9
D	5
E	8
F	0
G	0
H	2
J	3
K	0
L	1
M	2
N	1
P	2
Q	0

TABLE III

DISTRIBUTION OF SKIN MICROCOCCACEAE IN GROUPS OF INDIVIDUALS

No. of Patients Tested	*Site*	*No. of Strains Isolated and Classified*													
		SI	*SII*	*SIII*	*SIV*	*SV*	*SVI*	*M1*	*M2*	*M3*	*M4*	*M5*	*M6*	*M7*	*Unclassified*
Babies (0-12 months) in the same paediatric ward[1]															
	Axilla	0	17	2	2	3	0	1	0	0	0	1	0	1	0
19	Interscapular	0	23	0	1	3	0	0	2	0	0	0	0	0	0
	Nose	0	18	1	0	0	0	0	0	0	0	1	0	2	0
Babies (0-12 months) in other wards[2]															
50	Nose	6	61	4	7	11	8	0	0	0	0	3	6	5	4
17	Interscapular	1	39	2	1	10	5	0	1	0	0	0	2	0	1
Babies (0-12 months) in private households															
10	Axilla	0	5	2	3	5	2	0	1	0	0	1	2	3	2
	Interscapular	0	6	1	1	3	1	0	1	0	1	2	1	5	5
	Nose	0	5	0	1	0	0	0	0	0	0	0	1	1	1
Skin cultures from hospital staff[3]															
66		8	77	6	22	32	17	7	4	2	3	6	1	10	11

[1]These children had hydrocephalus and meningomyelocele, but showed no evidence of bacteraemia or colonized shunts. Cultures were made from various body sites.
[2]Children had no obvious skin infections.
[3]Either the upper arm or the interscapular region was cultured.

TABLE IV

COLLECTED RESULTS

No. of Strains Isolated and Classified													
SI	*SII*	*SIII*	*SIV*	*SV*	*SVI*	*M1*	*M2*	*M3*	*M4*	*M5*	*M6*	*M7*	*Unclassified*
701 isolates classified from all sources within the hospital													
45	354 (49%)	18	40	89	50	10	10	4	4	19	12	27	19
371 isolates from children and adults outside the hospital selected at random													
19	68 (18%)	26	15	54	33	6	13	12	7	29	14	37	38

classifying procedure, now well accepted, to organisms responsible for this low-grade yet extremely troublesome infection has revealed that almost without exception they belong to one group within the genus Staphylococcus. Since 1960 this hospital has seen only two cases where other organisms were responsible for the indolent colonization of shunts. In one case an enterococcus was responsible; *Candida albicans* was recovered from the revised shunt and the bloodstream in a second child (private communication, R. Hare).

Mitchell (1968) found Baird-Parker's group SII very frequently in urinary infection caused by coagulase-negative staphylococci, although he also reported that many infecting strains belonged to the group M3. Quinn *et al* (1965) noted that strains of coagulase-negative staphylococci isolated from cases with subacute and postcardiotomy endocarditis belonged to Staphylococcus subgroups II, III, IV, and V; they gave no indication of the relative proportions of each subgroup.

The marked dominance of Staphylococcus subgroup II in the investigation reported here is striking and suggests that the subgroup, although of mild pathogenicity even in debilitated babies, may have considerable invasive and survival powers. It is apparent that this subgroup is very common in the noses and on the skin of patients and staff in this hospital. Eighteen of 19 babies in the paediatric ward showed nasal carriage of one or more strains of SII, and almost every child had a strain of SII somewhere on its body.

The prevalence of this group in babies, children, and adults living in normal domestic surroundings was far less pronounced. It was still the most common group among babies and children at home, but represented only 25% of strains of micrococcaceae isolated from these sources. In adults other than hospital staff SII was slightly less common, being about 18% of all strains examined, followed by 14% of group SV.

The validity of the subtyping procedure within group SII is more open to question, and depends primarily on the constancy and stability of the biochemical characteristics used for differentiation. The three hexose solutions are notoriously unstable when heated, and for this reason were sterilized by cold filtration; every other technical precaution was taken to ensure standardization of procedure and, therefore, reproducibility of the result. Where subtypes differ by two or more of the five suggested criteria, this was accepted as reasonable evidence of biotype differentiation. Difference by only one characteristic was carefully rechecked; in many cases subtle colonial differences were apparent after three to four days' incubation, especially if the organism was lightly plated on MacConkey agar. Confirmation by an entirely different method, that of phage typing, was sought, and preliminary results are reported by Professor R. E. O. Williams in an addendum to this paper.

The value of evidence for the coexistence of more than one subtype in the bloodstream or shunt depends heavily upon the freedom of the collection and cultural procedures from any risk of contamination; this may be from the skin of the patient or from the manipulators. Since hospital patients and staff carry a high percentage of SII types, the risk of misinterpretation is high, although repetition of the result renders such mistakes less likely. It is noteworthy that in all cases where two types were found to coexist both were members of SII; contaminants might reasonably have been expected to be, on occasion at least, members of other groups of staphylococci and micrococci. The main safeguard, however, has been that the collection and handling of blood, fluid, and excised shunts was invariably in the hands of highly trained and experienced staff, fully aware of the misleading results which would follow from casual contamination, and with numerous sterile blood cultures to their credit. An entirely different reason for the existence of two types could conceivably be that one type had mutated or adapted to different metabolic activity after considerable time *in vivo* and under stress of continued antibiotic attack.

If the subtyping procedure is accepted, it is possible to offer tentative answers to some questions of interest. Successive recolonization of revised shunts may not be caused by the same type. It is possible that on some occasions two subtypes may colonize the shunt simultaneously. This could lead to misinterpretation of antibiotic sensitivity tests which, unless carried out individually on a selection of colonies, could give conflicting results. This in fact may furnish a reason for the inexplicable results obtained in some cases (Callaghan, Cohen, and Stewart, 1961). It may also be significant that strains of coagulase-negative staphylococci which are apparently fully sensitive by disc tests to benzylpenicillin are nevertheless capable of weak β-lactamase production (Holt, 1968). Where a long-term, indolent infection is involved, this property may assume practical importance, because in time these strains might be induced to strong β-lactamase production by continued therapy with penicillin derivatives.

No definite answers seem possible at present to several questions of more importance. (1) What is the origin of the colonizing strain, and by what route does it reach the valve? (2) How does it succeed in colonizing the valve, sometimes despite

the presence of excess of antibiotics to which it is sensitive? and, most momentous of all, (3) How may this colonization be prevented?

It has been suggested (Schimke, Black, Mark, and Swartz, 1961) that the colonization may originate from the introduction of bacteria at the time of surgery. While this may be true on many occasions, it is difficult to credit this cause when clinical and bacteriological signs of shunt colonization and bacteraemia first become apparent after many months or years of successful function. In some of the cases in this hospital there has been no evidence of colonization for over three years after the initial insertion. Perrin and McLaurin (1967) report that the established shunt infections in their six patients occurred between 20 and 82 months after insertion. If the idea of such prolonged inactivity in the shunt, followed eventually by a burst of growth, be postulated, this might perhaps be explained by the persistence of the original bacterium as an 'L' form; this change could be promoted by the antibiotics used as a cover when the shunt was originally inserted. Very little is known about the behaviour *in vivo* of L forms of coagulase-negative staphylococci. Their insensitivity to penicillin derivatives may furnish an explanation for the repeated failure of this form of prophylaxis. The same would apply to any other antibacterial drug which acts by inhibiting bacterial cell wall synthesis.

Nulsen and Becker (1966) have suggested that a low distal shunt catheter may damage the tricuspid valve, promoting the formation of thrombi, sometimes septic; the consequent bacteraemia might thus be mediated in much the same way as in subacute endocarditis. Bacteria from the bloodstream might then ascend the catheter to the valve chamber and even to the ventricles. The relative rarity, in our experience at least, of shunt colonization by green streptococci and other bacteria of low pathogenicity might be held to weigh against this hypothesis.

The presence of organisms of subgroup SII on the skin of many children with this syndrome can be quoted in support of either of the theories outlined above. The colonizing strain would be prevalent and might have ready access to the shunt at the time of surgery; however, the absence from this series of examples of colonization by diphtheroids is significant. On the other hand, if the theory of bacteraemia before colonization of the shunt is accepted, the colonizing staphylococcus would be continuously available to promote transient bacteraemia at any time; in some way not yet understood, the transient bacteraemia proceeds to establish a persistent, symptomatic infection when foreign body prostheses disturb the normal host-parasite relationship. The residence of these strains in the intestinal tract and nasopharynx may facilitate transient bacteraemia, although in this event faecal and oral bacteria should feature more commonly as organisms responsible for shunt colonization.

It would clearly be of considerable interest to classify micrococcaceae responsible for low-grade septicaemia associated with other types of prostheses implanted more or less permanently in patients of all age groups, and to investigate the skin and nasal flora of those patients by similar means. With the rapidly increasing use of internal devices of this kind, this fascinating problem will undoubtedly grow; the eventual solution will reveal much new evidence about the mechanisms of body defence.

ADDENDUM

A selection of the strains from 12 patients was examined by Professor R. E. O. Williams and Miss Jean Corse at St. Mary's Hospital Medical School with a set of 32 experimental typing phages isolated by them and by Professor K. C. Winkler, Mr J. Verhoef, and Dr C. P. A. van Boven in Utrecht.

From three of the patients all the strains were of one biotype; all showed a similar phage pattern in one case, all were untypable in one, but two distinct phage 'types' were observed in the third.

The remaining nine patients had yielded strains of two biotypes. With one of these patients all the strains had the same phage pattern, and with two all were untypable; in the rest the strains of each biotype were distinguishable by their reactions, or lack of reaction, to the phages. These results will be reported in more detail later.

R. E. O. WILLIAMS

Part of the investigation described here was undertaken during the preparation of a thesis, yet to be presented, for a higher degree of the Council for National Academic Awards.

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