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Nickel dermatitis hazards from prostheses

IN VIVO AND *IN VITRO* SOLUBILIZATION STUDIES

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SUMMARY

This report reviews data relating to the nickel hazard from implanted prostheses. It is shown that nickel is released from stainless steel prostheses by the action of sweat, blood and physiological saline solution. In laboratory animals, solubilized nickel is localized in the tissue near the implant.

Nickel-containing alloys have been implanted in man and in animals in a variety of therapeutic prostheses and devices. The most common alloys are those of stainless steel and cobalt–chromium (such as Vitallium). The stainless steel prostheses usually contain nickel in concentrations of 10–14%, but can contain concentrations as high as 35% (in the wire and probe leading to the heart muscle from a nickel–cadmium battery pacemaker). Common cobalt–chromium alloys for casting contain up to 2·5% nickel, while wrought alloys contain 9–10%.

In recent reports in the literature, instances of allergic reactions, urticarial (McKenzie, Aitken & Ridsdill-Smith, 1967; Symeonides, Paschaloglou & Papageorgiou, 1973) and eczematous dermatitis (Foussereau & Laugier, 1966; Tinckler, 1972; Brendlinger & Tarsitano, 1970; Barranco & Soloman, 1972; Pegum, 1974) to nickel have been attributed to implanted prostheses. Patch tests with nickel were positive in the patients with eczematous dermatitis. Removal of the metallic devices resulted in complete resolution of urticaria and involution of the eczemas. This would imply that nickel released from the metallic devices produced the allergic reaction in nickel-sensitive patients; a tenable thesis inasmuch as Ferguson *et al.* (1962) and Mears (1966) have reported increased nickel concentrations in parenchymal tissues from implantation of stainless steel rods containing nickel. Furthermore, Cohen (1962) has shown that corrosion of both stainless steel and cobalt–chromium alloys in simulated *in vivo* conditions is enhanced by cyclic stresses, such as are encountered in the use of weight-bearing orthopaedic implants. That this phenomenon does not occur in all such patients is noted in the case report by Lyell & Bain (1974). In their patient with proved nickel sensitivity, a Bjork–Shiley prosthetic

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valve (containing 300 mg of nickel) was used to replace the patient's diseased mitral valve. No adverse reactions were observed after a 22-month follow-up. However they do not dismiss the possibility that a reaction may arise especially as the valve is subject to constant trauma, and this may over a long period release significant quantities of metal. Pegum (1974) pointed out the importance of time; in his patient, who had a stainless steel plate inserted in the hip, all went well for 3 years, and then dermatitis appeared on various parts of the skin, and sterile suppuration developed around the plate.

Fisher (1972), commenting on the report by Barranco & Soloman (1972), rejected the possibility of such reactions on the grounds that nickel is so firmly bound physically in the alloy that body fluids and perspiration cannot 'leach' out the nickel to make it available to produce an allergic reaction. Fisher, however, has not considered the possibility of corrosion from implants. Samitz & Klein (1973) pointed out that corrosion of stainless steel orthopaedic prostheses has been well established (Cohen & Hammond, 1959; Scales, Winter & Shirley, 1961), and they suggested further investigation to determine if nickel is released from these materials. The variability of patient response and the variation in the detection of nickel reported here reflect the number of factors that affect corrosion *in vivo* including pH, PO_2, local stresses, and the presence of organic accelerating or passivating agents.

We have recently completed a laboratory investigation of the solubilization of nickel from stainless steel by sweat, whole blood, blood plasma, and physiological saline solution (PSS), and we have completed a small scale study of the translocation of nickel from implanted stainless steel to the surrounding tissue in laboratory animals. Several stainless steels, prostheses and surgical accessories were evaluated.

MATERIALS AND METHODS

Prostheses, suture wires, and screws were obtained from several manufacturers, and stainless steel samples were obtained through commercial sources. Large items were cut to a size that could be immersed in no more than 10 ml of 'leaching fluid' (sweat, blood, blood plasma or PSS). The test items, having surface areas of from 2 cm^2 to 5 cm^2, were washed in acetone and rinsed in distilled water. These items were then immersed in measured volumes of either sweat, blood, blood plasma, or PSS (contained in covered 50 ml polycarbonate beakers) for 1 week at room temperature (20–22°C). After this time, the liquid phases were analysed for nickel spectrophotometrically (Milner, 1963). The results of these measurements are summarized in Table 1.

Animal experiments

Incisions were made in both hind legs of each of five rabbits with a quartz scalpel. Stainless steel spheres were placed in the incisions in three animals, and polyethylene spheres were implanted as controls in the other two animals. The incisions were closed with nylon sutures. Three weeks later, biopsies were taken from the right leg of each animal with a quartz tube at the site of implant and 1, 2, 3, 4 and 5 cm from it. Biopsies were taken from the left side in the same manner 6 weeks after the implant. The biopsies were sealed in polyethylene tubing and analysed for nickel by neutron activation. These analyses were carried out at the University of Reading utilizing the facilities of the University of London Reactor Centre (ULRC). By careful control of the activation and cooling times, and by carrying out the activations with cadmium shielding, selective activation of nickel involving the ^{58}Ni (n, p)^{58}Co reaction was possible. Specific measurement of the ^{58}Co 810 KeV photopeak was made using the high-resolution Ge (Li) detector and 8196 channel analyser system at ULRC. Analysis of the data was by computer programme. The results of these measurements are listed in Table 2.

RESULTS

TABLE 1. Solubilization of nickel from stainless steel

Material tested	Nickel found in PSS, p.p.m.	Nickel found in sweat, p.p.m.	Nickel found in whole blood, p.p.m.	Nickel found in blood plasma, p.p.m.
302 s/s*	N.D.†	0·3		
303 s/s*	1·1	10·2		
316 L s/s	N.D.	N.D.	N.D.	N.D.
'Zimaloy' (Co–Cr type alloy)	0·1			
'Zimmer' 316 LVM	0·1			
Zimmer type 472 Jewett nail and plate	6·0	99·0	6·6	N.D.
	9·8	9·0	2·6	
Zimmer type 962 Jewett osteotomy plate	5·5	24·8	17·4	N.D.
'T & C' bone plate	1·8	12·1	15·3	1·0
Vitallium plate	0·6	7·2		
bone screw	3·0		N.D.	
suture wires (probably 316 L s/s)	0·5	0·6		
	0·7	N.D.		
Knowles pin	N.D.		N.D.	N.D.
Steinman pin	N.D.		N.D.	N.D.
Rush pin	N.D.		N.D.	N.D.

* Stainless steel from commercial channels (currently not used in prostheses)
† N.D., none detected, limit of detection ca. 1·0 μg

TABLE 2. Distribution of nickel in tissue near implanted stainless steel

Material implanted	Ni p.p.m. at distances indicated (cm)					
	0	1	2	3	4	5
after 3 weeks						
1 V4A s/s	46·2	N.D.†	N.D.	N.D.	N.D.	N.D.
2 V4A s/s	34·3	N.D.	N.D.	N.D.	N.D.	N.D.
3 V4A s/s	39·8	N.D.	N.D.	N.D.	N.D.	N.D.
4 polyethylene	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
5 polyethylene	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
after 6 weeks						
1 V4A s/s	53·3	N.D.	N.D.	N.D.	N.D.	N.D.
2 V4A s/s	46·2	N.D.	N.D.	N.D.	N.D.	N.D.
3 V4A s/s	49·7	N.D.	N.D.	N.D.	N.D.	N.D.
4 polyethylene	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
5 polyethylene	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.

† N.D., none detected, limit of detection ca. 0·5 μg

CONCLUSION

We conclude from these results that nickel is indeed released from stainless steel prostheses by the action of sweat, blood and PSS. From the limited study in animals it appears that the solubilized nickel is localized in the tissue near the implant, but a longer-term, more comprehensive study is required to confirm this finding.

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