Chapter 4

The Otto E. Aufranc Award Paper

Bone cement with and without antibiotics: a study of mechanical properties*

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Antibiotics have been added to polymethyl methacrylate (PMMA) bone cement in order to prevent and treat infection; these combinations are in especially common use in Western Europe. One can expect that antibiotics added to PMMA will modify the mechanical properties of the polymerized cement. Since the mechanical properties of PMMA are important parameters in the analysis of prosthetic failure, a sound understanding of alterations in these properties for polymerized cement with additions of antibiotics must be formed. This report describes studies of bone cement, with and without gentamicin, undertaken to determine the following properties: intrusion characteristics, dough time, elastic modulus, tensile strength, and fatigue strength with and without admixed blood. Thermal properties and the antibiotic pharmacology of Palacos-R and gentamicin bone cement are presented in detail elsewhere.[14,15]

METHODS

Palacos-R and Simplex-P bone cements were used in our studies. The Palacos-R was tested plain and with 0.5, 1.0, and, in some cases, 2.0 gm of gentamicin base. The antibiotic was premixed with 40 gm of powder by the manufacturer, and the acrylic mixture was formed by the addition of 20 ml of the liquid monomer. Simplex-P was tested without addition of antibiotic.

Specimens of PMMA used in the elastic modulus, tensile strength, and

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fatigue tests were cast in split metal molds and sanded smooth. Each specimen utilized a full 40-gm package of bone cement. The powder and liquid were mixed with a spoon in an open bowl at approximately 100 strokes/min until a surgical glove could be cleanly pulled away from the PMMA mixture following pressure contact. The PMMA was put in a large syringe and then injected into the mold. An aluminum cap was placed over the pour hole, and hand pressure was used to compact the material. Setting occurred free of external pressure.

The specimen had a modified hourglass shape. The end sections were 2.2 cm in diameter, and circular arc tapers reduced the diameter to a 1.3-cm diameter in the 0.65-cm–long central section.

The load tests were all conducted on an MTS 810.015 closed loop electrohydraulic materials testing system. The cylindric end sections were held in hydraulic grips. These end sections were 2.4 cm long, and 75% of their length was within the clamps.

Tension test loads were conducted by manually dialing increasing load levels. The change in length of the specimens was approximately 0.15 to 0.30 mm/sec. Times to failure were slow, ranging from 5 to 10 seconds. The load-displacement data were plotted on a Hewlett Packard X-X-Y plotter.

Strength data were taken directly from analog plots. The elastic modulus was determined by first establishing the stiffness (force/displacement) of the specimen. Since the material was homogeneous and the specimen shape known, it was then possible to determine the relative stiffness of each section of the specimen. The only unknown in the analysis of the specimen stiffness was the modulus of elasticity, and this was determined by relating the analysis to the experimental data. To simplify the analysis, the circular arc sections were approximated by a straight line taper; this approximation introduced an error of less than 1%.

Fatigue tests were also conducted on the MTS system and utilized the same specimen preparation method. All of the specimens were made from the same batch of Palacos-R. One gram of gentamicin had been added to half of the Palacos-R at the factory. All specimens were loaded in reversed axial loading under load control at ± 20.4 MPa (that is, tension and compression) at a loading frequency of 2 Hz. Since cyclic testing produces heat, the specimen temperature was kept cool to the touch by blowing shop air over the surface. All tests were conducted at room temperature, and specimen temperatures were not recorded.

For those tests in which blood was added to the PMMA it was mixed in at dough time and mixing occurred only until droplets were no longer observed and the specimen had a streaked appearance.

Onset of the cement dough time was determined by failure of the cement to stick to the surface of a surgical glove, while cement set time was taken as the time when the exothermic temperature rise was at a point midway between the ambient temperature and the maximum temperature attained. The working time was defined as the time interval between the dough time and the set time.

The temperature-time history of the specimen was monitored by inserting a type K (Nickel-Chromium versus nickel-aluminum) thermocouple into the center of the mold. Temperature was established using an ice bath reference, and data was recorded on a Hewlett Packard 7100B. The intrusion studies were conducted according to recommended methods of the American Society for Testing and Materials.

RESULTS

Tensile strength

The tensile strength test results suggest that the addition of up to 2.0 gm of gentamicin base to Palacos-R produces no significant reduction in quasi-static tensile strength (Fig. 4-1). These results are consistent with those reported in the literature, which show only a slight decrease in the strength of PMMA with the addition of barium sulfate or gentamicin. The relative tensile strength of Simplex-P and Palacos-R previously reported in the literature has normally been the reverse of our data, that is, Palacos-R has been reported to be slightly stronger than Simplex-P.[12] The results shown in Fig. 4-1 are for a single batch of Palacos-R to which varying amounts of gentamicin have been added. Our studies with other batches of Palacos-R indicate that the batch-to-batch variation in average tensile strength is on the order of 10%. This batch variation has been confirmed by other investigators.[13]

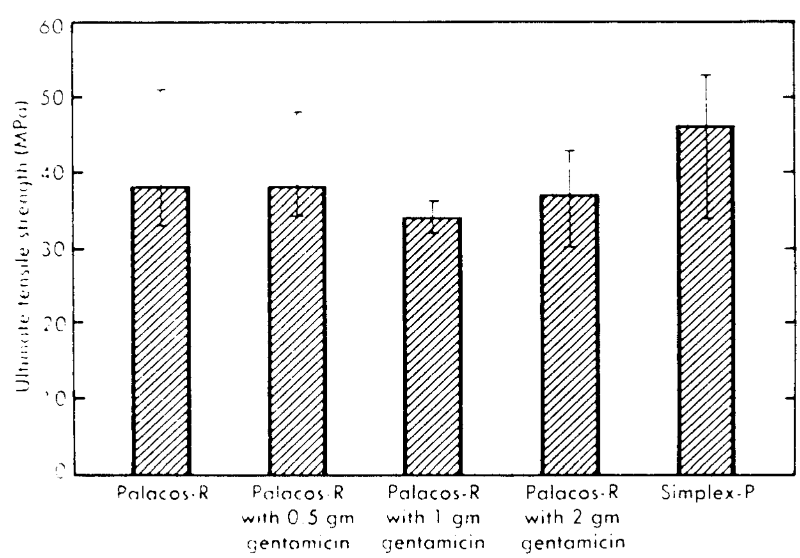

Fig. 4-1. Ultimate tensile strength for Palacos-R, plain and with gentamicin, and for Simplex-P

Separate experiments were conducted to determine the tensile strength of Palacos-R with and without the addition of 2 ml of fresh blood blended into the cement. In this study the average of four tests, with and without the addition of blood, resulted in ultimate tensile strengths of 39.4 MPa and 46.8 MPa, respectively. Thus a 16% decrease in strength was noted with the addition of this amount of blood. The results indicate that in tension the reduction in cement strength produced by the addition of blood is at least as significant as the addition of an antibiotic in powder form.

Elastic modulus

Static material tests measured the elastic modulus and tensile strength of Palacos-R, with and without gentamicin, and of Simplex-P. The load-deflection curves for all samples of cement were only slightly nonlinear, and the material showed no distinct yield point. The elastic modulus was taken as the tangent of the stress-strain curve at zero load. Elastic moduli were determined using six samples of Palacos-R without gentamicin and six samples with 1.0 gm of gentamicin. The addition of gentamicin had no significant effect on the data, and the average elastic modulus was 1950 MPa.

Fatigue strength

Fatigue strength data for specimens of Palacos-R from the same batch, with and without 1.0 gm of gentamicin and with and without 2.0 ml of blood are presented in Tables 4-1 and 4-2. A decrease in average cycles to failure with the addition of gentamicin was observed. Fatigue testing data follow a logarithmic mean distribution, and this was considered in our significance testing. The addition of 1.0 gm of gentamicin to Palacos-R reduced the mean cycles to failure from 36,625 to 7722 cycles ($p \leq 0.001$, Tests 1 and 2). The addition of 2.0 ml of blood to Palacos-R showed a reduction in the mean cycles to failure from 36,625 to 4600 cycles with a significance level of $p \leq 0.001$ (Tests 1 and 3). A comparison of Palacos-R with 1.0 gm of gentamicin with and without 2.0 ml of blood showed a reduction in the mean cycles to failure from 7722 to 2974 cycles ($p \leq 0.001$, Tests 1 and 2). Probably the most important comparison is between plain Palacos-R and Palacos-R with 1.0 gm of gentamicin, each mixed with 2.0 ml of blood. The average cycles to failure are reduced from 4600 to 2974 cycles. However, the difference is not statistically significant ($p = 0.20$).

The data presented in Tables 4-1 and 4-2 do not include any specimens in which voids greater than 1.0 mm in diameter were observed in the fracture region. While care was taken to produce "perfect" molds such inclusions appeared rather often. When such voids were present, the mean cycles to failure were on the order of 2000 cycles for all specimens. From these studies we conclude that the addition of gentamicin to Palacos-R significantly reduces its fatigue life in a controlled laboratory situation in which no foreign substances or voids are present. However, when 2 ml of blood are added to Palacos-R or

Table 4-1. Fatigue life of bone cement with and without gentamicin*

Sample	*Palacos-R plain* Cycles to failure N	$log_e N$	*Palacos-R with 1.0 gm gentamicin* Cycles to failure N	$log_e N$
1	11,250	9.328	4100	8.319
2	14,210	9.562	4300	8.366
3	14,300	9.568	4800	8.776
4	24,288	10.098	5030	8.523
5	37,032	10.519	6346	8.756
6	40,820	10.617	7560	8.931
7	42,466	10.656	9730	9.075
8	45,410	10.723	9560	9.165
9	56,510	10.942	12,899	9.465
10	79,960	11.289	13,890	9.539
	Mean cycles to failure = 36,625 Mean $\log_e N$ = 10.330 Variance ($\log_e N$) = 0.433 Standard deviation = 0.658		Mean cycles to failure = 7722 Mean $\log_e N$ = 8.892 Variance ($\log_e N$) = 0.181 Standard deviation = 0.426	

*Stress range of ± 20.4 MPa

Table 4-2. Fatigue life of bone cement with admixed blood*

Sample	*Palacos-R plain plus 2.0 ml rabbit blood* Cycles to failure N	$log_e N$	*Palacos-R with 1.0 gm gentamicin plus 2.0 ml rabbit blood* Cycles to failure N	$log_e N$
1	2954	7.991	1695	7.435
2	3201	8.071	2406	7.786
3	3688	8.213	3334	8.112
4	5203	8.557	3664	8.206
5	7951	8.981	3770	8.235
	Mean cycles to failure = 4600 Mean $\log_e N$ = 8.363 Variance ($\log_e N$) = 0.166 Standard deviation = 0.408		Mean cycles to failure = 2974 Mean $\log_e N$ = 7.995 Variance ($\log_e N$) = 0.116 Standard deviation = 0.341	

*Stress range of ± 20.4 MPa

Palacos-R with 1.0 gm of gentamicin, the difference in mean cycles to failure is small and not statistically significant. Given the clinical situation in which the surfaces of bone cement are rough because of intrusion into cancellous bone, blood or air is inadvertently mixed with the cement, and voids are present, the fatigue life will be dominated by these stress risers and impurities. Therefore, the addition of antibiotic to bone cement is unlikely to be of practical significance to its fatigue life in a clinical environment.

Some investigators have suggested that the metal prosthesis should be cooled before insertion in order to lower the peak temperature of the setting bone cement. We prepared bone cement that set under much reduced ambient temperature to see if there would be any effect in material properties. Both Palacos-R and Palacos-R with 1.0 gm of gentamicin were mixed and cured at 8° C. The curing time was approximately 60 minutes, and only three specimens of plain Palacos-R and two specimens of Palacos-R with 1.0 gm of gentamicin were studied. The plain Palacos-R underwent a reduction in the mean cycles to failure to 20,330 cycles, while the Palacos-R with gentamicin showed approximately the same cycles to failure (7900 cycles). While the sample size in this study is too small to make possible the drawing of any definitive conclusions, the preliminary results for the plain Palacos-R suggest that PMMA formed at reduced ambient temperatures may be weaker. We postulate that this weakness may be the result of incomplete polymerization.

Dough time

Dough, set, and working times are summarized in Fig. 4-2 for Palacos-R, Palacos-R with 0.5 gm gentamicin, Palacos-R with 1.0 gm gentamicin, and Simplex-P. The times represent averages of ten samples each from 10-ml molds with diameters of 2.0 cm, 1.0 cm, and 0.75 cm. The dough time for Palacos-R is very distinct and is approximately 2 minutes, with and without gentamicin. The dough time of Simplex-P is reached gradually, is not distinct, and is as long as 5 minutes. Palacos-R and Palacos-R with 0.5 gm and 1.0 gm of gentamicin all have working times essentially equal to that of Simplex-P. The working and setting times for the 10-ml samples consistently increased as the mold diameter decreased.

Intrusion characteristics

Palacos-R, Palacos-R with 1.0 gm of gentamicin, and Simplex-P were tested with regard to their ability to penetrate into small cylindric columns under a standard load. The results reported in the material following (p. 93) show the data from four individual columns (marked "holes") since there were some variations, as noted. The overall average intrusions were: plain Palacos-R, 2.37 mm, Palacos-R with 1.0 gm of gentamicin, 2.59 mm; and Simplex-P, 4.09 mm. The addition of antibiotics did not change the intrusion characteristics of Palacos-R significantly. However, if Palacos-R is compared with Sim-

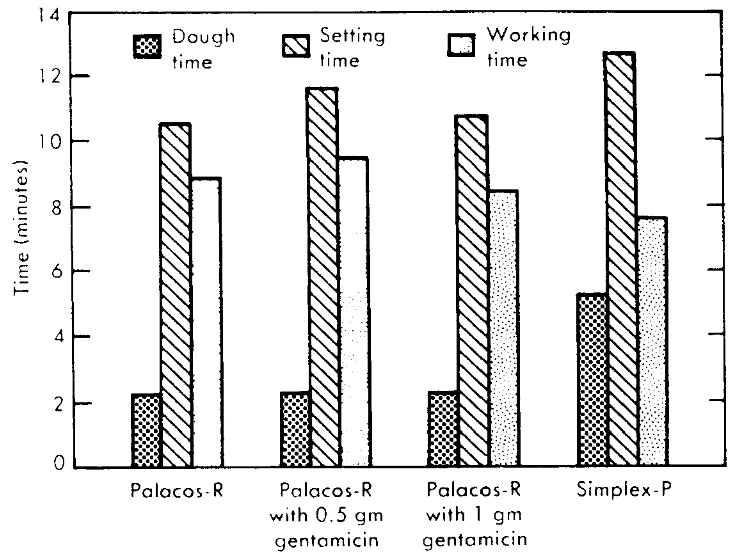

Fig. 4-2. Dough, set, and working times of bone cements with and without the addition of gentamicin.

Intrusion Study Results*

A. Palacos-R plain, five samples

Hole number	1	2	3	4
Mean value	2.46	2.11	2.49	2.42
Standard deviation	0.54	0.36	0.70	0.71

Overall average intrusion 2.37

B. Palacos-R with 1.0 gm gentamicin, five samples

Hole number	1	2	3	4
Mean value	2.98	2.35	2.24	2.80
Standard deviation	0.70	0.19	0.37	0.59

Overall average intrusion 2.59

C. Simplex-P plain, four samples

Hole number	1	2	3	4
Mean value	4.35	4.13	4.25	3.54
Standard deviation	0.52	0.38	0.53	0.58

Overall average intrusion 4.09

*Intrusion in millimeters.

plex-P, the differences are significant for each hole tested ($p = 0.05$ to 0.001) (see p. 93). Intrusion values are a strong function of the time at which the force is applied to the PMMA during polymerization. The time for the Palacos-R intrusion studies was taken as 120 seconds because dough time reliably began by then. The dough time for Simplex-P was less well defined, and the results on p. 93 are for an arbitrary dough time of 5 minutes. Other studies of intrusion versus dough time for Simplex-P produced average intrusions of 9.0, 4.1, 3.5, and 2.0 mm for dough times of 3.5, 5.0, 6.0, and 7.0 minutes, respectively.

DISCUSSION

There have been available for a number of years numerous studies* characterizing bone cements with respect to dough time, setting time, working time, modulus of elasticity, tensile and compressive strengths, and fatigue properties. The effects of adding radiopaque substances to the cement has also been investigated.[3,5,17] Recently, Bucholz[1] examined the effects of incorporating powdered gentamicin sulfate in Palacos-R and reported success in treating patients with infections.

Changes in PMMA handling characteristics exemplified by peak temperature and dough, set, and working times result from alterations in PMMA mass, kneading of the mixture, ambient temperature, and powder-to-liquid ratio.[3,8,11] Haas and associates[3] found that cement containing barium sulfate set somewhat more slowly and had a slightly longer handling time and dough time but had the same peak temperature as cement without barium. Our results do not show variations in setting and handling times as the concentration of gentamicin in bone cement is increased.

Review of the reported modulus of elasticity for PMMA shows a wide range of data† that generally extends from 1000 MPa to 2500 MPa. Our study found an insignificant variation in the elastic modulus of Palacos-R with the addition of gentamicin, and the average modulus was 1950 MPa.

Compressive strength of PMMA has been reported to range between 70 and 93 MPa.[3,5,10] Haas and associates[3] report a 1.5% reduction in the strength of Simplex-P with the addition of 0.5 gm of barium sulfate. The range of values for the shear strength has been rather consistent, extending from 40 to 50 MPa.[9,10,16] Gruen and co-workers[2] have recently discussed the shear and tensile strength of laminated PMMA specimens as functions of lamination time and for dry and wet interfaces. Their results have clinical implications and support early cement placement with dry surgical fields.

Tensile strength values for PMMA found in the literature[3,6,10] range from 25 to 53 MPa. Haas and associates[3] found an 11% reduction in the tensile

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* See references 3-7, 9, 10, and 16

† See references 3, 5, 9, 10, and 13

strength of Simplex-P with the addition of barium sulfate. Rawson[13] found a 20% reduction in the tensile strength of Palacos-R with the addition of 1.0 gm of gentamicin. Its strength then equaled the strength of Simplex-P without antibiotic.

Our tensile strength data were collected from a single batch of Palacos-R with 0, 0.5, 1.0, and 2.0 gm of gentamicin added. The maximum average reduction in strength (not statistically significant) was approximately 10% with 2 gm of added gentamicin. In contrast to other studies our data suggest that Simplex-P has a slightly higher tensile strength than Palacos-R. This may be a result of confining our studies to a single uniform production run, that is, batch.

The presence of gentamicin had a more dramatic effect on the fatigue characteristics of Palacos-R than it did on the static material properties. For a reversed axial tension-compression test of $\pm$ 20.4 MPa, the average cycles to failure were reduced from 36,625 to 7722 cycles at a significance level of $p \leq 0.001$ when 1.0 gm of gentamicin was added to Palacos-R. Previous fatigue studies by Jaffe and associates[5] used specimens loaded in cyclic compression only and, therefore, cannot be directly compared to the present study. However, the addition of 2.0 ml of blood to Palacos-R or the presence of voids of approximately 1-mm diameter or larger have a greater effect on fatigue life than the addition of gentamicin. Because of the strong dependence of fatigue life on stress concentrations, the environmental factors such as voids, admixed blood, and other foreign materials will most likely have a greater influence on material strength reduction than that caused by the addition of gentamicin in clinical practice.

SUMMARY

Tensile strength of Palacos-R cement varies by the batch up to 10% and may decrease 8% with the addition of 2.0 gm of gentamicin base and 16% with 2.0 ml of blood. Fatigue tests indicate that the addition of either antibiotics or blood weakens the bone cement but does not weaken it as much as small voids in cement or irregularities at the surface. Bone cement intrusion into small spaces decreases rapidly with increasing dough time. Palacos-R and Simplex-P have different intrusion properties. The addition of gentamicin to Palacos-R does not alter the dough, set, or working time.

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