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THE EFFECT OF AN ANTIMICROBIAL COATING ON METAL IMPLANTS

A Pilot Study in Goats

By

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Reconstructive surgery in which implants are used is an ever widening sphere in which the techniques demand highly integrated team work with considerable emphasis on the prevention of wound infection. It is well recognised that factors influencing sepsis are increasing age of the patient, the presence of a foreign body, the exposure of tissues for long periods of time, and the inability to use 'no touch' techniques. These factors operate when complicated procedures involving massive prosthetic replacements are undertaken. Implants separate the tissues and many of the prostheses used have cavities where bacteria can proliferate remote from attack via the blood stream.

There is a divergence of opinion concerning the value of locally applied antibacterial agents, especially when used in the presence of metal implants. No assessment of the use of these agents could be found in the literature. This investigation was undertaken to try and establish the value of a known bactericidal agent when carried in a vehicle with which implants could be coated. To be effective the agent should be slowly released at the site. Infection was deliberately introduced at the time of operation in the goats, which were the animals used in this pilot study.

Polyvinyl alcohol was chosen as the most suitable vehicle for the following reasons:

- (1) It is relatively inert in the body and has been used in the various forms in surgical procedures in both laboratory animals and man since 1951.

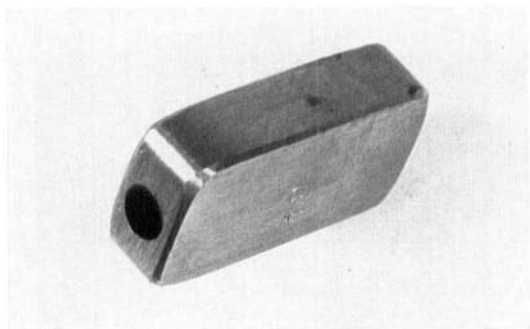


Figure 1.
Cobalt-chrome alloy implant.

- (2) It does not react with any of the known antimicrobial agents.
- (3) It can be sterilised by autoclaving.
- (4) It has flow characteristics such that it will penetrate small cavities and dries leaving a non-tacky intact continuous coating on the surface of the component.
- (5) The dry, sterilised film is firmly adherent to the metal and does not flake or peel. It is strong enough to withstand the manipulations of surgical implantation.
- (6) It is not absorbed from the metal surface, even after five months' implantation.

It was used as an aqueous solution of solvent for the stable di-isothionate salt of dibromopropamide (D. B. P. A.). D. B. P. A. has been shown to have a marked inhibitory action towards pyogenic cocci, but in strengths of 1.5 per cent it had some toxicity towards leucocytes (1-5).

Laboratory tests showed that 0.1 per cent D. B. P. A. in PVA dried as a film on test implants of cobalt-chrome alloy¹ exhibited a marked inhibitory action towards *staphylococcus pyogenes*. This action was retained for three to four days as shown by successive transplants of the metal on freshly inoculated plates. Autoclaving for a second time after two weeks did not appreciably diminish the activity of the D. B. P. A., and after six days in goat plasma at 37° C the coated implant still showed a minimal zone of inhibition (see Figures 1, 2 and 3).

¹ Composition of the alloy conformed with that specified in B.S.3531:1962 for cast cobalt-chrome alloy.

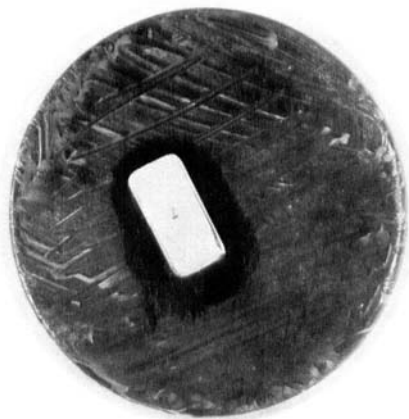


Figure 2. To show effect of alloy coated with 0.1 per cent D.B.P.A. in PVA on *G.17 staphylococcus*.



Figure 3. To show inhibitory zone after 4th transfer of coated implant

METHODS AND MATERIALS

Experimental Plan

Twelve drilled blocks of cobalt-chrome alloy were inserted in the paravertebral muscles of each of six month-old Saanen goats. The metal implants were classified into the following groups:—

- (1) Metal alone, with and without *G.17 staphylococcus*.
- (2) Metal coated with PVA without *G.17 staphylococcus*.
- (3) Metal coated with PVA and 0.1 per cent D. B.P.A., with and without test doses varying from 10–1 million organisms of *G.17 staphylococcus*.
- (4) Metal coated with PVA and 1.0 per cent D.B.P.A., with and without test doses varying from 50–100 organisms of *G.17 staphylococcus*.

Implants from more than one group were implanted into each of the six goats and the implantation times varied from six weeks to six months (see Table 1).

Goats

The female Saanen stock goats were obtained from the Agricultural Research Council, Compton, near Reading, Berks.

Implants

Cobalt-chrome alloy blocks measuring 25 mm × 6 mm × 11 mm were used with a cavity 3 mm in diameter drilled 22 mm in length (see Figure 1). These were prepared for use as follows:—

The blocks were degreased in trilene, left to drain on fat-free filter paper for two hours in a refrigerator and stored in degreased glass-stoppered jars, and then prior to use were washed in 1.18 per cent nitric acid for 20 minutes at 40°–60° C, rinsed thoroughly in distilled water and dried.

Table

<i>Implants without organisms</i>			
	No. of implants	No. of goats	Duration of implantation
Metal alone	4	4	10 weeks, 2 implants 5 months, 1 implant 6 months, 1 implant
Metal + Polyvinyl Alcohol	7	2	6 weeks, 6 implants 4 months, 1 implant
Metal + Polyvinyl Alcohol + 0.1 per cent D.B.P.A.	10	2	6 weeks, 6 implants 4 months, 4 implants
Metal + Polyvinyl Alcohol + 1 per cent D.B.P.A.	2	1	10 weeks, 2 implants

The polyvinyl alcohol chosen as the most suitable vehicle was Polyviol W 100/450 mixture No. 537, manufactured by Wacker-Chemie GmLH. It was supplied as an 11 per cent aqueous solution. The stable di-iso ethionate salt of dibromopropamidine was made up in strengths of 0.1 per cent and 1.0 per cent in the aqueous solution of PVA. The resultant solutions were colourless, transparent and rather viscous at room temperature. They were more easily used at 56° C.

The implants were submerged in the viscous field, care being taken to ensure the central core was completely filled. They were then inverted on thin degreased glass supports and dried in vacuo over P₂O₅ for 48 hours. The implants now had a thin plastic film firmly adherent to the metal and lining the cavity. Implants were also prepared having a film of PVA only.

All implants were sterilised in a high vacuum steam steriliser for 30 minutes at 136° C, care being taken to ensure proper drying took place. If this is not done, the implants remain tacky and difficult to use without damage to the film.

Staphylococcus Pyogenes

A strain, G.17, primarily isolated from a goat in whom it had caused severe mastitis was used. An 18-hour culture from blood agar was suitably diluted just prior to the goat operation and 0.1 ml was used in the case of each implant. Plate count control was made in triplicate from the two lowest doses, i.e. 10 and 50 organisms per 0.1 ml and in duplicate from the rest.

Method of Implantation and Removal

Insertion and removal of the implants was done with strict aseptic technique with the goats intubated and under general anaesthesia. The implants were put into the paravertebral muscles below deep fascia, with the core pointing towards the head. When organisms were used they were confined to the same side of the mid-

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<i>Implants with organisms</i>			
Number of organisms	No. of implants	No. of goats	Duration of implantation
50 organism per implant	2	2	5 months, 1 implant 6 months, 1 implant
Not done as polyvinyl alcohol not inhibitory to pyogenic cocci			
10, 10, 50 etc. organisms per 0.1 ml	10	3	4 months, 9 implants 6 weeks, 1 implant extruded
50, 100, 1,000 organisms per 0.1 ml	3	1	10 weeks, 3 implants

line of the vertebral column so that "clean" side and test dose side was maintained. X-ray examination was made prior to the removal of the implants as migration of the metal blocks occurred in the muscle planes.

Bacteriological examination was made at the time of removal, at the site and of the pus when this was present and all the implants were cultured. The capsules found round the implants on removal were examined histologically.

RESULTS

Bacteriological

Metal alone, implants coated with PVA, PVA + 0.1 per cent D. B. P. A. and PVA + 1.0 per cent D. B. P. A. No organisms.

The implants migrated frequently from site of insertion: all were embedded in smooth lined fibrous capsules containing straw coloured serous fluid with semi-solid plugs of clot in the cavity of the metal (see Figure 4). There were no abscesses found at any of these sites and there was no evidence of metastatic spread of infection, even to sites containing uncoated metal. Swabs taken from these sites and culture of the 23 implants concerned all proved sterile.

Metal alone + G. 17 Staphylococcus

A chronic abscess within a thick fibrous capsule surrounded the implants after five and six months. Culture of the pus and implants

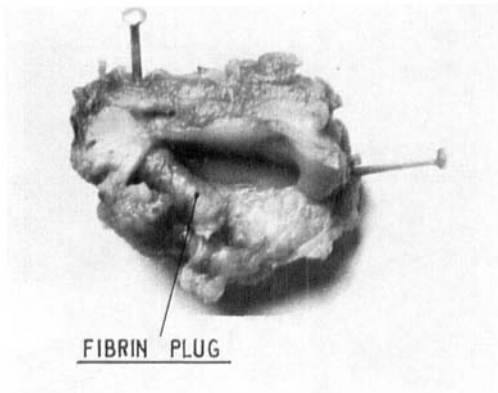


Figure 4. Thin, smooth-walled capsules showing plug.

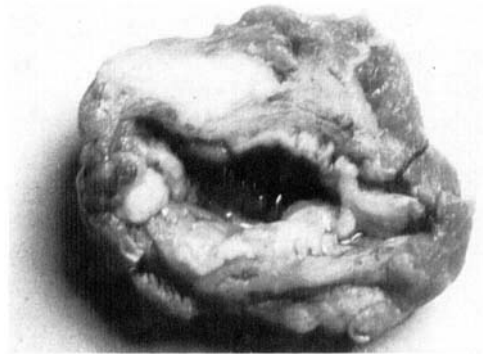


Figure 5. Chronic Abscess found within thick walled fibrous capsule.

resulted in recovery of an organism undistinguishable from the G. 17 staphylococcus (see Figure 5).

Implants Coated with 0.1 per cent D. B. P. A. + Varying Test Doses

The three implants recovered from sites with 10, 10 and 50 organisms per 0.1 ml challenge, all proved sterile as were the swabs taken from the smooth capsule. These three sites with test organisms did not develop abscesses, even after five to six months. The remaining seven implants with challenge doses of 50—1 million organisms per 0.1 ml all resulted in typical chronic abscess formation embedding the implants in thick pus and thick fibrous capsules. Recovery of the test organism resulted from all seven implants.

Implants Coated with 1.0 per cent D. B. P. A. in PVA

Here the strength of the antibacterial agent was ten times that used previously and the challenge doses with three implants were 50, 100

and 1,000 organisms per 0.1 ml. Fluctuant abscesses were felt at all three sites after ten weeks. Culture of both pus and implant resulted in recovery of a staphylococcus identical with the test organism.

Histology

The implants which did not contain organisms were enclosed in relatively thin fibrous tissue capsules in which inflammatory cells were minimal. Foamy areas which consisted of foci of macrophages with vacuolated cytoplasm, and voids, were obvious in the fibrous tissue surrounding the metal blocks coated with PVA alone and with PVA and D. B. P. A.

Implants containing 10 organisms were enclosed in mature fibrous tissue capsules in which there was a slight round cell infiltration. Implants which contained 50 organisms or more were embedded in a purulent exudate surrounded by organising granulation tissue of considerable depth. There was no apparent difference in the histological picture seen around the coated metal blocks and that seen around the uncoated blocks.

CONCLUSIONS

- (1) Polyvinyl Alcohol is a useful vehicle for coating surgical implants.
- (2) The inhibitory action of D. B. P. A. towards the test dose of staphylococcus was apparent in one goat only, where there was no evidence of infection with up to approximately 50 organisms with three implants coated with 0.1 per cent D. B. P. A. However, in two other goats with similar test doses of approximately 50 organisms chronic abscesses developed, even though one implant had in its film ten times the concentration of D. B. P. A. There was no evidence that this higher concentration had had any effect on the prevention of abscess formation.
- (3) There was no evidence of metastatic spread of abscesses from infected to "clean" side containing uncoated or coated implants.

RESUME

- (1) L'alcool polyvinyl est un produit utile pour enduire les implantations chirurgicales.
- (2) L'action inhibitive de l'alcool polyvinyl DB par rapport à la dose de staphylocoques du test est apparue chez une chèvre seulement, alors qu'il n'y eut pratiquement aucun signe d'infection dans environ 50 organismes avec trois implantations enduites de 0.1 pour cent d'alcool

DBPA. Quoi qu'il en soit, chez deux autres chèvres avec des doses de test similaires d'environ 50 organismes, des abcès chroniques se sont développés bien que l'une des implantations ait eu dans son film dix fois la concentration de DBPA. Il n'a pas été prouvé qu'une concentration plus élevée ait un effet quelconque pour prévenir la formation d'abcès.

(3) Il n'y a pas de preuve d'une propagation métastatique des abcès du côté intact contenant des implantations non enduites ou enduites.

ZUSAMMENFASSUNG

(1) Polyvinylalkohol ist ein brauchbares Lösemittel zur Überziehung chirurgischer Einpflanzungen.

(2) Die hemmende Wirkung von D. B. P. A. auf die Probedose von *Staphylococcus* zeigte sich nur bei einer Ziege, bei der kein Zeichen von Infektion mit bis zu ungefähr 50 Organismen auf drei Einpflanzungen, die mit 0.1 Prozent D. B. P. A. überzogen waren, nachweisbar war. Bei zwei anderen Ziegen jedoch mit ähnlichen Probedosen von ungefähr 50 Organismen entwickelten sich chronische Abscesse, obwohl ein Implantat in seinen Überzug die zehnfache Konzentration von D. B. P. A. hatte. Kein Beweis, dass diese höhere Konzentration irgendeine Wirkung auf die Verhinderung von Abscessbildung hat, war vorhanden.

(3) Keinerlei Beobachtung von metastatischer Ausbreitung von infizierten zu reinen Stellen, die nichtüberzogene oder überzogene Implantate enthielten, wurde gemacht.

It is a pleasure to thank *May and Baker Limited* for their supply of Polyviol W 100/450 and of the di-iso ethionate salt of Dibromopropamide.

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