



American Association of Oral  
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July 12, 2006

**To:** AAOMS House of Delegates  
AAOMS Board of Trustees

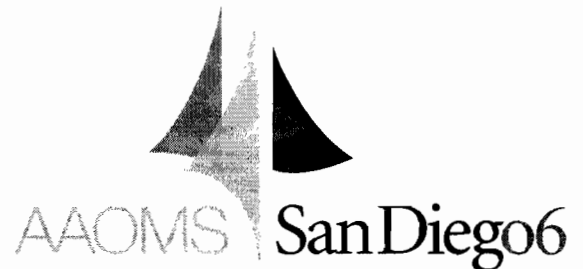
**Subject:** Interim Progress Report on Third Molar Clinical Trials

**cc:** Oral and Maxillofacial Surgery Foundation Board of Directors

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## INTERIM PROGRESS REPORT THIRD MOLAR CLINICAL TRIALS

July 12, 2006

This interim report on Third Molar Clinical Trials was requested by the AAOMS House of Delegates in 2005. This brief report and the attached appendices summarize a complex project spanning almost a decade.

Ash, Costich, and Hayward in 1962 alerted clinicians to the fact that 3<sup>rd</sup> molar periodontal pathology was common, and demonstrated that early 3<sup>rd</sup> molar removal in late teen years precluded periodontal problems <sup>(1)</sup>. Third molar removal in young adults was adopted widely as a preventive measure.

Subsequently, in a series of clinical trials with 3<sup>rd</sup> molar removal, Kugelberg demonstrated that periodontal defects detected presurgery on 2<sup>nd</sup> molars adjacent to 3<sup>rd</sup> molars were likely to repair if 3<sup>rd</sup> molars were removed before the mid 3<sup>rd</sup> decade of age. <sup>(2)</sup> Kugelberg's data also suggested 3<sup>rd</sup> molar removal in young adults.

Based on the only epidemiologic data published to date, Hugoson and Kugelberg reported in 1987 that 95% of young adults have at least one 3<sup>rd</sup> molar, 75% have four 3<sup>rd</sup> molars <sup>(3)</sup> According to the 2000 US Census, 4 million are in each age year from 15-25 years, a total of 40 million individuals. As 3<sup>rd</sup> molar removal was adopted almost universally, the magnitude of this health measure attracted attention from those who make health policy.

Responsibly, the AAOMS board endorses the concept that current recommendations for 3<sup>rd</sup> molar treatment are supported by clinical and biological data. A special committee was appointed in 1993 to critically review the existing literature. Though not current, data on clinical outcomes after 3<sup>rd</sup> molar removal still seemed accurate. Lacking was data on the prevalence of clinical pathology for those retaining 3<sup>rd</sup> molars, most often pericoronitis, periodontitis or coronal caries. The special committee believed that a prospective longitudinal trial enrolling subjects willing to retain 3<sup>rd</sup> molars was needed, but the estimated required length of such a trial, estimated then at a minimum of 7 years to evolve meaningful data, made the effort almost prohibitive. <sup>(4)</sup>

Wisely, the AAOMS board sought a comprehensive set of clinical trials to assess the risks of retaining 3<sup>rd</sup> molars as well as more current data on recovery after 3<sup>rd</sup> molar removal. I was asked to design and implement such trials to generate data as the basis for decision making for 3<sup>rd</sup> molar treatment. To the credit of those involved, the charge was "to look broadly at 3<sup>rd</sup> molar treatment", not limited to surgical problems. The collective clinical studies became known as Third Molar Clinical Trials.

When it became clear that others outside our specialty were not interested in funding research targeted to the special topic of 3<sup>rd</sup> molar treatment, Third Molar Clinical Trials was supported jointly by the Oral and Maxillofacial Surgery Foundation and the American Association of Oral and Maxillofacial Surgeons. In addition departmental funds from the participating university academic centers, supporting the effort since the initiation of these clinical studies, have been substantial and critical to the success of the project

A longitudinal trial conducted at the University of Kentucky and the University of North Carolina enrolling asymptomatic patients retaining 3<sup>rd</sup> molars was unique and a key component of the clinical research. This trial became the "center piece" of Third Molar Clinical Trials. Subjects (356) were enrolled over a 4 year period ending in 2002 and have at least one follow-up visit. Fifty-three percent are female, 78% Caucasian, and half are above age 25 years. The enrolled young adult subjects are a diverse sample of the United States population with only Hispanic subjects under represented.

As of January 2006, data from 195 subjects with follow-up at least 4 years after enrollment were available for analyses. Median follow-up was 5.9 years (Interquartile range 4.6 – 6.9y) and median age at enrollment was 26.3 years (Interquartile range 22.0 – 34.0y). Data collection from these subjects continues at the University of Kentucky and the University of North Carolina.

Though no one knew what or how quickly data might emerge, the plan was to fund the trial for at least 4 years. If important data was derived, the longitudinal trial could be extended. To the surprise of those directly involved in the research, baseline data from these young adults at enrollment documented substantial periodontal pathology affecting the 3<sup>rd</sup> molar region as well as coronal caries on exposed 3<sup>rd</sup> molars. These findings are documented in peer reviewed publications, almost all in the Journal of Oral and Maxillofacial Surgery. (See Appendix A)

Data from the subjects followed over time suggest that in a considerable number of young adults periodontal pathology initiates in the mandibular 3<sup>rd</sup> molar region, spreads forward in the lower jaw, up to the 3<sup>rd</sup> molar region of the maxilla, and subsequently forward in that jaw. These findings are compatible with current biological models of periodontal disease, though no other data exists, gathered over this time frame time from young asymptomatic subjects.

Although the focus has been on pathology affecting the 3<sup>rd</sup> molar region, we find that we have data which is unique, addressing periodontal disease and caries on individuals in the 3<sup>rd</sup> decade of life. Our data on chronic oral inflammation implicating 3<sup>rd</sup> molars has emerged at the same time as the data suggesting that chronic oral inflammation has a systemic impact with negative cardiovascular, obstetric, metabolic, and renal health outcomes. Our analyses suggest that 3<sup>rd</sup> molar periodontal pathology contributing to chronic oral inflammation in young adults, is a major contributor to a systemic inflammatory response with immediate negative consequences for affected pregnant women, elevated serum C-reactive protein or preterm birth

Clinicians following the publications in our Journal emanating from the longitudinal trial have raised multiple questions which might be answered by further data collection and analyses. However, our current focus is on documenting further the initiation and spread of periodontal pathology from the 3<sup>rd</sup> molar region, the impact of 3<sup>rd</sup> molar removal on the inflammatory process with the disease, and the fate of impacted 3<sup>rd</sup> molars which could not be probed at baseline. In addition 1<sup>st</sup> and 2<sup>nd</sup> molar caries experience in the enrolled subjects as risk indicators for the incidence of 3<sup>rd</sup> molar coronal caries is being explored.

The inclusion/exclusion criteria from the longitudinal trial, requiring subjects have no 3<sup>rd</sup> molar symptoms at enrollment, precluded study of a common outcome of retaining 3<sup>rd</sup> molars, pericoronitis. An exploratory trial of consecutive subjects having 3<sup>rd</sup> molars removed after mild symptoms of pericoronitis, suggested that affected individuals might be distinguished by an exaggerated inflammatory response to the colonization of periodontal pathogens in biofilm established in the lower 3<sup>rd</sup> molar region.(5) To address this topic further, a clinical trial was begun in late 2005 studying pericoronitis; the oral inflammatory response, the potential systemic inflammatory response, and the genetic tendency predisposing the individual to a hyperinflammatory reaction to the pathogens in the oral biofilm in the 3<sup>rd</sup> molar region. To date 20 subjects of the anticipated 50 required have been enrolled, and half have had 3<sup>rd</sup> molars removed after baseline data collection. Subjects will be followed for at least six months after 3<sup>rd</sup> molar removal.

Third Molar Clinical Trials is distinguished by having multiple investigators and clinicians participating. Seventeen non-surgeons with recognized expertise in their respective fields have contributed along with 25 surgeons. An initially unrecognized benefit from these multiple interactions has been access to 3<sup>rd</sup> molar data derived from NIH sponsored clinical studies. Third molar data has been published from Oral Conditions and Pregnancy (OCAP), the dental components of Piedmont 65+ and Atherosclerosis Risk in Communities (DARIC). Particularly important has been the analyses from OCAP whose subjects have considerably more periodontal pathology during pregnancy than subjects in our longitudinal trial. Periodontal pathology in the 3<sup>rd</sup> molar region is a major contributor to disease severity in OCAP, and data from OCAP and Third Molar Clinical Trials suggest a disease progression not addressed in prior clinical studies. Keeping these key non-surgeon investigators involved in our efforts offers continued access to 3<sup>rd</sup> molar data emerging from other NIH sponsored trials.

In addition to the longitudinal trial of subjects retaining 3<sup>rd</sup> molars over time cited above, primary data also has been collected from multi-site clinical trials of recovery after 3<sup>rd</sup> molar surgery. These clinical studies have a unique aspect as well. The experimental design targeted recovery data from the patients' perspective, quality of life outcomes, as well as clinical data. An important initial step was the design and validation of an

instrument to collect health related quality of life data affecting several domains: lifestyle, oral function, pain and other symptoms related specifically to recovery after 3<sup>rd</sup> molar surgery. This instrument has subsequently been modified by other clinical investigators to monitor quality of life recovery from oral and maxillofacial procedures such as orthognathic surgery and implant surgery. To date, recovery data after 3<sup>rd</sup> molar surgery has been collected from over 1,100 patients across 8 states involving 7 academic clinical centers and 12 community practices. Data collection and analyses continue to confirm and further validate what we have reported as risk indicators of delayed recovery.

This research endeavor has been quite successful. Over 65 abstracts and papers have been published, almost all in our Journal. (See Appendix A) An annotated bibliography of peer reviewed publications is in Appendix B. The clinical data we report has been recognized for the quality of the science on multiple occasions, including the Laskin Award for best paper in the Journal and the Oral and Maxillofacial Surgery Foundation Research Award in 2003, and the best clinical research paper from the UNC faculty in 2004. Abstracts presented by residents won awards for best presentations at the AAOMS meetings in 2004 and 2005. UNC dental students won two of the seven awards for posters at the UNC Dental Research Day in 2006, and one of these was selected as the sole UNC submission for the American Dental Association Meeting in 2006. I am particularly proud that we have been able to involve 19 students/residents/ fellows in our clinical research efforts. All have contributed beyond the experience gained from participation.

Two questions might be raised at this point in time. Should AAOMS in concert with the Foundation continue to support targeted clinical research? Certainly the experience we report suggests a positive response. Two topics surrounding this issue must be considered for the future. A formal process led to the recognition of the need for Third Molar Clinical Trials. A similar project might not be successful without a concerted planning exercise. Secondly, if our specialty does not continue to support targeted clinical research on topics of special interest to our specialty, no one else will do it!

What is the future of Third Molar Clinical Trials? From my perspective, important clinical questions regarding 3<sup>rd</sup> molar treatment remain. Some are cited above. If the longitudinal trial is terminated it is unlikely to be repeated soon. However, I must accept that my personally gratifying academic career is coming to a close. I remain committed to the project, and I am comfortable with addressing the topic of continuing the project annually with the recognition that my involvement must be short term.

On behalf of all who have participated in Third Molar Clinical Trials, I offer thanks to AAOMS and to the Foundation for their support which made the project possible.

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## REFERENCES

- 1) Ash MM, Costich ER, Hayward JR: A study of periodontal hazards of third molars. J Periodont 33:208, 1962
- 2) Kugelberg CF, Ahlstrom U, Ericson S, Hugoson A, Kvint S: Periodontal healing after impacted lower third molar surgery in adolescents and adults. Int J Oral Maxillofac Surg 20: 18, 1991
- 3) Hugoson A, Kugelberg CF: The prevalence of third molars in a Swedish population. An epidemiological study. Comm Dent Health 5: 121, 1987
- 4) Report of the special committee. J Oral Maxillofac Surg 52:1104, 1994

## Appendix A

### Annotated Bibliography Third Molar Clinical Trials

(July 2006)

After an AAOMS sponsored, comprehensive review of the literature (JOMFS 52:1104,'94), it became obvious that more data must be generated to evolve data based decision making for 3<sup>rd</sup> molar treatment. Wisely, the AAOMS Board sought a comprehensive set of clinical trials to assess the risks of retaining 3<sup>rd</sup> molars as well as data on recovery after 3<sup>rd</sup> molar removal.

A unique aspect of the clinical studies is a longitudinal trial of patients retaining 3<sup>rd</sup> molars. Though the time frame required to generate adequate data might be too short, this initial trial was planned for 5 years. Since this "exploratory trial" led to meaningful clinical data, the trial has been extended.

Concurrently, prospective, multisite clinical trials were implemented addressing both clinical and Health Related Quality of Life (HRQOL) recovery after 3<sup>rd</sup> molar surgery. A prospective, longitudinal design with primary data collection involving investigators from multiple disciplines as well as surgeons, has led to a rich set of data about 3<sup>rd</sup> molar treatment.

AAOMS and the OMS Foundation continue to support "Third Molar Clinical Trials".

The following citations and comment summarize progress to date:

#### A) RECOVERY after THIRD MOLAR SURGERY

Shugars DA, Benson K, White RP Jr, Simpson KN, Bader JD: Developing a measure of patient perceptions of short-term outcomes of third molar surgery.

J Oral Maxillofac Surg 54:1402,'96

*Validation of condition specific, Health Related Quality Of Life questionnaire, designed to capture the patients' perception of recovery after 3<sup>rd</sup> molar surgery for 14 days post surgery.*

Conrad SM, Blakey GH, Shugars DA, Marciani RD, Phillips C, White RP Jr: Patients' perception of recovery following third molar surgery.

J Oral Maxillofac Surg 57:1288,'99

*Average HRQOL recovery after 3<sup>rd</sup> molar surgery for 300 patients from 2 academic centers with bivariate analysis.*

White RP Jr, Shugars DA, Shafer DM, Laskin DM, Buckley MJ, Phillips C: Recovery after third molar surgery: Clinical and health related quality of life outcomes.

J Oral Maxillofac Surg 61: 535, '03

UNC Clinical Research Award '04

*Average HRQOL and clinical recovery after 3<sup>rd</sup> molar surgery for 630 patients from 9 community practices across 5 states and 5 academic centers.*

Phillips C, White RP Jr, Shugars D, Zhou X: Risk factors associated with prolonged recovery and delayed clinical healing after third molar surgery.

J Oral Maxillofac Surg 61:1436, '03

*What predicts delayed recovery, identified by multivariate analysis from 547 patients with clinical data and data from 14 days post surgery. Age above 18 years, female, and both lower 3<sup>rd</sup> molars below the occlusal plane increased the odds of delayed HRQOL recovery. Prior 3<sup>rd</sup> molar symptoms, female and the surgeon's estimate of difficulty at surgery increased the odds of delayed clinical recovery.*

Ruvo A, White RP Jr, Shugars DA, Phillips C: Delayed clinical recovery and health related quality of life outcomes after third molar surgery.

J Oral Maxillofac Surg 63:929, '05

*If delayed clinical recovery, significant negative impact on HRQOL recovery. Risk doubled for delay in recovery for lifestyle, oral function, and pain. Adds to justification for interventions to prevent delayed clinical recovery.*

Snyder M, Shugars DA, White RP Jr, Phillips C: The role of pain medication after third molar surgery in recovery for lifestyle and oral function.

J Oral Maxillofac Surg 63:1130, '05

*Another predictor for delayed recovery: if patients taking pain meds, NSAID or OPIOID as a behavioral indicator of perceived pain, recovery delayed for lifestyle and oral function.*

Hull D, Shugars DA, White RP Jr, Phillips C: Radiographic proximity of lower third molars to the inferior alveolar canal as a predictor of delayed recovery.

In press J Oral Maxillofac Surg 9/06

*If a lower 3<sup>rd</sup> molar was close the inferior alveolar canal, recovery twice as likely for delayed recovery for oral function and pain.*

Foy SP, Shugars D, Phillips C, Marciani RD, Conrad SM, White RP Jr: Outcomes following third molar surgery with intravenous antibiotics in patients at risk for delayed recovery. J Oral Maxillofac Surg 62:15, '04

*IV antibiotics at surgery improved clinical recovery for targeted higher risk patients, but not HRQOL recovery.*

Tiwana PS, Foy SP, Shugars DA, Marciani RD, Conrad SM, Phillips C, White RP Jr:

The Impact of Intravenous Corticosteroids with Third Molar Surgery in Patients at High Risk for Delayed Health Related Quality of Life and Clinical Recovery.

J Oral Maxillofac Surg 63:55, '05

*For targeted higher risk patients, IV corticosteroids at surgery with no antibiotics did not delay clinical recovery. Minimal, but positive impact on HRQOL recovery. Did reduce patient reports of the impact of nausea post surgery.*

Stavropoulos F, Shugars D, Phillips C, Conrad SM, Fleuchaus P, White RP Jr: Outcomes following third molar surgery with topical minocycline in patients at risk for delayed recovery. J Oral Maxillofac Surg 64:1059, 2006

*For targeted higher risk patients topical antibiotics at surgery, minocycline in slow release PLGA microspheres, placed in lower 3<sup>rd</sup> molar extraction sites, significantly improved clinical recovery and recovery for oral function. Clinical outcomes with topical antibiotics could be differentiated from clinical outcomes with IV antibiotics.*

Noori H, Hill D, Shugars DA, Phillips C, White RP Jr: Lower third molar root development and recovery from 3<sup>rd</sup> molar surgery. Accepted J Oral Maxillofac Surg 2/06

Poster award UNC Dental Research Day '06

*Removing 3<sup>rd</sup> molars when the lower 3<sup>rd</sup> molar roots incomplete gave no advantage in recovery as compared to surgery with roots complete! Also, no disadvantage in recovery was incurred.*

Shugars DA, Gentile MA, Ahmad N, Stavropoulos MF, Slade GD, Phillips C,

Conrad SM, Fleuchaus PT, White RP Jr: Assessment of Oral Health Related Quality Of Life Before and After Third Molar Surgery. Accepted 4/06 J Oral Maxillofac Surg

Poster award UNC Dental Research Day '06, ADA '06

*Complementary instruments to measure quality of life outcomes, the more global Oral Health Impact Profile (OHIP-14) and the condition specific Health Related Quality of Life (HRQOL) instrument, provide a broader understanding of recovery after 3<sup>rd</sup> molar surgery.*

## B) EPIDEMIOLOGY / POPULATION STUDIES

Elter JR, Cuomo C, Slade GD, Offenbacher S, White RP Jr: Relationship of third molars to periodontal health in NHANES III. *J Oral Maxillofac Surg* 62:440, '04

*Sample of US population 18-34 years representing four million persons in US each age year. If examiner could see a 3<sup>rd</sup> molar in the quadrant, increased risk of periodontal probing depth  $\geq 5\text{mm}$  on the adjacent 2<sup>nd</sup> molar, OR 2.1, (95% CI 1.6 - 2.8).*

Elter JR, Offenbacher S, White RP Jr: Third molars associated with periodontal pathology in older Americans. *J Oral Maxillofac Surg* 63:179, '05

*Sample of US population, 7,000 men and women aged 52 – 64 years, being studied over time for cardiovascular disease. If examiner could see a 3<sup>rd</sup> molar in the quadrant, increased risk of periodontal probing depth  $\geq 5\text{mm}$  on adjacent 2<sup>nd</sup> molar, OR 1.6, (95% CI 1.4 - 1.8).*

Moss KL, Mauriello S, Offenbacher S, White R, Beck JD: Systemic impact and reliability of third molar probing measures. *J Dent Res* 84 (Spec Iss A) Abs 1067, '05

*Third molar periodontal probing depths as accurate as probing other teeth.*

*For Oral Conditions and Pregnancy Clinical Trial (1020 subjects) multivariate analysis for moderate/severe periodontal disease, >15sites PD  $\geq 4\text{mm}$  including 3<sup>rd</sup> molars, odds were increased for preterm birth, OR 1.7, (95%CI 1.1 - 2.6). Not significant for preterm birth if 3<sup>rd</sup> molars not included.*

Moss KL, Ruvo AT, Mauriello SM, Offenbacher S, White RP Jr, Beck JD:

The Systemic Impact of Third Molar Periodontal Pathology.

*J Oral Maxillofac Surg* 64:652, '06

*For Oral Conditions and Pregnancy Clinical Trial (405 subjects with a visible 3<sup>rd</sup> molar) multivariate analysis for outcomes; if upper quartile 3<sup>rd</sup> molar PD  $\geq 4\text{mm}$  alone was considered, odds were increased for preterm birth, OR 2.4 (95% CI 1.4 - 4.4). Upper quartile of 3<sup>rd</sup> molar PD  $\geq 4\text{mm}$  alone was associated with elevated serum CRP levels, OR 2.3 (95%CI 1.3 - 4.3), and elevated serum d8iso levels, OR 3.4 (95%CI 1.9- 6.4), at enrollment.*

Moss KL, White RP Jr, Mauriello SM, Offenbacher S, , Beck JD:

Third Molar Periodontal Disease and Caries in the Elderly.

Accepted *J Oral Maxillofac Surg* 11/05

*For elderly subjects, mean age 73 years, 3<sup>rd</sup> molar caries experience and periodontal pathology were associated with that of non-3<sup>rd</sup> molars. Few subjects, 17%, had clinical evidence of both caries and periodontal pathology affecting 3<sup>rd</sup> molars. In this elderly population of subjects no periodontal pathology or caries experience were detected in 21%.*

Moss KL, Beck JD, Mauriello SM, Offenbacher S, White RP Jr: Risk Indicators for Third Molar Caries and Periodontal Disease in Senior Adults. Accepted *J Oral Maxillofac* 4/06

*African American subjects had more retained 3<sup>rd</sup> molars and were likely to have periodontal pathology with 3<sup>rd</sup> molars. Caucasians were more likely to have 3<sup>rd</sup> molar caries experience.*

Moss KL, Ruvo AT, Offenbacher S, Beck JD, Mauriello SM, White RP Jr: Third molars and progression of periodontal pathology during pregnancy.

Submitted *J Oral Maxillofac Surg* 4/06

*In multivariable models, either 3<sup>rd</sup> molar PD  $\geq 4\text{mm}$  at enrollment (RR 1.4, 95% CI 1.1- 2.0), or 3<sup>rd</sup> molar Bleeding On Probing at enrollment (RR 1.7, 95% CI 1.3 – 2.3) were associated with periodontal disease progression between enrollment and postpartum, 4 or more probing sites with at least 2mm increasing depth, all being at least 4mm.*

## C) RETAIN THIRD MOLARS – PERICORONITIS

Slade GD, Foy SP, Shugars DA, Phillips C, White RP Jr: The impact of third molar symptoms, pain and swelling, on oral health related quality of life.

*J Oral Maxillofac Surg* 62:1118, '04

37% of 480 patients had pain or swelling in 3 months prior to surgery sufficient to seek removal of 3<sup>rd</sup> molars before symptoms occurred again. One quarter of the symptomatic patients reported by the 12 item global oral health impact profile before surgery, that their lifestyle measures were affected "fairly often" or "very often". Difficulty relaxing, feeling irritable, feeling tense, interruptions to meals reported most frequently.

Blakey GH, White RP Jr, Offenbacher S, Phillips C, Delano EO, Maynor G: Clinical/biological outcomes of treatment for pericoronitis.

J Oral Maxillofac Surg 54:1150, '96

Only "orange complex" bacteria and GCF IL-1  $\beta$  inflammatory mediators elevated, distinguishing acute pericoronitis from periodontitis. Removal of 3<sup>rd</sup> molars eliminated the "orange complex" bacteria from the patients' biofilm.

#### D) RETAIN THIRD MOLARS Longitudinal Trial- PERIODONTITIS

Blakey GH, Marciani RD, Haug RH, Phillips C, Offenbacher S, Pabla T, White RP Jr: Periodontal pathology associated with asymptomatic third molars.

J Oral Maxillofac Surg 60:1227, '02

At baseline one quarter of 329 asymptomatic patients enrolled in a longitudinal clinical trial had at least one periodontal probing depth  $\geq 5$ mm on the distal of 2<sup>nd</sup> molars or around 3<sup>rd</sup> molars with at least 2mm attachment loss. If patients  $\geq 25$  years old, 33% of mandibular 3<sup>rd</sup> molars affected. Third molars at the occlusal plane and vertical affected with the same frequency as mesioangular/horizontal 3<sup>rd</sup> molars below the occlusal plane. Prevalence periodontitis higher than NHANES III data which did not assess 3<sup>rd</sup> molar region.

White RP Jr, Madianos PN, Offenbacher S, Phillips C, Blakey GH, Haug RH,

Marciani RD: Microbial complexes detected in the second/third molar region in patients with asymptomatic third molars. J Oral Maxillofac Surg 60:1234, '02

At baseline "orange and red" complex periodontal bacteria detected greater than  $10^3$  in 80% and greater than  $10^5$  in 44% of 295 asymptomatic patients with periodontal PD  $\geq 5$ mm in the 3<sup>rd</sup> molar region. "Red" complex pathogens not detected without "orange".

White RP Jr, Offenbacher S, Haug RH, Blakey GH, Phillips C: Inflammatory mediators and periodontitis in patients with asymptomatic third molars.

J Oral Maxillofac Surg 60:1241, '02

For 316 asymptomatic patients at baseline, if PD  $\geq 5$ mm in the third molar region, GCF IL-1 $\beta$  significantly elevated as compared to patients with PD  $< 5$ mm. GCF PGE<sub>2</sub> not significantly elevated, confirming early periodontitis in affected patients.

Nance PE, White RP Jr, Offenbacher S, Phillips C: Change in third molar angulation/position and periodontal pathology. J Oral Maxillofac Surg 64: 424, 2006

Periodontal pathology more likely if 3<sup>rd</sup> molars vertical or distal in angulation and at the occlusal plane. PD  $\geq 4$ mm in 52% erupted mandibular 3<sup>rd</sup> molars.

Nance PE, White RP Jr, Offenbacher S, Phillips C, Blakey GH, Haug RH:

Third Molar Periodontal Pathology in the Third Decade and Periodontal Pathogens

J Oral Maxillofac Surg Suppl 1 63:69, 2005

Of the 3<sup>rd</sup> molar regions in the maxilla with  $\geq 10^5$  pathogens at baseline, 22% had PD  $\geq 4$ mm at follow-up. In the mandible with  $\geq 10^5$  pathogens at baseline, 63% had PD  $\geq 4$ mm at follow-up. If pathogens  $\geq 10^5$  are detected with PD  $\geq 4$ mm, both are likely in the same quadrant.

Blakey GH, Jacks MT, Offenbacher S, Nance PE, Phillips C, Haug RH, White RP Jr:  
Progression of Periodontal Disease in the Second/Third Molar Region in Subjects with Asymptomatic Third Molars. J Oral Maxillofac Surg 64:189, '06  
*Among 254 subjects at enrollment, 59% had at least one PD  $\geq 4$ mm in the 3<sup>rd</sup> molar region. When the same subjects were followed for a median of 2.2 years, 38% had a change PD $\geq 2$ m if baseline PD $\geq 4$ mm. If PD $< 4$ mm at baseline, only 3% had a change PD $\geq 2$ mm.*

White RP Jr, Offenbacher S, Blakey, Haug RH, GH, Jacks, MT, , Nance PE, Phillips C:  
Chronic Oral Inflammation and the Progression of Periodontal Pathology in the Third Molar Region. J Oral Maxillofac Surg 64:880, 2006  
*For 250 subjects, baseline PD  $\geq 4$ mm in the 3<sup>rd</sup> molar region or baseline "orange and red" complex periodontal bacteria  $\geq 10^5$  were significantly associated a change in PD  $\geq 2$ mm.*

Vandersea B, Hambright T, Offenbacher S, Phillips C, Blakey G, Haug, R, White R  
Clinical periodontal outcomes in the third molar region after third molar removal.  
J Oral Maxillofac Surg Suppl 1 63:70, 2005  
*For 38 of 39 subjects at least 6mo post surgery, PD on the distal of 2<sup>nd</sup> molars was  $< 4$ mm. However, levels of "orange and red" complex periodontal bacteria  $\geq 10^5$  were unchanged from baseline to 2.2 year follow-up.*

Blakey GH, Hull D, Haug RH, Offenbacher S, Phillips C, White RP Jr: Changes in Third Molar and non-Third Molar Periodontal Pathology Over Time.  
Submitted J Oral Maxillofac Surg 7/06  
*Data from 195 subjects, median follow-up 5.9 years (IQ 4.6 - 6.9y), median age at enrollment 26.2 years (IQ 22.0 - 34.0y). Periodontal pathology worsened incrementally over time for non-3<sup>rd</sup> molars. This was more likely if PD  $\geq 4$ mm was detected in the 3<sup>rd</sup> molar region.*

#### **E) RETAIN THIRD MOLARS - OCCLUSAL CARIES**

Shugars DA, Jacks TM, White RP Jr, Phillips C: Occlusal caries in patients with asymptomatic third molars. J Oral Maxillofac Surg 62:973, '04  
*At baseline 28% of 303 asymptomatic patients had at least one 3<sup>rd</sup> molar with occlusal caries; 39% if age  $\geq 25$  years. Lower 3<sup>rd</sup> molars more often affected than upper. Less than 2% 3<sup>rd</sup> molars had occlusal caries if 1<sup>st</sup> and 2<sup>nd</sup> molars caries free.*

Shugars DA, Elter JR, Jacks TM, Phillips C, White RP Jr, Haug RH, Blakey GH: Progression of third molar occlusal caries in patients with asymptomatic third molars.  
J Oral Maxillofac Surg 63:341, '05  
*For 211 patients with median 2.9 year follow-up 33% had 3<sup>rd</sup> molar caries as compared to 29% at baseline. All the increase in caries was in the cohort  $< 25$  years old; most in the mandible. Only 1% 3<sup>rd</sup> molars had occlusal caries if 1<sup>st</sup> and 2<sup>nd</sup> molars caries free.*

## Appendix B

### ABSTRACTS/PAPERS THIRD MOLAR CLINICAL TRIALS (July 2006)

#### ABSTRACTS

- Blakey G, *Offenbacher S*, White RP, *Maynor G*, *Socransky S*: Identification of risk markers for pericoronitis. J Oral Maxillofac Surg Suppl 4 53:110,'95
- Conrad SM, Blakey GH, Marciani RD, *Shugars D*: Patient perception of recovery following third molar surgery. J Oral Maxillofac Surg Suppl 3, 54: 63,'96
- Conrad S, Blakey G, Marciani R, *Shugars D*, *Phillips C*: Recovery following third molar surgery. J Dent Res Suppl 76: 289,'97
- Conrad SM, Blakey GH, Marciani RD, *Shugars DA*, *Phillips CL*: Factors affecting patients' perception of recovery following third molar surgery. J Oral Maxillofac Surg Suppl 3 55:53,'97
- Folck M, *Shugars D*, *Phillips C*, Laskin D, White R: Patients' perceptions of recovery following third molar surgery. J Dent Res Suppl 79:340,'00
- Foy SP, *Shugars D*, *Phillips C*, Laskin D, White R: Patients' perception of recovery following third molar surgery. J Oral Maxillofac Surg Suppl 1 58:37,'00
- Blakey GH, Haug R, *Offenbacher S*, *Phillips C*, White R: Periodontal pathology in patients with asymptomatic third molars. J Oral Maxillofac Surg Suppl 1 59:56,'01
- Foy SP, *Shugars D*, *Phillips C*, Marciani RD, Conrad SM, White R: Recovery after third molar surgery with intravenous antibiotics. J Dent Res Special Issue A 81:A317,'02
- Cuomo C, *Elter JR*, *Slade GD*, *Offenbacher S*, White R: Relationship of third molars to periodontal measures in NHANES III. J Dent Res Special Issue A 81:A317,'02
- Bowen SM, White RP, *Madianos PN*, *Offenbacher S*, Blakey GH, Haug RH, *Phillips C*: Microbial complexes detected in the second/third molar area in patients with asymptomatic third molars. J Dent Res Special Issue A 81:A317,'02
- Phillips C*, *Gai F*, White R, *Offenbacher S*, Blakey G, Haug R: Prediction modeling for the periodontal pocketing around third molars. J Dent Res Special Issue A 81:A449,'02
- Foy SP, *Shugars D*, *Phillips C*, White RP Jr: Predictors of prolonged recovery after third molar surgery. J Oral Maxillofac Surg Suppl 1 60:43,'02
- Jacks M, *Shugars D*, White RP Jr, *Phillips C*: Occlusal caries in patients with asymptomatic third molars. J Oral Maxillofac Surg Suppl 1 60:72,'02
- Bowen SM, White RP Jr, *Shugars D*: The impact of inferior alveolar nerve deficit on Health related Quality of Life outcomes after third molar surgery. J Oral Maxillofac Surg Suppl 1 60:43,'02

Elter JR, Cuomo C, Offenbacher S, White RP Jr: Relationship of visible third molars to periodontal disease in NHANES III. J Oral Maxillofac Surg Suppl 1 60:45, '02

Foy S, Slade GD, Shugars DA, Phillips C, White RP Jr: The impact of third molar symptoms on oral health related quality of life. J Oral Maxillofac Surg Suppl 1 61:25, '03

Tiwana P, Foy SP, Shugars DA, Marciani RD, Conrad SM, Phillips C, White RP Jr: The impact of IV corticosteroids on oral health related quality of life outcomes and clinical recovery after third molar surgery. J Oral Maxillofac Surg Suppl 1 61:55,'03

Jacks TM, Shugars DA, White RP Jr, Phillips C, Haug RH, Blakey GH: Progression of occlusal caries experience in patients with asymptomatic third molars. J Oral Maxillofac Surg Suppl 1 61:26, '03

Jacks TM, White RP Jr, Offenbacher S, Blakey GH, Haug RH, Phillips C: Progression of periodontitis in the second/third molar region in patients with asymptomatic third molars. J Oral Maxillofac Surg Suppl 1 62:22, '04  
AWARD for Best Abstract Presentation!

Ruvo A, White RP Jr, Shugars DA, Phillips C: Delayed clinical recovery and health related quality of life outcomes after third molar surgery. J Oral Maxillofac Surg Suppl 1 62:23, '04

Hull D, White RP Jr, Shugars DA, Phillips C: Proximity of the third molar to the inferior alveolar canal as a predictor of clinical and health related quality of life outcomes after third molar removal. J Oral Maxillofac Surg Suppl 1 62:33, '04

Elter JR, Offenbacher S, White RP Jr: Association of third molars with periodontal pockets: The Dental ARIC Study. J Oral Maxillofac Surg Suppl 1 62:73,'04

Steen M, Shugars DA, White RP Jr, Phillips C: Pain after third molar surgery and lifestyle/oral function recovery. J Dent Res 84 (Spec Iss A) Abs 0096, '05

Nance PE, White RP Jr, Offenbacher S, Phillips C: Change in third molar angulation/position and periodontal pathology. J Dent Res 84 (Spec Iss A) Abs 3497, '05

Moss KL, Mauriello S, Offenbacher S, White RP Jr, Beck JD: Systemic impact and reliability of third molar probing measures. J Dent Res 84 (Spec Iss A) Abs 1067, '05

Nance PE, White RP Jr, Offenbacher S, Phillips C, Blakey GH, Haug RH: Third Molar Periodontal Pathology in the Third Decade and Periodontal Pathogens. J Oral Maxillofac Surg Suppl 1 63:69, 2005

Ruvo AT, Moss KL, Mauriello SM, Offenbacher S, White RP Jr, Beck JD: The systemic impact of third molar periodontal pathology. J Oral Maxillofac Surg Suppl 1 63:69, 2005

Vandersea B, Hambricht T, Offenbacher S, Phillips C, Blakey G, Haug, R, White R: Clinical periodontal outcomes in the third molar region after third molar removal. J Oral Maxillofac Surg Suppl 1 63:70, 2005  
AWARD for Best Abstract Presentation!

Stavropoulos MF, Shugars DA, Phillips C, Conrad SM, Fleuchaus PT, White RP Jr: Outcomes following third molar surgery with topical minocycline in patients at risk for delayed recovery. AADR '06

*Moss KL, White RP Jr, Mauriello SM, Offenbacher S, Beck JD:*  
Third molar periodontal disease and caries in senior adults. AADR '06

Noori H, Hill D, Shugars D, Phillips C, White R: Third molar root development and recovery from 3<sup>rd</sup> molar surgery. AADR '06  
AWARD Dental Research Day 2/06

*Shugars D, Gentile M, Ahmad N, Stavropoulos M, Slade G, Phillips C, Conrad S, Fleuchaus P, White R:* Assessment of Oral Health Related Quality Of Life Before and After Third Molar Surgery. Accepted AAOMS '06  
AWARD Dental Research Day 2/06

Ruvo A, Moss K, Beck J, Mauriello S, White R, Offenbacher S: Third molars and progression of periodontal pathology during pregnancy. Accepted AAOMS '06

Hull D, Blakey G, Haug R\*, Offenbacher S, Phillips C, White R: Changes in Third Molar and non-Third Molar Periodontal Pathology Over Time. Accepted AAOMS '06

**OMFS residents, fellows or dental students underlined,  
non surgeon faculty investigators in *italics***

## PAPERS

Blakey GH, White RP Jr, Offenbacher S, Phillips C, Delano EO, Maynor G: Clinical/biological outcomes of treatment for pericoronitis.  
J Oral Maxillofac Surg 54:1150,1996

Shugars DA, Benson K, White RP Jr, Simpson KN, Bader JD: Developing a measure of patient perceptions of short-term outcomes of third molar surgery.  
J Oral Maxillofac Surg 54:1402,1996

Conrad SM, Blakey GH, Shugars DA, Marciani RD, Phillips C, White RP Jr: Patients' perception of recovery following third molar surgery.  
J Oral Maxillofac Surg 57:1288,1999

Blakey GH, Marciani RD, Haug RH, Phillips C, Offenbacher S, Pabla T, White RP Jr: Periodontal pathology associated with asymptomatic third molars.  
J Oral Maxillofac Surg 60:1227, 2002

White RP Jr, Madianos PN, Offenbacher S, Phillips C, Blakey GH, Haug RH, Marciani RD: Microbial complexes detected in the second/third molar region in patients with asymptomatic third molars. J Oral Maxillofac Surg 60:1234, 2002

White RP Jr, Offenbacher S, Haug RH, Blakey GH, Phillips C: Inflammatory mediators and periodontitis in patients with asymptomatic third molars.  
J Oral Maxillofac Surg 60:1241, 2002

White RP Jr, Shugars DA, Shafer DM, Laskin DM, Buckley MJ, Phillips C: Recovery after third molar surgery: Clinical and Health Related Quality of Life outcomes.  
J Oral Maxillofac Surg 61: 535, 2003

Phillips C, White RP Jr, Shugars DA, Zhou X: Risk factors associated with prolonged recovery and delayed clinical healing after third molar surgery.  
J Oral Maxillofac Surg 61:1436, 2003

Foy SP, Shugars DA, Phillips C, Marciani RD, Conrad SM, White RP Jr: Outcomes following third molar surgery with intravenous antibiotics in patients at risk for delayed recovery. J Oral Maxillofac Surg 62:15, 2004

Shugars DA, Jacks TM, White RP Jr, Phillips C, Haug RH, Blakey GH: Occlusal caries in patients with asymptomatic third molars. J Oral Maxillofac Surg 63:973, 2004

Elter JR, Cuomo C, Slade GD, Offenbacher S, White RP Jr: Relationship of third molars to periodontal health in NHANES III. J Oral Maxillofac Surg 62:440, 2004

Slade GD, Foy SP, Shugars DA, Phillips C, White RP Jr: The impact of third molar symptoms, pain and swelling, on oral health related quality of life. J Oral Maxillofac Surg 63:1118, 2004

White RP Jr: Recovery after Third Molar Surgery: Conference Summary. Am J Orthod Dentofac Orthoped 126:289, 2004

Tiwana PS, Foy SP, Shugars DA, Marciani RD, Conrad SM, Phillips C, White RP Jr: The impact of intravenous corticosteroids with third molar surgery in patients at high risk for delayed Health Related Quality of Life and clinical recovery. J Oral Maxillofac Surg 63:55, 2005

Elter JR, Offenbacher S, White RP Jr: Third molars associated with periodontal pathology in older Americans. J Oral Maxillofac Surg 63:179, 2005

Shugars DA, Elter JR, Jacks TM, Phillips C, White RP Jr, Haug RH, Blakey GH: Incidence of occlusal dental caries in asymptomatic third molars. J Oral Maxillofac Surg 63:341, 2005

Ruvo A, Shugars DA, White RP Jr, Phillips C: Delayed clinical recovery and health related quality of life outcomes after third molar surgery. J Oral Maxillofac Surg 63:929, 2005

Phillips C, Preisser J, Fang G, Offenbacher S, White R Jr, Blakey G, Haug R: Prediction modeling for periodontal pathology around third molars. In press '06 Commun Dent Health

Snyder M, Shugars DA, White RP Jr, Phillips C: The role of pain medication after third molar surgery on recovery for lifestyle and oral function. J Oral Maxillofac Surg 63:1130, 2005

Nance PE, White RP Jr, Offenbacher S, Phillips C, Blakey GH, Haug RH: Change in third molar angulation/position and periodontal pathology. J Oral Maxillofac Surg 64: 424, 2006

Moss KL, Mauriello SM, Ruvo AT, Offenbacher S, White RP Jr, Beck JD: Reliability of third molar probing measures and the systemic impact of periodontal pathology. J Oral Maxillofac Surg 64:652, 2006

Stavropoulos MF, Shugars DA, Phillips C, Conrad SM, Fleuchaus PT, White RP Jr: The impact of topical Minocycline with third molar surgery on clinical recovery and Health Related Quality of Life Outcomes. J Oral Maxillofac Surg 64:1059, 2006

Hull D, Shugars DA, White RP Jr, Phillips C: Radiographic proximity of lower third molars to the inferior alveolar canal as a predictor of delayed recovery. In press 9/06 J Oral Maxillofac Surg

Blakey GH, Jacks MT, Offenbacher S, Nance PE, Phillips C, Haug RH, White RP Jr: Progression of periodontal disease in the second/third molar region in patients with asymptomatic third molars. J Oral Maxillofac Surg 64:189, 2006

White RP Jr, Offenbacher S, Blakey GH, Haug RH, Jacks MT, Nance PE, Phillips C: Chronic oral inflammation and the progression of periodontal pathology in the third molar region. J Oral Maxillofac Surg 64:880, 2006

Moss KL, Beck JD, Mauriello SM, Offenbacher S, White RP Jr:  
Third molar periodontal disease and caries in senior adults.  
Accepted 11/05 J Oral Maxillofac Surg

Noori H, Hill D, Shugars DA, Phillips C, White RP Jr: Lower third molar root development and recovery from 3<sup>rd</sup> molar surgery.  
Accepted 2/06 J Oral Maxillofac Surg

Shugars DA, Gentile MA, Ahmad N, Stavropoulos MF, Slade GD, Phillips C, Conrad SM, Fleuchaus PT, White RP Jr: Assessment of Oral Health Related Quality Of Life Before and After Third Molar Surgery. Accepted 4/06 J Oral Maxillofac Surg

Moss KL, Beck JD, Mauriello SM, Offenbacher S, White RP Jr: Risk Indicators for Third Molar Caries and Periodontal Disease in Senior Adults.  
Accepted 4/06 J Oral Maxillofac Surg

Moss KL, Ruvo AT, Offenbacher S, Beck JD, Mauriello SM, White RP Jr: Third molars and progression of periodontal pathology during pregnancy.  
Submitted J Oral Maxillofac Surg 4/06

Blakey GH, Hull D, Haug RH, Offenbacher S, Phillips C, White RP Jr: Changes in Third Molar and non-Third Molar Periodontal Pathology Over Time.  
Submitted J Oral Maxillofac Surg 7/06