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METAL IMPLANTS IN THE HUMAN BODY

A Histopathological Study

By

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Most implants used in orthopaedic surgery are of metallic origin. Metals and alloys employed during the last 20 years are as a rule tolerated by the human body for several years, though they always evoke a foreign body reaction.

Metallic implants can produce the following side-reactions in the contiguous tissue.

1. Mechanical or physical irritation.
2. Chemical or electro-chemical irritation.
3. Oligodynamic or catalytic effect.
4. Carcinogenic effect.

Our knowledge of the last two types (3 and 4) of reaction is very meagre. Experimental investigations have shown that metal implants can induce neoplasms in rats, mice and hamsters (*Oppenheimer et al.* 1956, *Oberling* 1959, *Kaplan* 1959). Despite some case reports (*Schinz* 1942, *Mc Douggal* 1956) long experience has taught that such reactions are extremely rare in man and may therefore be ignored.

Though much has been written about reaction 1 and 2 in experimental animals the literature on these effects in man is scanty. *Zierold* (1924) and *Key* (1946) discuss some problems of this type.

At autopsy of all together 13 cases *Collins* (1953) studied the structural changes of human bone around collum nails and plates with screws of stainless steel. He found no corrosion of the steel (18–8) but only what he considered a more or less mechanical reaction of the tissue. The possibility of a chemical reaction was not discussed. It is

now known (*Emnéus* 1961) that 18–8 steel often corrodes and thereby makes a chemical reaction with the surrounding tissue likely. The reaction of the soft tissue is important, especially around plates and screws, wires and nails projecting into the surrounding soft tissue.

Baeckstroem & Block (1953), *Cater & Hicks* (1956 and 1962) and *Hicks* (1958) investigated cases where metals had caused abscesses or chemical irritation, and discussed the problem very thoroughly.

Emnéus (1957) reported cases with supposedly electro-chemical tissue reaction and described the histopathological picture. *Cohen* (1959) published a detailed account of a fatal case of supposedly electrolytic origin. *Scales et al.* (1955, 1956 and 1959) have given much attention to the subject but their papers include no systematic description of the histopathology. Tissue reaction around nylon prostheses were thoroughly investigated by *Scales* (1957). Most of these papers concern cases where chemical reaction was suspected. Knowledge of the normal or average tissue reaction can be obtained only from the previously mentioned autopsy studies. According to *Hicks* (1958) evidence of iron pigment is often demonstrable around vitallium implants but not of chemical intolerance.

In view of the fragmentary nature of our knowledge of the effects of metal implants on contiguous tissue we decided to examine soft tissue biopsies from cases, where the clinical course strongly suggested mechanical or chemical irritation, and from cases where the implants were removed for prophylactical reasons, and cases in which treatment of a fracture with a metal implant failed because of factors that could not be ascribed to the implants on clinical grounds.

MATERIAL AND METHODS

The biopsy material consisted of almost all cases seen at the department of orthopaedics in the years 1956–1962 with obvious clinical symptoms of mechanical and/or chemical irritation. A few outstanding severe cases of massive bone absorption caused by mixed appliances (steel + vitallium) referred to us from elsewhere are not included in the material. The biopsies from cases where the implants were extracted for prophylactic reasons were selected at random from a total of 238 cases seen during the same time period. The group of non-healing fractures consisted of cases of fractures of the femoral neck with necrosis or pseudarthrosis, where *MOORE*-arthroplasty or osteotomy was made.

The biopsies were taken where the reaction, if any, seemed to be most pronounced. Most of the biopsy specimens were taken by one (*Hans Emnéus*) of us. The specimens were as a rule the size of a hazel nut or a walnut. They were immediately fixed in 10 per cent formol. Sections were stained with hematoxylin-eosin and the

Turnbull blue method. With the latter method ionized iron stains blue. Ionized cobalt stains dark-brown and ionized nickel gives a yellow precipitate with potassium ferricyanide. Ionized chromium is green but gives no precipitate with potassium ferricyanide (*Emnéus, Petersen* 1960). Pigment that turned blue when treated with this method is called Turnbull positive pigment; all other pigments, Turnbull negative. So-called formalin pigment was dissolved and removed from the sections before staining, as in our previous studies (*Emnéus & Stenram* 1960). The amount of pigment, when present, was subjectively evaluated and classed as + to ++++ (Tables 1 and 2).

Table 1 comprises simple implants such as screws, pins or nails; and Table 2, compound implants such as screws and plates, while Table 3 covers all the implants. The groups in the table are:

Group 1. Prophylactically extracted implants. Patients with healed fractures with no complaints at all. They had only a screw, pin, plate or all three, and were offered extraction.

Group 2. Cases where fracture treatment failed for reasons not clinically related to the osteosynthetic materials.

Group 3. Cases with clinically obvious mechanical irritation *i.e.* hip nails or Kuentscher nails and Rush pins projecting into the musculature or adjacent tissue. In this group co-existing chemical irritation was considered unimportant.

Group 4. Cases with clinically obvious chemical irritation, co-existing mechanical irritation was considered unimportant. An abscess with abundant pus was seen in 13 out of 21. The pus was sterile in 5 cases. Culture gave growth of non-pathogenic Staphylococcus albus in 2 and of Staphylococcus aureus sensitive to all antibiotics in 4. In 2 cases culture was not done. All 13 healed by first intention after extraction of the implants.

In the remaining 8 cases there was spontaneous pain, swelling, tenderness and rarefaction of bone but no purulent liquefaction. Symptoms ceased after extraction of the implants. The interval between insertion and onset of symptoms ranged from 6 weeks to 8 years (average 22 months).

OBSERVATIONS AND COMMENTS

All biopsies showed a small amount of fibrous tissue around the implants with a rather small number of lymphocytes and fibrocytes and a few macrophages and occasionally giant cells. In this respect the specimens differed but slightly.

The amount of pigment in the tissues varied considerably from case to case (Tables 1–3 and Figs. 1–2). There was nearly always Turnbull positive pigment.

Turnbull negative pigment was sometimes seen around the implants. As formalin pigment had been dissolved and removed from the sections the Turnbull negative pigments most probably originated from the implants, either as a transfer from instruments during the operation or dissolved by corrosion. Since clinical evidence of chemical irritation

TABLE

Imlants Consisting of

	Number of cases	Phagocytized pigment									
		Turnbull pos.					Turnbull neg.				
		−	+	++	+++	++++	−	+	++	+++	++++
Group 1.											
Vitallium	6		4	2					1		
Steel	*13*		*6*	*4*	*3*			*2*			
Group 2.											
Vitallium	11	1	3	7				1	1		
Steel	*5*		*2*	*1*	*2*			*1*			
Group 3.											
Vitallium	5		4	1							
Steel	*14*	*1*	*9*	*2*	*2*						
Group 4.											
Vitallium	1*				1						
Steel	*4*		*1*	*2*		*1*					

* Smith-Petersen nail of vitallium with a piece of the threading of the driver remaining in the threading of the nail. This is a type of abundant transfer of tool steel. It appears to be the only significant case of "chemical inflammation" caused by "Laing's transfer". The vitallium nail cannot be blamed for this.

in form of sterile abscesses was seen in several cases, the latter alternative seems the more likely, at least in these instances. Turnbull-negative pigment was yellow-green or yellow-brown and sometimes black and therefore probably as a rule consisted of Cr- and Co- or Ni-salts (of. section on Material and Methods). In a few randomly selected cases X-ray spectographic analyses of tissue around vitallium implants with a method described elsewhere (*Emnéus et al.* 1960) usually showed Co and Cr (see Fig. 3). The specimens were not studied for nickel. X-ray fluorescence analysis is the method of choice for tracing heavy metals in tissue. The tissue is not destroyed. One section may be examined by histological methods and the adjacent one by X-ray analysis.

The tables show that there was, as a rule, more pigment around compound implants than around single screws and nails. This may be due not only to the larger size of the compound implants, for experimental work has revealed a greater risk of corrosion of implants composed of several details than of simple implants of equal size (*Emnéus* 1961, *Bechtol et al.* 1959).

1
Single *Screw, Pin or Wire.*

Non phagocytized pigment											
Turnbull pos.					Turnbull neg.						
–	+	++	+++	++++	–	+	++	+++	++++		
	1	*1*				*1*					
		1	*1*			*2*					
		1				*1*					
	1										
			1			*1*					

Table 1, 2 and 3.

Group 1. Prophylactically extracted implants. Patients with healed fractures with no complaints at all. They had only a screw, pin, plate or all three, and were offered extraction.

Group 2. Cases where fracture treatment failed for reasons not clinically related to the osteosynthetic materials.

Group 3. Cases with clinically obvious mechanical irritation *i.e.* hip nails or Küentscher nails and Rush pins projecting into the musculature or adjacent tissue. In this group co-existing chemical irritation was considered unimportant.

Group 4. Cases with clinically obvious chemical irritation, co-existing mechanical irritation was considered unimportant. An abscess with abundant pus was seen in 13 out of 21. The pus was sterile in 5 cases. Culture gave growth of non-pathogenic Staphylococcus albus in 2 and of Staphylococcus aureus sensitive to all antibiotics in 4. In 2 cases culture was not done. All 13 healed by first intention after extraction of the implants.

Vitallium is Co-Cr-Mo-alloy.

Steel is Cr-Ni- and Cr-Ni-Mo-steel, *i.e. STAINLESS STEEL.*

We have decided not to deal with metallurgy in this paper. The osteosynthetic materials of stainless steel used in this investigation are of Scandinavian, British, American and possibly German origin.

We have very much to say about corroding metals. However, this paper is not devoted to the etiology of corrosion, but the metal pigmentation of tissues and its relation to the strength and type of foreign body reaction.

TABLE
Compound Implants, i.e.

	Number of cases	Phagocytized pigment									
		Turnbull pos.					Turnbull neg.				
		–	+	++	+++	++++	–	+	++	+++	++++
Group 1.											
Vitallium	8	1	3	4				1			
Steel	*10*		*5*		*3*	*2*		*4*			
Group 2.											
Vitallium	6	2	2	2					2		
Steel	*3*		*1*	*1*	*1*				*1*		
Group 3.											
Vitallium	4	1	1	2				2			
Steel	*3*		*1*	*1*	*1*			*1*			
Group 4.											
Vitallium	7		1	5	1			1			
Steel	*13*		*2*	*2*	*3*	*6*		*1*	*1*		

TABLE
All Implants, i.e.

	Number of cases	Phagocytized pigment									
		Turnbull pos.					Turnbull neg.				
		–	+	++	+++	++++	–	+	++	+++	++++
Group 1.											
Vitallium	14	1	7	6				1	1		
Steel	*23*		*13*	*2*	*6*	*2*		*6*			
Group 2.											
Vitallium	17	3	5	9				1	3		
Steel	*8*		*3*	*2*	*3*				*1*		
Group 3.											
Vitallium	9	1	6	2				2			
Steel	*17*	*1*	*10*	*3*	*3*						
Group 4.											
Vitallium	8		1	5	2			1			
Steel	*17*		*3*	*4*	*4*	*6*		*1*	*1*		
Total	113										

2
Screw or Pin and Plate.

Non phagocytized pigment										
Turnbull pos.					Turnbull neg.					
–	+	++	+++	++++	–	+	++	+++	++++	
	1	*2*	*1*	*1*		*4*				
		2					*1*			
		1	*1*				*1*			
	2									
		1	*4*	*4*		*3*	*5*			

3
the whole Material.

Non phagocytized pigment										Colour of the Turnbull neg. pigment	
Turnbull pos.					Turnbull neg.						
–	+	++	+++	++++	–	+	++	+++	++++	Black	Brown or green
		1								1	1
	2	*4*	*1*	*1*		*5*				*2*	*8*
										2	1
		3	*1*			*2*	*1*			*1*	*2*
	1										2
	1	*2*	*1*			*1*	*1*				*2*
	3										1
	1	*1*	*5*	*4*		*3*	*5*			*1*	*7*

Fig. 1.

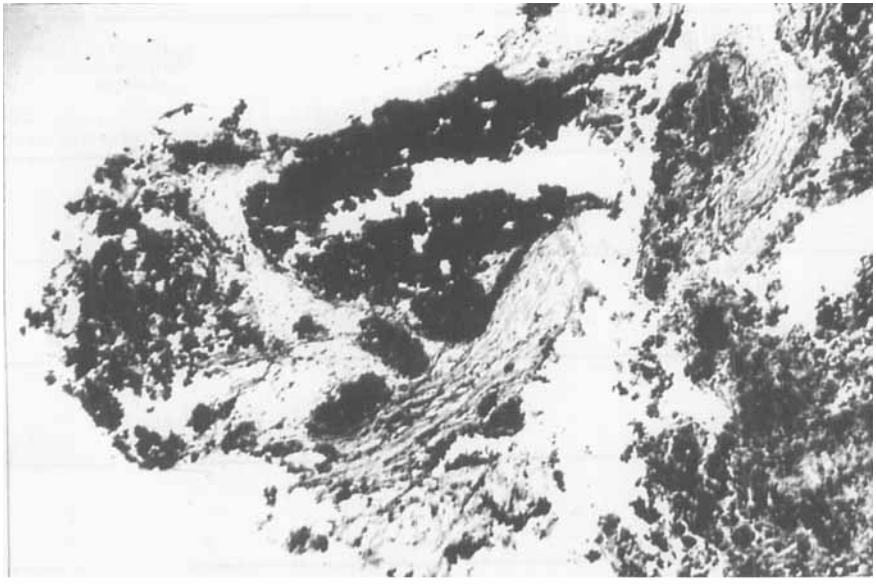

Fig. 2.

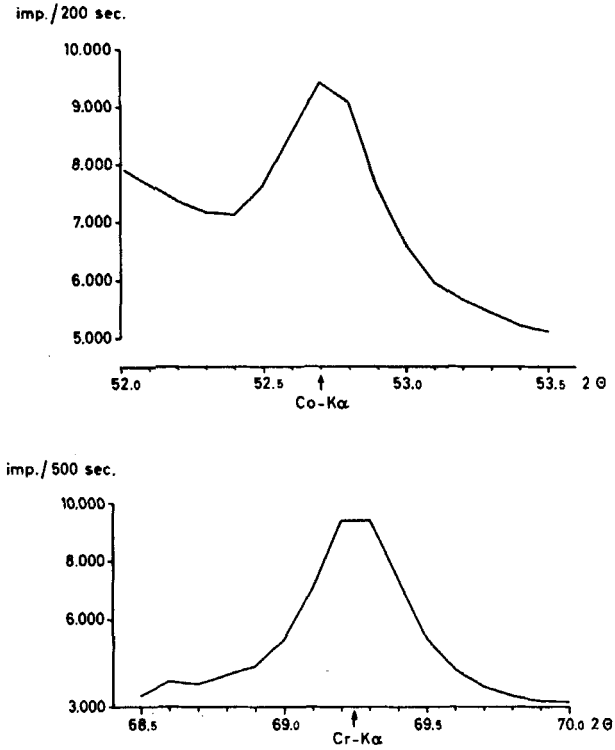

Fig. 3.

X-ray fluorescence curve for cobalt (upper diagram) and chromium (lower diagram). The analysis was made on a piece of tissue along a McLaughlin nail and plate of vitallium that was extracted because of mechanical irritation. The X-ray intensity of Co/Cr is about 5/2, which corresponds to their proportions in the vitallium alloy.

Figs. 1 and 2.

Histological sections of two different biopsies. The sections were stained according to the Turnbull blue method. All pigment appears black in the photographs. Each photograph covers about one fourth of the section and shows about one fourth of the pigment present in the sections. × 115. In the biopsy shown in *Fig. 1* the pigment was evaluated as phagocytized Turnbull-positive pigment +. The larger dots represent the pigment. The biopsy shown in *Fig. 2* was evaluated as phagocytized Turnbull-positive pigment ++++, non-phagocytized Turnbull-positive pigment ++++, non-phagocytized Turnbull-negative pigment +. Large accumulations of non-phagocytized pigment are seen in the upper part of the picture and in the right half of the middle part, while most of the pigment in the lower part of the picture is phagocytized.

The presence of Turnbull positive pigment around vitallium implants may be explained in several ways:

1. It may derive from corrosion of vitallium, which contains 0,5–1 per cent iron as a contamination.
2. Iron from steel tools, screw drivers, drills and guide wires used during the operation can be transferred to the implants (*Bowden et al.* 1955).
3. It may be a sequal of bleeding during the operations.

Surprisingly, Turnbull negative pigment is more often seen around steel than around vitallium implants. However, the steel is an alloy containing Fe, Ni, Cr and Mo. These elements may be dissolved from the corroding implants or possibly be scraped off during the operation.

From what has been said above and from our previous experimental studies (*Emnéus* 1960, 1961, *Emnéus & Stenram* 1960, *Emnéus & Baecklund* 1960), it appears that Turnbull negative pigment and large amounts of Turnbull positive pigment, especially when non-phagocytized and situated close to the implants, indicate corrosion and chemical irritation. But such pigment may exist in the tissue around steel implants without any accompanying clinical symptoms or signs of chemical irritation (Tables 1 and 2). Vitallium shows the same tendency, though not so marked. The reason is most probably that corrosion exists without producing obvious clinical signs. The cases showing the strongest clinical evidence of chemical irritation, however, always showed large amounts of non-phagocytized pigment. It thus appears that corrosion of an implant is one of the causes of chemical irritation. It cannot be excluded from a clinical study of the present type that transfer metal from tools used can also cause chemical irritation.

SUMMARY

The material consisted of clinical cases where metallic implants were extracted for prophylactic reasons or due to failure of the fracture to heal, mechanical irritation, or, as judged clinically, chemical irritation. The soft tissue around the implants was examined by histological methods including the Turnbull blue method for ionized iron. In several cases Turnbull-negative pigment and large amounts of Turnbull-positive pigment were found, often non-phagocytized and situated close to the implants. It is suggested that the pigment is due to corrosion of

the implants. Corrosion sometimes causes clinically obvious chemical irritation. The transfer of metals from tools used may also be a cause of tissue pigmentation.

RESUME

Le matériel d'observation se compose de cas cliniques chez lesquels des implants métalliques ont été extraits pour des raisons prophylactiques, par suite du défaut de guérison de la fracture, d'une irritation mécanique ou, selon ce que l'on a pu juger cliniquement, d'irritations chimiques. Le tissu mou autour des implants a été examiné par des méthodes histologiques y compris celle du bleu de Turnbull pour le fer ionisé. Dans plusieurs cas le pigment Turnbull négatif et de larges quantités de pigment Turnbull positif ont été trouvés, souvent non phagocytés, localisés à proximité des implants. Il est suggéré que le pigment est dû à la corrosion des implants. La corrosion cause parfois une irritation chimique cliniquement observable. Le transfert des métaux des instruments utilisés peut aussi être la cause de la pigmentation du tissu.

ZUSAMMENFASSUNG

Das Material bestand aus klinischen Fällen in denen metallische Implantate aus prophylaktischen Gründen oder wegen mangelnder Bruchheilungstendenz infolge mechanischer oder auch, bei klinischer Beurteilung, chemischer Irritation, entfernt wurden. Die Weichteile um das Implantat wurden mittels histologischer Methoden, einschliesslich der Turnbull Blaumethode für ionisiertes Eisen, untersucht. In mehreren Fällen wurde Turnbull-negatives und grosse Mengen von Turnbull-positivem Pigment gefunden, das oft nicht phagozitiert und dicht am Implantat gelegen war. Man nimmt an, dass das Pigment durch die Zersetzung des Implantates entsteht. Zersetzung ruft manchmal klinisch eine deutliche chemische Reizung hervor. Die Überführung von Metallen von den Werkzeugen, die gebraucht wurden, kann auch eine Ursache der Gewebspigmentation sein.

REFERENCES

Bechtol, C. O., Ferguson, A. B. Jr. & Laing, P. G.: Metals and engeneering in bone and joint surgery. The Williams & Wilkins Co., Baltimore 1959.

Block, W. & Baeckstroem, J.: Langenbecks Arch. u. Dtsch. Z. Chir. *277*: 89–103, 1953.

Bowden, F. P., Williamsson, J. B. P. & Laing, P. S.: J. Bone Jt Surg. *37-B*: 676, 1955.

Cater, W. H. & Hicks, J. H.: The Lancet, Oct. 1956, pp. 871–873.
Cater, W. H. & Hicks, J. H.: J. Bone Jt Surg. *44-B*: 122, 1962.
Cohen, J. & Hammond, G.: J. Bone Jt Surg. *41-A*: 524, 1959.
Collins, D. H.: J. Path. Bact. *65*: 109, 1953.
Emnéus, H.: Acta orthop. scand. *26*: 236, 1957.
Emnéus, H.: Acta orthop. scand. Suppl. 44 B.
Emnéus, H. & Peterson, P.: Acta orthop. scand. *29*: 331, 1960.
Emnéus, H. & Stenram, U.: Acta orthop. scand. *29*: 315, 1960.
Emnéus, H., Stenram, U. & Baecklund, J.: Acta orthop. scand. *30*: 226, 1960.
Hicks, J. H.: In: Modern Trends in Surgical Materials. Ed. Gillis, London 1958.
Kaplan, H.: Cancer Res. *17*: 791, 1959.
Key, J. A.: Surg. Gynec. Obstet. *82*: 319, 1946.
Mc Dougall: J. Bone Jt Surg. *38-B*: 709–713, 1956.
Oberling, C.: Ann. Rev. Med. *10*: 233, 1959.
Oppenheimer, B. S., Oppenheimer, E. T., Danishefsky, I. & Stout, A. P.: Cancer Res. *16*: 439, 1956.
Scales, J. T.: J. Bone Jt Surg. *38-B*: 754, 1956.
Scales, J. T. & Zarek, J. M.: J .Bone Jt Surg. *37-B*: 527, 1955.
Scales, J. T., Winter, G. D. & Shirley, H. T.: J. Bone Jt Surg. *41-B*: 810, 1959.
Scales, J. T.: Acta orthop. scand. *27*: 13, 1957.
Schinz, H. R.: Schweiz. med. Wschr. *72*: 1070, 1942.