Surface ultrastructure of silicone rubber aortic valve poppets after long-term implantation

A scanning electron microscope study of four poppets

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Allwork, Sally P. and Norton, R. (1976). Thorax, 31, 742–752. Surface ultrastructure of silicone rubber aortic valve poppets after long-term implantation. A scanning electron microscope study of four poppets. The surface ultrastructure, demonstrated by scanning electron microscopy, is described in four implanted Silastic aortic valve poppets. Ball variance was discovered at necropsy in two patients and clinically in one in whom the poppet was replaced. The fourth patient underwent reoperation, but ball variance was neither suspected nor found. All four poppets were densely coated with biological debris and microthrombi. The 'coat' was soluble in a weak solution of sodium hydroxide. The true Silastic surface beneath the coat was little altered compared with unimplanted poppets, even after 10 years' implantation.

Although valve prostheses with Silastic poppets are implanted less often than in previous years, they are still used, and patients with Silastic poppets occasionally require a replacement of the poppet. This event in one of the patients considered here stimulated the present study.

Despite meticulous attention to anticoagulant control, thromboembolic episodes have frequently been reported in patients with various models of both Starr-Edwards and Magovern aortic valve prostheses (Friedli *et al.*, 1971; Reed *et al.*, 1971; Cleland and Molloy, 1973). Ball variance, due to absorption of plasma proteins and lipids into the Silastic poppet, and increased platelet adhesiveness have been implicated in peripheral embolic complications (Krosnick, 1965; Laforet, 1967; McHenry *et al.*, 1970; Myhre *et al.*, 1971). The radiological, phonocardiographic, and gross macroscopic appearances of variant poppets are well recognized (Hysten *et al.*, 1968; Hysten *et al.*, 1969), but we are aware of only one other report of the surface ultrastructure of Silastic poppets after clinical implantation (Rodman, Dity, and Caughey, 1974). We studied the poppets recovered from four patients and compared the appearances with those of unimplanted Silastic poppets.

MATERIAL

The clinical data of the four patients are summarized in the Table. The poppets were recovered

from cases 1 and 2 at necropsy and from cases 3 and 4 at reoperation. Case 1 died of his second major cerebrovascular accident, and case 2 was found dead after a street brawl. Ball variance had not been suspected in either patient during life but was evident at necropsy. Case 3 underwent a change of prosthesis for ball variance four and a half years after his original valve replacement, and case 4, although ball variance was neither suspected nor found, was reoperated upon after two cerebral embolic episodes 10 years after the original operation. Cases 1 and 4 had their original operation for congenital aortic valve stenosis, and cases 2 and 3 had had acquired valve disease.

METHODS

The two necropsy specimens had been fixed and stored in formalin for a number of years, and the two surgical specimens had been washed in distilled water, allowed to dry, and stored dry thereafter.

Small slices were cut from macroscopically 'good' and 'bad' areas of each of the four test poppets, and at random from poppets taken from unused Starr-Edwards and Magovern prostheses. These slices were mounted on specimen stubs with double-sided adhesive tape, then coated *in vacuo* with gold, gold-palladium or carbon. The slices

T A B L E
CLINICAL DATA OF THE FOUR PATIENTS

Case	Sex	Age at Operation	Operation for	Prosthesis	Clinical Ball Variance	Reoperation	Postop. Anticoag.	Postop. Course	Outcome
1	M	55	Congenital AS	S-E 1000	0	0	+	CVA 1971	Died 1973
2	M	23	Rheumatic AR	Magovern	0	0	+	Uneventful	Died 1970
3	M	35	AR due to IE	S-E 1000	+	S-E 1260 1968	+	CVA 1970	A/W 1976
4	F	40	Congenital AS	S-E 1000	0	S-E poppet 1975	+	?CVA 1969 and 1975	A/W 1976

AR=aortic valve regurgitation; AS=aortic valve stenosis; IE=infective endocarditis; S-E=Starr-Edwards valve; CVA=cerebrovascular accident; A/W=alive and well; M=male; F=female.

FIG. 1a. Seam area of an unimplanted radioopaque Starr-Edwards poppet ($\times 700$). Particles of dust cover the surface.

FIG. 1b. Unimplanted transradiant Starr-Edwards poppet ($\times 740$). The surface shows some microscopic dust.

FIG. 1c. Unimplanted Magovern poppet ($\times 750$). The surface is essentially similar in appearance to 1a and 1b.

were examined in a Cambridge Stereoscan electron microscope at an accelerating voltage of 20.8 kV. The angle of tilt varied between 30° and 60° but was usually about 45°.

Further slices were cut from each specimen and the control (unused) poppets and cleansed of biological debris by immersion and intermittent agitation in several changes of 2% sodium hy-

FIG. 1b.

FIG. 1c.

FIG. 2a. Case 1. 'Good' area of untreated poppet (see text). The micrograph ($\times 675$) shows a 'coat' of debris. A microthrombus and an erythrocyte are seen in the centre.

FIG. 2b. Similar area from case 2 ($\times 640$). The coat is cracked and features structures which may resemble erythrocytes, but comparison with 2a confirms that they are not.

FIG. 2c. Case 3 ($\times 660$). The micrograph shows an irregularly cracked coat together with some debris.

FIG. 2d. The poppet from case 4 ($\times 700$). The upper border of the micrograph shows a 'coat', and the lower part contains some debris. This was the only patient in the series who did not exhibit 'ball-variance'.

dioxide over a period of two or three days, then washed in deionized water, and immersed for a short period in 2% hydrochloric acid. The slices were then rinsed in several changes of deionized

water and allowed to dry. They were then mounted and coated in exactly the same way as the untreated samples.

FIG. 3. Case 3 ($\times 650$). Micrograph of a macroscopically 'bad' area (see text). The Silastic surface is pitted and irregular, and microthrombi abound.

RESULTS

UNTREATED SPECIMENS Figure 1 shows micrographs of untreated samples of (a) an unimplanted radiolucent poppet, (b) an unimplanted radioopaque poppet, and (c) an unimplanted Magovern poppet. All the samples show minor surface irregularities, fine cracks and pits, and dust. The two Starr-Edwards poppets were taken from stock, ie, ready for clinical use, while the Magovern valve had been a demonstration model.

Figure 2 shows comparable magnifications of macroscopically good areas of untreated samples of the poppet from each of the four patients. The micrographs all show biological debris consisting of platelets, both singly and in clumps, erythrocytes, and occasionally fibrin. The debris appears as a relatively dense but incomplete 'coat' over the surface. Figures 2b and c show a regular pattern of cracks in the coat in cases 2 and 3, and Fig. 3 is an uncoated area in the same sample of case 3, which shows pits in the Silastic surface as well as debris. Figure 4a is a very low-power micrograph of two patches of fibrin in the coat of a sample from patient 3. Figure 4b shows the fibrin at higher magnification. Figure 5a is a low-power view of a groove worn by the cage in patient 1, and Fig. 5b shows the floor of the groove. Figures 6a–d are micrographs of macroscopically bad areas of the untreated poppets. These specimens were selected for cracks, ridges,

and grooves worn by the cage. In these specimens the surface coating shows aggregates of debris, and in Fig. 6a a number of blood cells are trapped in the ridges worn by the cage.

TREATED SPECIMENS Figures 7a–c show the surface of unused poppets after treatment in sodium hydroxide and hydrochloric acid. Compared with

FIG. 4a. Case 3. Macroscopically 'good' area ($\times 35$). The surface is very irregular, and two patches of fibrin are associated with the surface cracks.

FIG. 4b. The fibrin patch in the background of 4a ($\times 360$).

FIG. 5a. Case 1. An edge of a groove in the Silastic poppet caused by the cage of the valve ($\times 640$). The surface is worn into ridges, and erythrocytes, leucocytes (arrowed), and platelets adhere to the ridges.

FIG. 5b. The floor of the groove illustrated in 5a ($\times 640$). The Silastic surface is obscured by the coat which is worn into peaks and folds.

the untreated group these micrographs are relatively featureless, but small cracks and surface irregularities are to be seen in each specimen.

Figures 8a-e are micrographs from both good and bad areas of the implanted poppets after treatment. The coat is largely abolished but remains in a few areas. The surface structures in Fig. 8c resemble erythrocytes but are very much larger and are seen in uncoated areas (compare with Figs 2a and 6a). A similar appearance was noted in patient 2, also in an uncoated region. Figure 9 shows a somewhat rippled surface from a good area of the poppet after complete removal of the coat, together with some crater-like structures, similar to those in Figures 8c and d.

DISCUSSION

The present study was stimulated by the second operation on patient 4. The Starr-Edwards valve poppet was removed after 10 years, looking macroscopically similar to its new replacement except for a slight yellow discolouration. The first micrographs of this poppet showed a dense coat of biological debris when compared with micrographs of an unused poppet. As the surface was viewed from above, measurement of the thickness of the coat was not possible. We considered it necessary to remove the coat to reveal the Silastic surface of the poppet so that a true comparison could be made. The other three specimens were drawn from the files and, as has been illustrated, a similar coat was observed in them all, irrespective of how they had been obtained or stored, or whether clinical ball variance was present or absent. It appears, therefore, that the coat is neither a cause nor an effect of ball variance.

The appearance of the coat was relatively constant in all four poppets despite considerable variations in the time they had been implanted (Table) so that it is not really possible to assess the time of its initiation. The studies of Sawyer *et al.* (1974) in cattle indicate that coating is established within a year of placement of the valve. However, as their study compared several types of prosthesis over variable periods of time, it cannot with certainty be deduced that the coat 'grows' by accretion of debris as time passes.

The coat of debris on the poppets was quite difficult to remove, and, as Fig. 8a shows, it was not entirely abolished by the procedure used in the authors' department for removing blood from silicone rubber products. Sawyer *et al.* (1974) described and illustrated coats on both Silastic and metal poppets which appear to be identical

FIG. 6a. Case 1. Macroscopically 'bad' area, untreated. Rim of the groove worn by the cage ($\times 620$). The surface is rippled and partly coated. A few erythrocytes are scattered about the surface.

FIG. 6b. Case 2. Macroscopically 'bad' area ($\times 625$). The surface has been gouged out by the cage, and the coat is rippled.

FIG. 6c. Comparable area in case 3 ($\times 360$). The Silastic surface is coated with debris. There are scattered microthrombi.

FIG. 6d. Case 4 ($\times 880$). A small area of uncoated Silastic is seen to the left of the micrograph. The coat is irregular and 'shaggy', and an erythrocyte is trapped in the centre of the field.

FIG. 7a. Unimplanted radioopaque Starr-Edwards poppet ($\times 15$) after chemical cleaning (see text). The diagonal ridge is the seam uniting the two halves of the poppet.

FIG. 7c. Low-power micrograph ($\times 170$) of unimplanted Magovern poppet. There are small cracks on the surface and some dust.

FIG. 7b. Enlarged detail of seam area ($\times 380$). There are some small irregularities in the surface and a few dust particles.

FIG. 8a. Case 1. Cleaned surface of the poppet ($\times 745$). The Silastic surface is irregular, and a few platelets are still adherent to it.

with those described here. Rodman *et al.* (1974), in their description of a Braunwald-Cutter mitral prosthesis recovered after 14 months, illustrated platelets both singly and in clumps on the poppet surface but did not describe a coat. The absence of a coat of debris in the poppet described by

Rodman *et al.* (1974) may reflect a difference in reaction to prosthetic material between cattle and man, as Sawyer *et al.* (1974) also placed their prostheses in the atrioventricular position, albeit the tricuspid as opposed to the mitral location of the Braunwald-Cutter valve.

FIG. 8b. Case 2. Cleaned surface ($\times 745$). The silicone surface is essentially similar in appearance to 8a.

FIG. 8d. One of the craters in 8c ($\times 1700$).

FIG. 8c. Case 3. Cleaned surface of a macroscopically 'good' area ($\times 465$). The crater-like structures on the surface resemble erythrocytes. Comparison with Fig. 2a confirms that they are not, but appear to be pushing the surface from below, rather than resting upon it. This feature was observed in all three patients with ball-variance.

FIG. 8e. Case 4. Cleaned area of the non-variant poppet ($\times 390$). The surface is very little altered from that of an unimplanted poppet.

FIG. 9. Case 2. Cleaned area of the Magovern poppet ($\times 155$). The surface has a slightly 'rippled' appearance, and some 'craters' similar to those in Figs 8c and d are present.

Comparison of the true surfaces of the poppet shows that they alter but little during long periods of implantation. The microscopic cracks seen in new poppets seem neither to enlarge particularly nor to be related to the formation of the coat. Our findings confirm those of other investigators (Rodman *et al.*, 1974; Sawyer *et al.*, 1974) that even new poppets have some surface irregularities, in addition to a variable amount of surface dust. Sawyer *et al.* (1974) found that this surface dust was increased after steam sterilization.

As the cracks do not contain platelets or debris, they do not seem, despite their dramatic appearance, to be associated with the formation of the coat. They may, however, be a route whereby lipid can enter the poppet in susceptible persons. When the variant poppet from patient 3 was transected, droplets were seen on the cut surface, and these contained plasma lipids (Dr. B. Lewis, personal communication). The other three poppets were not cut at the time of removal. More than 50 000 silicone rubber poppets had been distributed up to 1970 (Hysten *et al.*, 1970) and ball variance is a relatively uncommon complication, particularly in the later models of the valves (Behrendt and Austen, 1973), due probably to alteration in the curing time of the silicone rubber during manufacture (Hysten, Hodam, and Kloster, 1972).

Ridolfi and Hutchins (1974) described dissemination of poppet material, especially in the liver, in three patients who had died with ball variance. Disseminated Silastic is observed only in the presence of ball variance (Hameed, Ashfaq, and Waugh, 1968; Kloth and Spagnuolo, 1972). The craters containing fibrin (Figs 4a and b) in a variant poppet suggest a source of poppet emboli. Similar craters were also seen in case 1 in the present series but not in case 2 (Magovern valve) nor in case 4, who did not have ball variance. Information about Silastic material in other organs is not available for our two dead patients, but it seems reasonable to speculate that fragments of the poppet might well have been present in their livers.

Although fragments of poppet material may embolize in patients with ball variance, a far commoner cause of embolism in persons with prosthetic valves is an alteration of the coagulation mechanism, due to enhanced platelet adhesiveness (Myhre *et al.*, 1971), associated with a degree of haemolysis (Dale, Myhre, and Rootwelt, 1975). The findings of these authors respectively are supported by the work of Rodman *et al.* (1974) and the present study.

The majority of the cells in the micrographs illustrating this communication show the morphological characteristics of platelets, although Figs 5a and 6a also show both leucocytes and erythrocytes. The platelets vary quite considerably in size. This observation was also made by Rodman *et al.* (1974) and is well illustrated by Sawyer *et al.* (1974).

Normally platelets range in size from 1 μm to 3 μm . They are larger when they are 'activated' than during the resting or inactive phase (Rodman *et al.*, 1974). As platelet function in patients with prosthetic valves is often deranged (Myhre *et al.*, 1971), the finding of both large and small cells is not surprising. Haemolysis is commonly found in patients with prosthetic valves (Myhre, Dale, and Rasmussen, 1970), and the agent which stimulates platelets to aggregate, adenosine diphosphate, is released during haemolysis (Dale *et al.*, 1975). Our case 3 demonstrated considerable haemolysis before his valve was changed.

(All the patients in the present series underwent their first operation before the introduction of dipyridamole (Persantin) to modify platelet function. The two reoperated patients now receive this preparation in their drug regime.)

The present findings, far from indicating that the coat on the poppets is a storage or preparation artefact, support the view that the deposition of

FIG. 10. Case 3. Microthrombus on the uncleaned surface of the poppet ($\times 640$). Several similar microthrombi were observed in this specimen.

debris on the poppet is a phenomenon which should be anticipated. Blood cells interact rapidly with injured vascular surfaces and with prosthetic surfaces. Variations in electrical potential between different parts of a prosthetic surface may occur when that surface is contaminated by dust, oil or even glove powder, and such potential differences are sufficient to cause platelet aggregation (Sawyer *et al.*, 1974).

Arterial emboli are characteristically composed of fibrin strands and platelets (Mustard and Packham, 1970; Jørgensen *et al.*, 1967). Fibrin was identified in two samples (Figs 4a and b) but the shaggy coats in Figs 5b and 6d are probably fibrin, at least in part. The microthrombi on the poppet surface thus contain the matrix of arterial emboli (Fig. 10). The mechanism whereby fibrin strands attach even to smooth Silastic is obscure, but their presence has been demonstrated *in vivo* and *in vitro* (Sawyer *et al.*, 1974).

Thus it appears from the observations of ourselves and others (Rodman *et al.*, 1974; Sawyer *et al.*, 1974) that platelet aggregates are commonly found on Silastic surfaces exposed to the bloodstream. We have not had the opportunity to examine poppets from patients who have received drugs which inhibit platelet aggregation, but a comparison of the two may be helpful in assessing the role of these drugs in patients with Silastic poppets.

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