Tissue Responses to Endoprosthesis Experience of 495 Cases

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ABSTRACT: As the use of implanted materials has becomes more popular in orthopaedic surgery, pathologists are likely to encounter increasing number of cases containing such materials. The lesions induced by these particle sometimes simulate neoplasms, infections, granulomas etc. We report our experience in Department of Pathology, the Hospital for Special Surgery, Cornell Medical College, U.S.A. of 495 cases during a one-year period. This experience involves metals, bone cement, polyethylene, silicone and carbon. The responses ranged from fibro-histocytic cells infiltration to granulomas consistings of epithelioid and giant cells. The materials were either differactile or refractile and were most easily detected using polarising filters. Specific identification was confirmed using Energy-Dispersive X-ray Analysis. It is therefore very important that pathologists be familiar to such reactions so as not to mistake them as other stimulating lesions.

INTRODUCTION

After the first fixation of fracture of bone with iron-wire in 1775,[1] several other materials such as vitallium,[2,3] stainless steel,[4] titanium,[5] etc. were introduced for orthopaedic implants. In 1960, Sir John Charnley utilized bone cement (poly methyl methacrylate) to fix metallic prostheses to bones, and in 1967 he used polyethylene as material for acetabular cup in total hip replacement.[6,7] Since then total hip replacement has become popular and one of routine procedures in orthopaedic surgery as it was noted that the incidence of total hip replacement for osteoarthritis in U.S.A. changed from 19.9 in 1960 to 34.9 in 1970 per 100,000 population.[8] It was also currently estimated that since 1980 a national requirement for United States people had been over 100,000 total hip arthroplasties per year.[9,10] General pathologists, therefore, are likely to encounter increasing number of cases containing implanted materials. It is the purpose of this report to present the histologic features of tissue responses and characteristic optical appearances of various common orthopaedic implants in our experience of 495 cases during a period of one year by using routine light and polarising microscopes. The confirmation of these materials was done by using energy Dispersing Analysis of X-rays (EDAX).

The poster-exhibition of this work was presented in United States – Canadian Division, Interntional Academy of Pathology, 75th Annual Meeting, New Orleans, March 10-14, 1986.

MATERIALS AND METHODS

The report is based on material from 495 cases examined in the Department of Orthopaedic Pathology of Hospital for Special Surgery during the 12 month-period from January to December 1985. The original procedures for implantations of prostheses include 190 hip joint replacements, 49 knee joint replacements, 4 elbow joint replacements, 1 shoulder joint replacement, 143 fixations of fractures and 108 corrections of deformities. The percentage of various implant materials are: metals 93, cement 38, polyethylene 27, carbon 2, and silicone 2.

Tissue was routinely fixed in formalin embedded in paraffin and cut 4 micron thick for H & E stained section for examination in plain and polarising light microscope. For confirmation, selected sections from the paraffin-embedded tissue were placed on carbon planchesttes and prepared for electron microscopic examination in an AMRAY 1000 A Scanning Electron Microscope. Elemental analysis was performed using a EDAX 9100/40 attached to the SEM by analysis of dispersed X-rays.

RESULT

Generally, tissue responses to various endoprosthetic materials in our study included fibrohistiocytic cells, chronic inflammatory cells, capillary-vessels proliferation, and peri-vascular cuffing

TABLE 1
Characteristics of Various Implanted Materials and Their Responses

Implanted material	Material	Polarization	Cellular response
Metals	Black Minute Irregular Shapes	Diffracticle	None or Histiocytic and Giant cell Slight Chronic Inflammatory
Cement	Clear, (Dissolved) Variable Size Fragmented Granulra (Barium)	Not Visible	Histiocytic and Giant Cell
Polyethelene	Clear, Colorless Variable Size Shards Refractile	Bright	Histiocytic and Giant Cell
Carbon	Black Variable Size Rectangular	Diffractile	Histiocytic (Slight)
Silicon	Clear, Colorless Small Granular Refractile	Not Visible	Histiocytic Slight Chronic Inflammatory

with chronic inflammatory cells. The proportions of cellular components vary upon types of material and the optical appearance of various types of material are also different. The unique features of individual material are, therefore, described as the followings (See also Table 1):

Metals

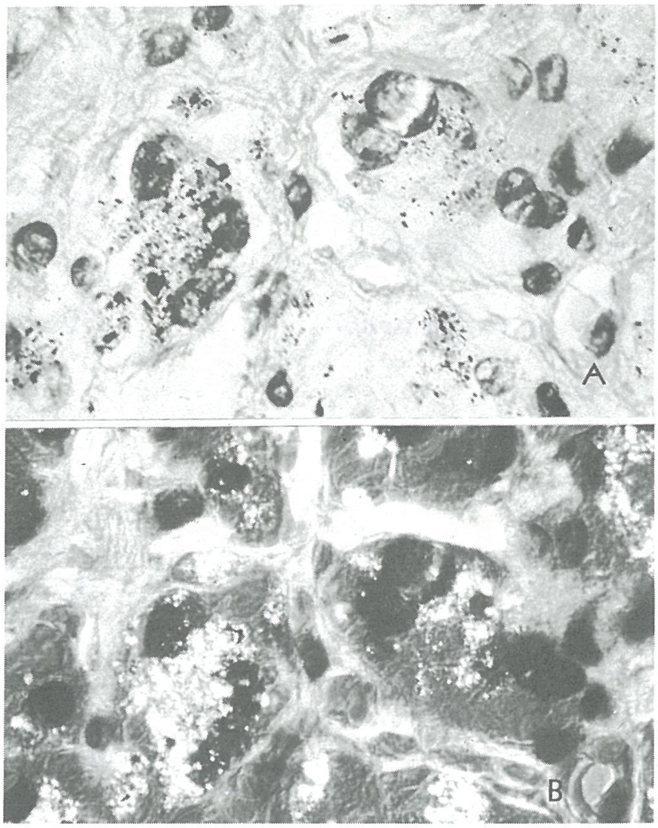
Majority of cases show fibro-histiocytic responses with mild chronic inflammation and fibrosis. The histiocytes are predominantly mononuclear cells. Metal particles are identified as black spheres or rods varying from 1 to 4 microns and confined mostly in mono-nuclear histiocytes (Figure 1A). Under polarized light, these particles diffract light and shows illumination around the edges (Figure 1B). In some cases, unusual perivascular infiltrations by lympho-plasma cells are observed. (Figure 1C).

Polyethylene

Most cases show fibro-histiocytic responses with varying degree of chronic inflammation and fibrosis. Large aggregations of histiocytes with predominant multi-nucleated giant cells are also frequent findings. Polyethylene are recognized as irregular, colorless and strongly refractile shards ranging in sizes from 0.5 to 500 microns and confine mainly in multinucleated giant cells. This material is strongly birefringent when viewing under polarized light (Figure 2A & B). In some cases, the histiocytic response is so exuberant that the lesion simulate histiocytic neoplasma, so-called *"pseudo-tumor"* (Figure 2C).

Cement

Most cases show focal aggregations of fibrohistiocytic cells with predominant multinucleated giant cells (intermingling with large areas of necrosis and fibrosis). Fibrinous materials are noted covering the surfaces and distributing focally in connective tissue stroma. Histiocytes and multinucleated giant cells show fine-granular cytoplasm. Cement in paraffin-embedded sections appear as spaces varying in shapes and sizes upto 1000 microns and contain golden brown granules of 1-2 microns; the spaces are surrounded by several multinucleated giant cells and fibrosis (Figure 3A). These granules aggregate in clusters or honey-comb pattern and are non-polarizable. Analysis of these granules by using X-ray microprobe show peaks of barium and sulfur which are consistent with ba-



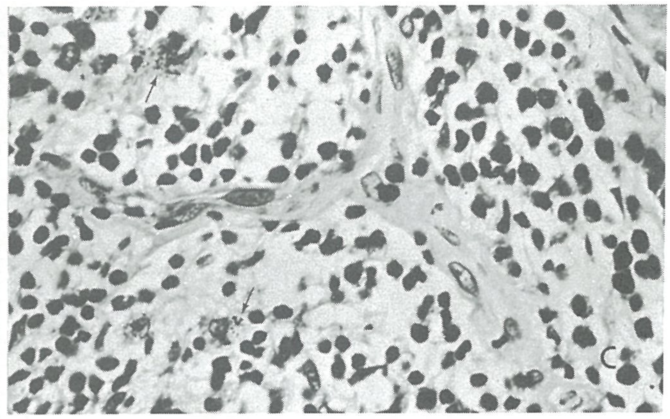


Fig. 1A (H & E; original magnification x 400): Showing clusters of histiocytes containing black minute particles in their cytoplasm.

B: Viewing under polarising filter of the same area as in Fig 1A showing diffractile particles corresponding with the dark particles as viewing under ordinary light microscope.

C: (H & E; original magnificantion x 100): Showing perivascular inflammation consisting of lympho-plasma cells and occasional histiocytes; Black minute particles are also present in the histiocytes (ARROWS)

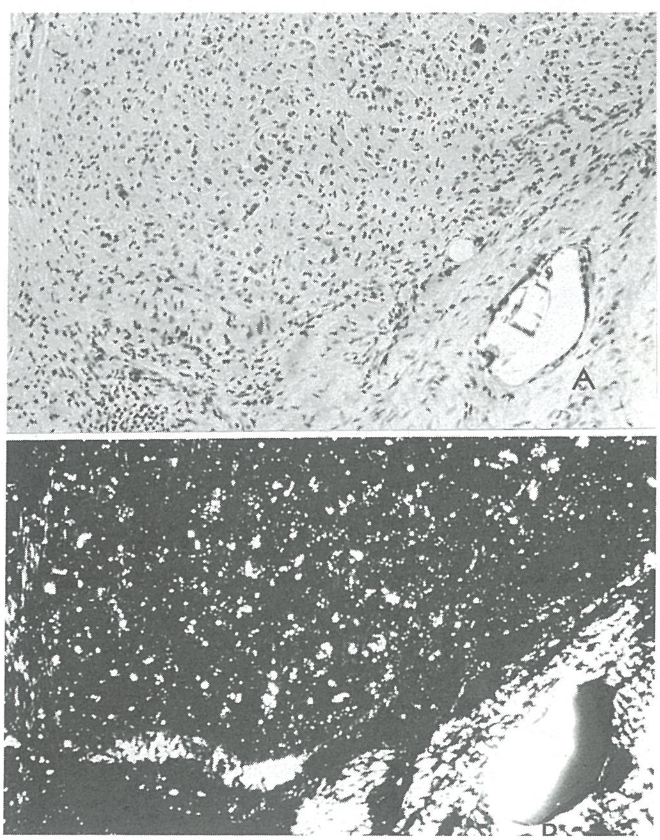


Fig. 2A (H & E; original magnification x 40) Showing large lobule of histiocytic aggregation and a cavity containing refractile material and surrounding with flattening multi-nucleated giant cells.

B: Viewing under polarising filter of the same area as in Fig. 2A showing numerous strongly birefringent particles in histiocytic aggregation and a large strong-birefringent piece of material in the cavity.

C: (H & E; original magnification x 20) Showing aggregations of histiocytes and fibroblast simulating tumor in the fibro-fatty stroma.

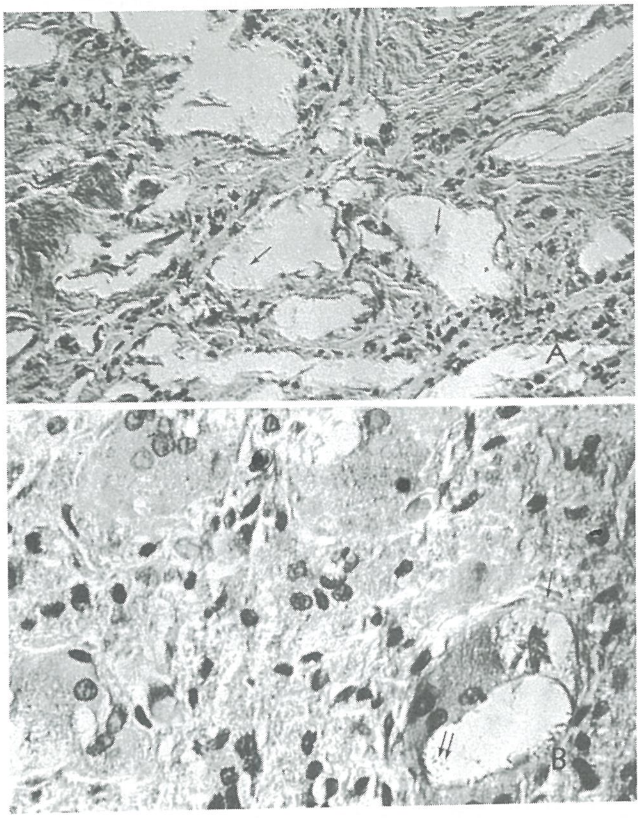


Fig. 3A (H & E; original magnification x 100)
Showing several spaces lined by fibro-histiocytic cells and containing granular materials. (ARROW) These granules represent barium-sulphate in the bone-cement.
B: (H & E; original magnification x 400)
Showing epithelioid granuloma consisting of giant cells having asteroid body (arrow) and vacuolar space containing granular material (double arrows)

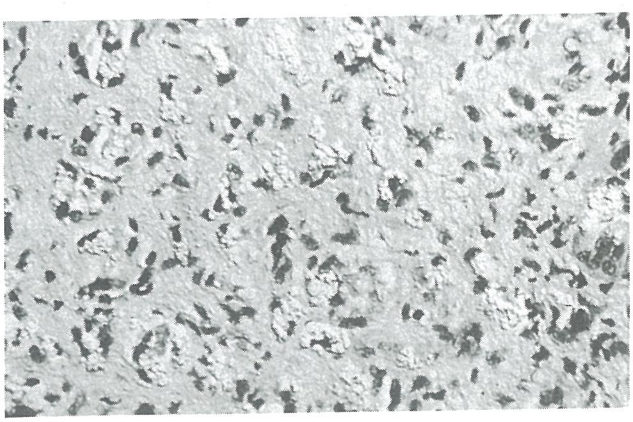


Fig. 4A (H & E; original magnification x 100)
Showing fibro-histiocytic lesions with occasional multinucleated giant cells. Amorphous granular, refractile globules are present in the histiocytes.

riuim sulfate (a radioopaque additive in bone cement). Therefore, the detection of radioopaque of these granules reflects the presence of bone cement which is polymers of methylmethacrylate and has been dissolved during the histological process. In minority of cases, epithelioid granuloma with or without asteroid bodies are observed. (Figure 3B)

Silicones

The tissue responses include fibro-histiocytic cells with varying degree of inflammatory cells and fibrosis. Giant cell macrophages are also preponderant and phagocytize silicones which appear as amorphous, colorless, refractile globules varying from 15 to 150 microns (Figure 4). These globules are non-polarizable and by energy-dispersive X-ray analysis reveal a peak of silicon.

Carbon

Most cases show fibro-histiocytic cells with prominent fibrosis. Carbon is recognized as either

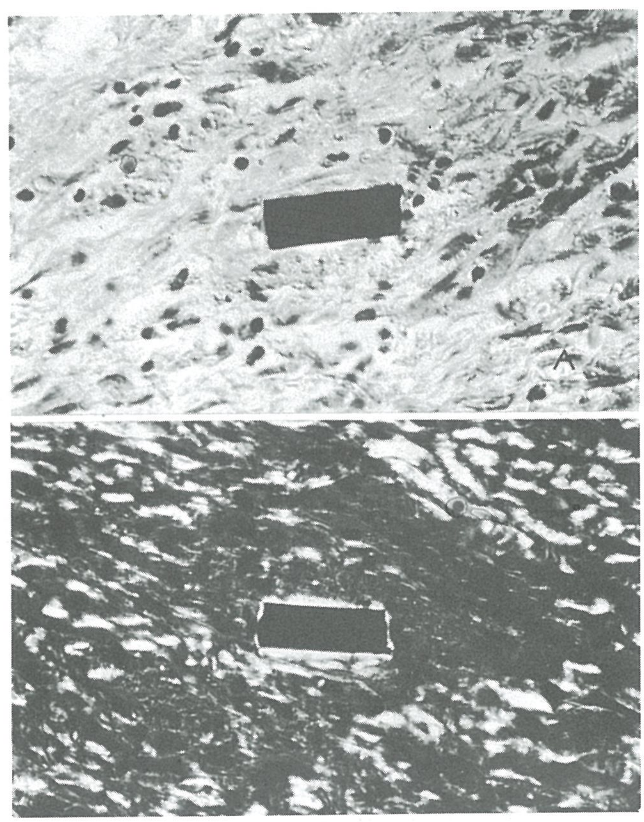


Fig. 5A (H & E; original magnification x 100)
Showing fibro-histiocytic stroma and a black rectangular fragments of carbon in the center.
B: Viewing under polarizing filter showing illumination around the edges of the carbon fragment.

tiny, irregular black granules varying from 1 to 5 microns or black fragments with sharp edges varying in sizes upto 300 microns in length and varying in shapes such as rectangles, triangles etc. (Figure 5A). The tiny granules are usually confined in histiocytes but the large fragments are often found entrapped in dense fibrous stroma. Under polarized light, carbon diffracts light and gives illumination around the edges (Figure 5B) and by X-ray microprobe analysis does not show any significant peak of element.

DISCUSSION

Common materials used currently as orthopaedic implants are metal alloys, polymers, ceramics, carbon and silicones. Metal alloys are used in making instruments for internal fixations of fractures and joint arthroplasties such as intramedullary rods, screws, plates, wires, etc. Polymers such as polyethylene are used as one of the articulating surface component of hip joint replacement or tibial component of total knee joint prosthesis; another type of polymer such as methyl methacrylate (bone cement) are used as a fixation interface between prosthesis and bone. Ceramics are used as load-bearing devices such as acetabular component. Carbon sometimes used for reenforcement the polyethylene in knee or hip prostheses and silicones used in prosthesis of finger and wrist joints. Implant materials ideally serve to withstand the mechanical and biological demands. As for mechanical demands, they should be able to withstand maximal compressive and tensile forces without deformity, break or wear-off. As for biological demands, they should not elicit any local or systemic reactions or carcinogenic effect to hosts.[11,16] Much of progress attributable to the development of new materials during the past half century but as yet unattained goal has been achieved to find an ideal one. Wear-off debris from materials due to abrasion, fatigure erosion and corrosion seem to be one of unsolved problems and play major role in evoking local tissue reaction.[12-14] In the early stages of local tissue reaction, granulation tissue containing fibroblasts, newly-formed capillaries, histiocytes, giant cell macrophages, lymphocytes and neutrophils similar to tissue response to wound healing are seen and in the later stages granulation tissue is replaced by fibroconnective tissue.[15] The composition and proportion of cellular responses vary upon the sizes, and types of wear debris; mononuclear histiocytes are predominant in response to small particles such as metal, whereas multinucleated giant cells are found predominantly in response to larger particles such as polyethylene, cement, and silicone. Our findings parallel with those of others.[14] The type of implant materials also plays important role in modifying tissue responses; cements tend to cause more necrosis and fibrosis. In addition, perilymphatic spaces inflammations are sometimes seen and occasionally polarizable particles can be detected in lymphatic spaces. The finding is in correspondance with the conviction that lymphatic systems play role in elimination of other small wear-off particles.[14]

Occasionally, other responses include granuloma with asteroid bodies in cases of cement and polyethylene, pseudo-tumor simulating fibro-histiocytic neoplasms in case of polyethylene or perivascular lympho-plasma cell infiltration in case of metals.[14] These findings are consistent with those of several investigators;[13] the complexes formed between host-proteins and foreign material may be responsible for these unusual reaction.[17]

The lesions induced by implant materials, therefore, can mimic sarcoidosis and infections ranging from non-specific to specific types such as syphilis, tuberculosis and fungus.[18] It is important that general pathologists not misdiagnose such lesions as infections and vice versa. Our observation was similar to other investigation that polymorphonuclear cells are not prononunced in the lesions that are not superimposed with infection[14-16] and it is sufficiently consistent to exclude the foreign bodies by simply using plain and polarizing microscopy. But in some cases, however, either the histologic features are not typical or the history of implant materials is uncertain; the use of a special technique such as Energy Dispersive Analysis of X-rays (EDAX) may be necessary to identify the foreign materials.

REFERENCES

1. Laing PG. Clinical experience with prosthetic material: historical perspectives, current problems, and future directions. In: Syrett BC, Acharya A, Corrosion and degradation of implant materials. Baltimore: American Society for Testing and Materials, 1979:199-211.
2. Smith-Petersen MN. Arthroplasty of the hip-a new method. J Bone Joint Surg 1939; 21:269-88.

3. Venable CS, Stuck WG, Bech A. The effect on bone of the presence of metals: based upon electrlytes – an experimental study. Ann Surg 1937; 105:917-38.
4. Hudack S. High Chromium, Low Nickel Steel in the operative fixation of fractures. Arch Surg 1940; 40:867-84.
5. Leventhal GS. Titanium, a Metal for surgery. J Bone Joint Surg (Am) 1951; 33A:473-4.
6. Charnley J. Arthroplasty of the Hip-a New operation. Lancet 1961; 27:1129-32.
7. Charnley J. Symposium on lubrication and wear in living artificial human joints. London: Institute of Mechanical Engineers, 1967.
8. Potter BE, Potter RA. Surgery in the United states-a Summary Report of the study on surgical services for the United States. Vol 2. The American College of Surgeons and the American Surgical Association, 1976:1568.
9. Melton J, Stauffer RN, Chao EYS, Ilstrup DM. Rates of total hip arthroplasty-a Population-Based Study. N Engl J Med 1982; 307:1242-5.
10. Wilson PD, Gordon SL NIH Concensus Development conference total hip replacement. National Institutes of Health, Bethesda, Maryland. March 1-3, 1982. J Orthop Res 1983; 1:189-234.
11. Gibbons DF. Materials for Orthopaedic joint prosthesis. In: Williams DF, ed. Biocompatibility of orthopaedic Implants. Vol 1. Boca Raton, FL: 1982:111-37.
12. Dowson D, Wright V. Wear Characteristics of prosthetic materials In: Williams D, ed. Biocompatibility of Implant Materials. London: Sector Publishing, 1976:15-20.
13. Evans EM, Freeman MA, Miller AJ, Vernon-Roberts B. Metal Sensitivity as a Cause of Bone Necrosis and Loosening of the Prosthesis in Total Joint Replacement. J Bone Joint Surg (Br) 1974; 56B:626-42.
14. Willert HG. Reaction of the Articular Capsule to plastic and Metallic Wear Products from Joint Endoprostheses. Congress of Dutch-Swiss Orthopaedic Societies, Lausanne, 1974.
15. Gross UM, Pickartz H, Taube K-J, and Strunz V. Tissue Reaction During the Incorporation of Glass Ceramic Material. In: Winter GD, Leray JL, de Groot K, eds. Evaluation of Biomaterial. John Wiley 1980; 413-9.
16. Autian J. Toxicology of Degradation Products of Plastics. In: Syrette BC, Acharya A. Corrosion and Degradation of Implant Materials. Phildelphia: American Society for Testing and Materials, 1979:5-19.
17. Merritt K, Mayor MB, Brown SA. Evaluation of Sensitivity to Metallic Implants. In: Winter GD, Leray L, de Groot K, eds. Evaluation of Biomaterials. John Wiley, 1980; 315-24.
18. Robbins SL. Syphilis. In: Robbins SL. Pathologic basis of disease. Philadelphia: WB Saunders, 1974; 378-84.