

## METHYLMETHACRYLATE HYPERSENSITIVITY IN ORTHOPAEDIC SURGERY

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The sensitivity to methylmethacrylate monomer in 25 patients undergoing orthopaedic surgery was studied. No relation could be found between the cardiovascular reactions observed during the cementation of the femoral prosthesis and the complement system, investigated by measuring the serum concentration of the haemolytic complement, components 3 and 4.

*Key words:* complement; hip surgery; methylmethacrylate cement

Accepted 14.x.77

Although the study of the cardiovascular phenomena observed during fixation of endoprostheses with methylmethacrylate cement (MMC) has demonstrated evidence of the significant role of the methylmethacrylate monomer (MMM) (Deichmann 1941, Homsy 1969, Monteny et al. 1975, Peebles et al. 1972, Pelling & Butterworth 1973, Phillips et al. 1971, Wagner et al. 1969) and fat embolism (Cohen & Smith 1971, Hausberger & Whitenack 1972, Sevitt 1972), the importance of other factors or a combination of these factors have also been pointed out. Attention has been drawn to the exothermic polymerization reaction of the cement (d'Hollander et al. 1976, Frost 1970, Homsy 1969, Ohnsorge 1971), the anaesthesia techniques (Cadle et al. 1972, Fearn et al. 1972), uncompensated blood loss (Berman et al. 1974, Deutman 1974, McMaster et al. 1974), stimulation of receptors (Milne 1973, Pelling & Butterworth 1973, Phillips et al. 1971), pronounced hypothermia (Pasteyer et al. 1976), coagulation disorders (Modig et al.

1973) and allergic reactions (Kepes et al. 1972).

To assess the importance of these possible allergic reactions, the cardiovascular system and the complement system (CS) were studied during the endoprosthesis fixation with and without use of MMC. A significant decrease of the enzymatic complexes might explain an eventual haemodynamic alteration occurring during the introduction of the MMC.

### PATIENTS AND METHODS

The complement system (CS) was investigated by measuring the serum concentration of total haemolytic complement (C'H50), component 3 (C3) and 4 (C4).

The study involved 25 patients undergoing orthopaedic surgery. The C'H50, C3 and C4 were first studied in 11 patients during McKee-Farrar hip replacement (THA). In order to evaluate the relative importance of the anaesthesia, the surgical stimuli and the use of MMM, 14 patients were studied during Moore arthroplasty with (CHP) and without use of methylmethacrylate cement (NCHP).

The age and sex of the patients and type of operation performed are presented in Table 1.

#### Technique of anaesthesia

About 1 hour prior to the induction of the anaesthesia each patient received atropine 0.25 mg and diazepam 5 to 10 mg i.m. Anaesthesia was induced by intravenous administration of flunitrazepam (0.008 to 0.03 mg/kg) + fentanyl (0.025 to 0.05 mg/kg) + pancuronium (0.1 mg/kg). The patients were intubated and normoventilated (pCO<sub>2</sub> 34–42 Torr; pO<sub>2</sub> 110–180 Torr). Anaesthesia was maintained with O<sub>2</sub>/N<sub>2</sub>O (1/3–2/3, v/v) and small doses of fentanyl and pancuronium were given intravenously when necessary. Compensation for blood loss by whole blood was accurate throughout the operation.

#### Measurements

Venous blood was collected with a venous catheter inserted into the vena cava superior via the vena jugularis interna. The samples were immediately refrigerated in ice, centrifuged at 4°C and frozen at –40°C, until assayed. Haemolytic complement (C'H50) was titrated with a Technicon Auto-analyser as described by Vargues & Tagnon (1967). Results are expressed in Units/ml (normal range: 300–600 U/ml). The serum concentration in C3 and C4 was measured by an immunoprecipitation technique using a Technicon Auto-analyser as indicated by Carson et al. (1972). Results are expressed in mg/100 ml serum (normal values of C3: 100–200 mg/100 ml; of C4: 30–50 mg/100 ml).

An arterial catheter was placed in the radial artery in order to measure the arterial O<sub>2</sub> con-

Table 1. Distribution of age, sex and type of operation

| Type of operation              | Total | Sex |    | Age*       |
|--------------------------------|-------|-----|----|------------|
|                                |       | M   | F  |            |
| Total hip arthroplasty         | 11    | 2   | 9  | 65.4 ± 6.9 |
| Non-cemented hemi-arthroplasty | 7     | 1   | 6  | 76.2 ± 7.4 |
| Cemented hemi-arthroplasty     | 7     | —   | 7  | 76 ± 5.8   |
| Total                          | 25    | 3   | 22 | 71.2 ± 4.5 |

\*Mean age in years ± S.D.

Table 2. Sampling times during total hip arthroplasty (THA), non-cemented hemi-arthroplasty (NCHP) and cemented hemi-arthroplasty (CHP)

| Sampling time  | Arterial blood |             | Venous blood |             |
|--|----------------|-------------|--------------|-------------|
|  | THA            | NCHP<br>CHP | THA          | NCHP<br>CHP |
| 1. Start of anaesthesia  | +              | +           | +            | +           |
| 2. Hip dislocation   | +              | +           | +            | +           |
| 3. 1 min after the introduction of the cement into the acetabulum                  |                |             | +            |             |
| 4. 10 min after Step 3   |                |             | +            |             |
| 5. Before introduction of the cement and/or the prosthesis into the femur          | +              | +           |              |             |
| 6. 1 min after the introduction of the cement and/or the prosthesis into the femur |                |             | +            | +           |
| 7. 10 min after Step 6   | +              | +           | +            | +           |
| 8. 20 min after Step 6   |                |             | +            | +           |
| 9. 30 min after Step 6   |                |             | +            | +           |

centration ( $\text{PaO}_2$ ), the arterial  $\text{CO}_2$  concentration ( $\text{PaCO}_2$ ) and to monitor the blood pressure (BP) and pulse continuously (EMT 34 Elema transducer + Mingograf 81 recorder).  $\text{PaO}_2$  and  $\text{PaCO}_2$  were measured directly by means of membrane electrodes (macrotechnique: ILPO2-20335, ILPCO2-20334 Instrumentation Laboratory 313).

The timing of arterial and venous samplings and the operative events are indicated in Table 2.

**RESULTS**

*C'H50, C3 and C4 variations during total hip replacement, Moore arthroplasty without MMC and with MMC (Figures 1-5).*

The modifications of C'H50, C3 and C4 can be related to the two phases of the procedure:

*Phase I: Induction of the anaesthesia* (samples 1, 2). The serum concentrations of C'H50, C3 and C4 were significantly decreased after the induction of the anaesthesia. The effect extended slightly into the first stage of the operation.

*Phase II: Surgery* (samples 3 to 9). During surgery we observed a stabilization of C'H50, C3 and C4. During total hip surgery there was a slight but not significant decrease of

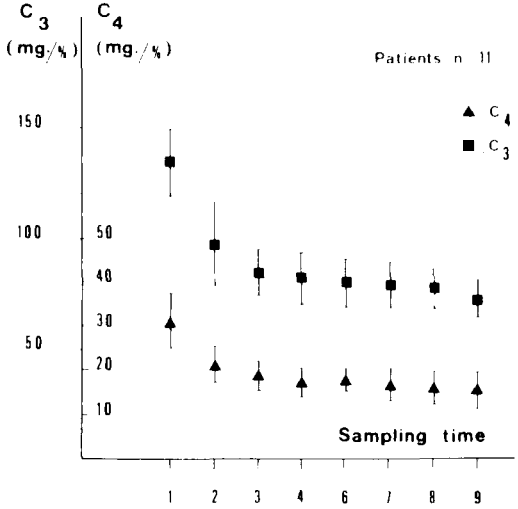


Figure 2. Variations of components 3 (C3) and 4 (C4) during total hip replacement (THA).

C'H50 after the introduction of the cement and the prosthesis into the femur (Figure 1, samples 6, 7).

*Blood pressure and pulse (Table 3)*

No modification of blood pressure or pulse were recorded during cementing of the acetabulum with MMC. After the impaction of the femoral prosthesis a decrease in blood

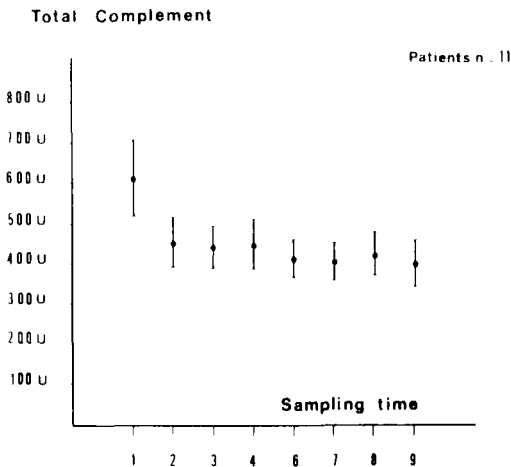


Figure 1. Variations of total haemolytic complement (C'H50) during total hip replacement (THA).

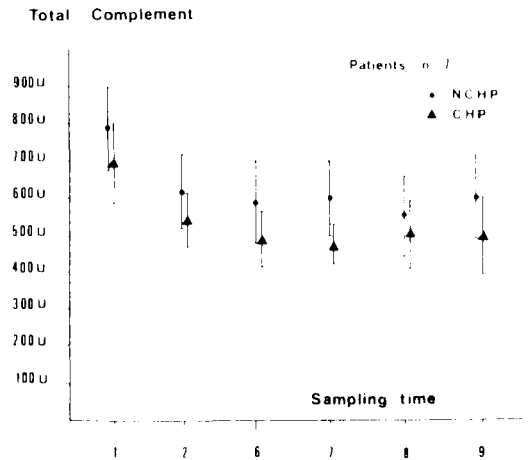


Figure 3. Variations of total haemolytic complement (C'H50) during cemented hemiarthroplasty (CHP) and non-cemented hemiarthroplasty (NCHP).

Table 3. Blood pressure changes after introduction of the cement and/or the prosthesis into the femur

| Type of operation              | Blood pressure |           |            |            |           |              |
|--------------------------------|----------------|-----------|------------|------------|-----------|--------------|
|                                | Total          | Elevation |            | Drop       |           | Minor change |
|                                |                | >20%      | >10%       | >20%       | >10%      |              |
| Total hip arthroplasty         | 11             | 1         | 2          | 3          | 1         | 4<br>(36.4%) |
| Cemented hemi-arthroplasty     | 7              | —         | 2          | 1          | —         | 4<br>(57%)   |
| Non-cemented hemi-arthroplasty | 7              | —         | —          | 1          | —         | 6<br>(86%)   |
| Total                          | 25             | 1<br>(4%) | 4<br>(16%) | 5<br>(20%) | 1<br>(4%) | 14<br>(56%)  |

pressure equal to or greater than 20 per cent was observed in five patients (20 per cent). In 14 patients (56 per cent) the variation was less than 10 per cent. After impaction of the femoral prosthesis we noted an increase in the pulse greater than 20 per cent in one patient (4 per cent) and a decrease of more than 20 per cent in three patients (12 per cent).

#### *PaO<sub>2</sub> and PaCO<sub>2</sub> variations*

Ten minutes after fixation of the femoral prosthesis a decrease in PaO<sub>2</sub> of more than 10 per cent was registered in eight patients (32

per cent) and an increase in PaCO<sub>2</sub> greater than 10 per cent was noted in five patients (20 per cent).

#### DISCUSSION

The possibility of an abnormal sensitivity to MMM during orthopaedic surgery has been suggested by Kepes et al. (1972) who observed sudden death just after fixation of the femoral prosthesis with MMC.

Neither the surgery nor the introduction of the MMC affected the complement system in

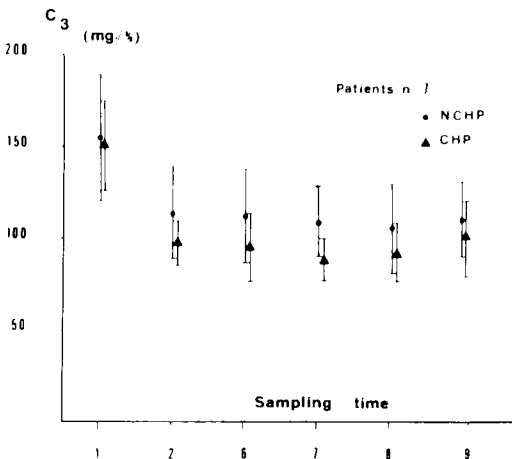


Figure 4. Variations of component 3 (C3) during cemented hemi-arthroplasty (CHP) and non-cemented hemi-arthroplasty (NCHP).

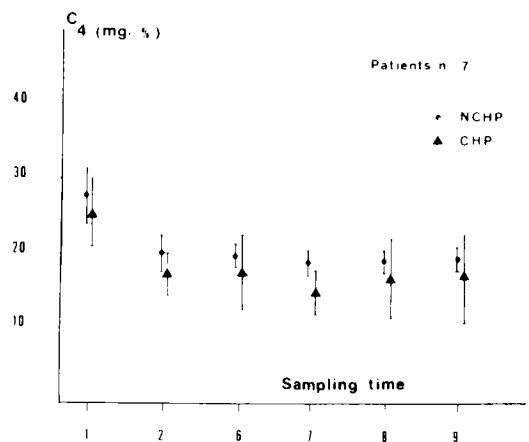


Figure 5. Variations of component 4 (C4) during cemented hemi-arthroplasty (CHP) and non-cemented hemi-arthroplasty (NCHP).

the 25 patients undergoing hip surgery. After recording a significant decrease of C'H50, C3 and C4 serum concentrations during the induction of the anaesthesia, we noted a stabilization of the CS during the surgical procedure. This emphasizes the importance of the interaction and the method of administration of the anaesthetic drugs on the CS. No relation could be found between the cardiovascular reactions and the CS variations observed. In our series 20 per cent of the patients presented a BP decrease in excess of 20 per cent. Parallel to this BP decrease no drop in the C'H50, C3 and C4 serum concentrations was recorded. Furthermore, the CS showed no significant changes during Moore arthroplasty with (CHP) or without (NCHP) the use of MMC.

The minor, statistically insignificant diminution of the CS components registered throughout the operation could be attributed exclusively to the effect of anaesthesia (repeated injections of drugs, plasma substitutes and transfusion). Haemodilution is not responsible for the initial drop of C'H50, C3 and C4 serum concentrations because all the patients received about 200 cm<sup>3</sup> of 5 per cent glucose solution during the induction of the anaesthesia which represents less than 5 per cent of the blood volume. The reduction of the serum concentration in C'H50, C3 and C4 observed in the induction phase results very likely from an activation of the complement system. Indeed this observation cannot be explained by a haemodilution (as explained above) nor by a non-specific hypercatabolism.

## CONCLUSION

The study of the complement system during endoprosthesis fixation with methylmethacrylate cement allows two conclusions to be drawn:

1. After an important activation of the complement system during the induction of the anaesthesia with flunitrazepam, fentanyl and pancuronium, surgery does not modify the complement significantly.

2. The introduction of the cement does not induce an activation of the complement. If an immunological process should be involved in some of the cardiovascular phenomena occurring during hip arthroplasty MMC is not responsible for an activation of the complement system.

## ACKNOWLEDGEMENTS

We wish to thank the Orthopaedic Department (Prof. de Marneffe) of the Brugmann University Hospital for allowing us to study patients under their care.

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