1991 Research Report

Department of Orthopaedics

UNIVERSITY OF WASHINGTON

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Department
of Orthopaedics
University of Washington
Seattle, Washington 98195

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COVER ILLUSTRATION: These computer-generated images show three-dimensional motions of the shoulder complex. The images are not the result of a simulation or model, but rather show the actual glenohumeral and scapulothoracic motions of a living subject. In this case the computer is used as tool to help develop a deeper undestanding of the mechanics of the shoulder. These images were produced on an IRIS workstation using software written by Dr. John Sidles.

Contents


AMERICAN SHOULDER and ELBOW SURGEONS
1982


THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS
INC.
Ορθόν Παιδίον
MCMXXXIII


International Society for the Study of the Lumbar Spine
1974

Foreword

The University of Washington Department of Orthopaedics has three primary missions:

1. To provide outstanding education to the orthopaedic leaders of the future.
2. To provide excellent service to the patients and referring physicians of our region.
3. To make important contributions to the body of knowledge on which the practice of orthopaedics is based.

This report presents some of the ways we are achieving the third goal. Clinical and basic research are vital to the progress of orthopaedics as a clinical science. This Department is concerned with a broad range of challenging questions, for example:

- What physical and non-physical factors are associated with complaints of low-back pain by a worker?
- Can nerve transplantation be used to bridge otherwise irreparable defects in peripheral nerves?
- Can the break-down products of bone excreted in the urine be used as an assay for the early detection of osteoporosis?
- What are the factors controlling the repair of articular cartilage?
- What factors control the functional outcome of treatment for serious musculoskeletal injuries?
- Can bioactive substances be used to strengthen fractured or weakened bone?
- What is the structure of articular cartilage?
- What role does the scapula play in optimal function of the shoulder joint?

The Department is attaining substantial national recognition for its accomplishments in investigating such questions. At the March 1991 combined meetings of the American Academy of Orthopaedic Surgeons and the related specialty societies, Department faculty delivered more than 70 major presentations. Three of these presentations were awarded accolades for research excellence: Dr. Stan Bigos and his co-workers received the Kappa Delta Award for their study of factors affecting back-pain reporting in workers. The Volvo Award was presented to Dr. Michele Battié and her co-workers for their investigations on the relationship of smoking to degeneration of the intervertebral disk. The Charles Neer Award went to Drs. Doug Harryman and John Sidles for their work on glenohumeral laxity in normal subjects.

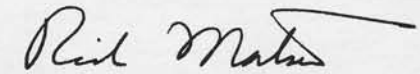
The excellence of departmental research also has been recognized by the National Institutes of Health. Under the principal investigatorships of Drs. David Eyre, Linda Sandell, and Stan Bigos, our Department ranks third nationally in total NIH grant dollars awarded. It is well recognized that the competition for NIH dollars is becoming increasingly intense. The ascendance of the Department of Orthopaedics in this competition is a remarkable accomplishment.

One of the factors that has promoted departmental research productivity is the institution of departmental Research Support Grants. Support for these grants comes from private donations and from dollars generated by the clinical practice of the faculty. Faculty and residents are encouraged to submit grant requests to the Department's Research Advisory Committee. These grants are peer-reviewed exactly as they would be if they were submitted to the National Institutes of Health and then are prioritized for funding. As can be seen in this report, departmental grants have been instrumental in many of our important investigative programs.

The Department recognizes the need for attracting new creative minds to the challenge of improving orthopaedic patient care through quality research. To this end we have substantially enhanced the resident research program. Each resident now defines a major research topic in the first year and submits it for review by the Department's Resident Research Committee. Yearly progress reports culminate in written and oral formal presentations by the chief residents at Resident Research Day, this year scheduled for June 14-15. A noted orthopaedic surgeon and investigator is invited each year to discuss these research presentations. Our inaugural guest research professor will be Dr. Bill Garrett from Duke University, an authority in sports medicine research and patient care. The University of Washington orthopaedic alumni are generously supporting this program.

Resident research also is supported to a major degree by the resources of the new D.K. Clawson Library at Harborview and the Clinical Research Center at the University, both of which were made possible by contributions from the Department's many supporters. In recognition of our growing profile in resident research, we have been asked to host the 1993 American Orthopaedic Association Resident Research Conference.

In conclusion, I would like to thank all those who have participated in the organization, conduct, and support of the Department's research activities. This volume presents only a sampling of the clinically relevant research that would not have been possible without the efforts of these individuals. Through our support of meaningful investigations we can contribute to orthopaedic knowledge and improve the care of our patients.



Frederick A. Matsen III, M.D.
Professor and Chairman

Low Back Pain Reporting in the Workplace

Stanley J. Bigos, M.D.
Michele C. Battié, Ph.D.

Back problems are one of the most expensive health care problems in persons aged 20 to 50, the most expensive industrial injury, and the most common cause of disability in adults under 45 years of age. The impact on the lives of individuals, on industry, and on society poses a challenge for orthopaedists. Our efforts to treat patients with back problems are undermined by our lack of good scientific data and useful knowledge about this condition. The cause of symptoms in the vast majority of back pain patients remains unknown, and many of the approaches to restoring function or preventing disability are undependable.

1991 Kappa Delta Award

This most prestigious award in orthopaedics, presented by the American Academy of Orthopaedic Surgeons, this year went to Dr. Stanley J. Bigos, principal investigator of "A Longitudinal, Prospective Study of Industrial Back Injury Reporting." This landmark report is the culmination of the 11-year "Boeing Study." Dr. Michelle Battié is a co-investigator on the seven-member study team that also includes Professor Alf Nachemson of Sweden. This is the fourth time that Department investigators have won the Kappa Delta Award.

Prospective Study

Back symptoms are very common among workers; each year up to 50% complain of back symptoms or experience activity limitations for at least one day. Yet, only 2% to 5% of workers file a back injury claim. Certainly the severity of symptoms and the physical demands of the job are likely to influence decisions to report a back injury, but factors other than the presence of symptoms play a role as well.

Our investigation is the first major prospective study of psychosocial and physical factors contributing to the reporting of back pain by industrial workers. From July 1982 through September 1983, 3,020 hourly employees from the Boeing-Everett plant volunteered to participate in the study, representing approximately 75% of the workers solicited.

Employees underwent a physical examination to measure anthropometric variables, flexibility, isometric lifting strength, and estimated aerobic capacity. A back examination included lower extremity girths, straight leg raise testing, and evaluation of reflexes. At the time of the physical examination, we also obtained medical history, demographic, and psychosocial information. All subjects were asked to complete the Minnesota Multiphasic Personality Inventory (MMPI), which assesses traits that have been associated clinically with back pain disability and chronic pain. The Modified Work APGAR was used to examine perceptions of support at the workplace and job enjoyment.

Over the next four years we tracked the study participants during their employment with the Boeing Company to identify those who filed an incident report or a claim for back injury complaints. The data analysis used survival analysis techniques to identify associations with back pain reporting. During four years of follow-up, more than 279 subjects reported acute back problems.

Results

Data analysis led to the following findings and conclusions:

1. The strongest variables for predicting the report of subsequent acute back injury report were: (a) the amount of work time lost for back pain during the previous six months, and (b) acute back symptoms that precluded strength testing at the time of the initial physical examination.

2. Factors commonly used in preemployment screening, such as range of motion and general isometric lifting strength, were not helpful in predicting acute back injury reports.

3. Smoking was associated with a 40% increased risk of reporting back pain as compared to workers who did not smoke.

4. The strongest physical factor associated with the subsequent report of acute back problems was pain in the back or limbs prior to any rocking of the pelvis when raising the straight leg in the supine position. Nevertheless, straight leg raising was not a very good predictor, as it only doubled the risk of reporting acute back injury (20% vs. 10% within a four-year follow-up). More notable was that four out of five workers with symptoms on straight leg raising did not file a back injury claim during follow-up.

5. Other than current or recent back problems, the strongest predictors of future reports were perceptions of the workplace such as low job enjoyment. Work APGAR responses of "hardly ever enjoying job tasks" and relatively high scale 3 scores on the MMPI, indicating tendencies toward somatic complaints and denial of emotional distress, were strongly associated with subsequent back injury reports.

As orthopaedic surgeons, we must accept that nonphysical stresses in a person's life or work can influence the response to back problems. Symbolically, back pain may be the "straw" that breaks the back of the already burdened camel. Concomitantly, removal of the straw may not allow the camel to bounce right back to its feet. Concentrating only on eliminating back pain may not spring the patient back to his or her feet to resume normal life activities. Back problems may be only one component of the person's overall predicament.

Orthopaedists who provide primary care and surgical treatment for patients with back disorders see the full spectrum of back pain, back injury claims, back pain disability, and the ensuing negative social consequences. This broad perspective provides a basis for understanding the findings of our study. Orthopaedists have the opportunity to assume a leadership role in altering the course of the low back pain epidemic.

In summary, our longitudinal, prospective, interdisciplinary study has led to a more scientific and meaningful analysis of back pain complaints. It points out why a focus on purely physical and injury factors has met with little success in dealing with what has become society's most expensive orthopaedic problem. The data do not support continued emphasis on unalterable markers such as age and sex, or on physical capacities such as strength and flexibility. Instead, this study demonstrates that nonphysical factors can significantly impact the reporting of back injuries and also may affect how a patient responds to medical treatment. This research opens the door to a more educated, positive, and effective approach for screening workers, treating patients, and preventing disability.

Supported by a grant from the National Institutes of Health, by the Boeing Corporation, and the University of Washington Department of Orthopaedics.

Smoking and Lumbar Intervertebral Disc Degeneration

A Study of Identical Twins Using MRI

Michele C. Battié, Ph.D.
Tapio Videman, M.D., Ph.D.
Kevin Gill, M.D.
Giovanni B. Moneta, Ph.D.
Rickard Nyman, M.D.
Jaakko Kaprio, M.D., Ph.D.
Markku Koskenvuo, M.D., Ph.D.

Recently smoking has been added to the list of suspected risk factors for back pain complaints. Several theories have attempted to explain the association between smoking and back problems. One theory is that smoking affects the intervertebral disc. This assumption is not surprising, since many clinicians and scientists believe the disc is most likely responsible for symptoms, particularly when sciatica is present.

Our study attempted to determine whether disc degeneration, as assessed through MRI, is greater in smokers than in nonsmokers. To control for the maximum number of potentially confounding variables, carefully selected pairs of identical twins highly discordant for cigarette smoking were chosen as study subjects. Twenty pairs of identical twins were selected from the Finnish Twin Cohort. The subjects were all men, ranging from 36 to 60 years of age. The mean difference in cigarette smoking between the exposed and control co-twins was 31 pack-years.

An extensive, structured interview was conducted with each subject to obtain information on smoking history, as well as occupational exposures, leisure activities, traumatic injuries, and general medical history. While one twin was interviewed, the co-twin underwent MRI of the lumbar spine. The MRI examinations were performed with a Siemens Magnetom, with an operating field strength of 0.5 Tesla, using surface coils. Two independent investigators highly experienced in MRI conducted blinded evaluations of T2-weighted images.

These evaluations resulted in a degeneration score for the anterior, middle, and posterior portion of each disc using a four-point scale. The final degeneration score for each disc was the mean of the three partial scores. The spines of identical twin pairs showed a high degree of similarity, underscoring the value of using appropriately selected twins to control for many potentially confounding factors, and isolating the effects of smoking to the greatest degree possible. The high correlation coefficient of the degeneration scores between co-twins increases the power of the analysis for detecting the effects of smoking, and supports the choice of study design.

Data analyses revealed 18% greater mean disc degeneration scores in the lumbar spines of smokers as compared to nonsmokers. The effect was present across the entire lumbar spine, implicating a systemic mechanism (Figure).

1991 Volvo Award

The Volvo Awards are given each year by the Society for the Study of the Lumbar Spine (ISSLS) for outstanding research related to spinal disorders and back pain. This study on smoking and lumbar disc degeneration won the award in the basic science category. Michele Battié (photo on page 2) presented the paper on May 15 at the ISSLS Annual Meeting in Heidelberg, Germany. The paper also will be featured in the September 1991 issue of *Spine*.

Smoking could cause disc degeneration through several possible mechanisms. Vasospasms or arteriosclerotic changes caused by smoking may have a negative effect on the blood supply to the vertebral bodies and other structures surrounding the discs, and subsequently affect disc nutrition. Toxic substances in cigarette smoke also may have deleterious effects on disc metabolism and accelerate degeneration. However, further study is needed to determine the specific mechanism through which smoking may act.

To our knowledge, this is the first study to examine the effects of smoking on the human intervertebral disc. This efficient study design using identical twins is likely to be a valuable tool in further identifying and understanding other risk factors for disc disease, and eventually in the broader study of back symptoms.

Supported by an NIH grant entitled "Spine Pathology and Low Back Pain Determinants in Identical Twin Pairs."

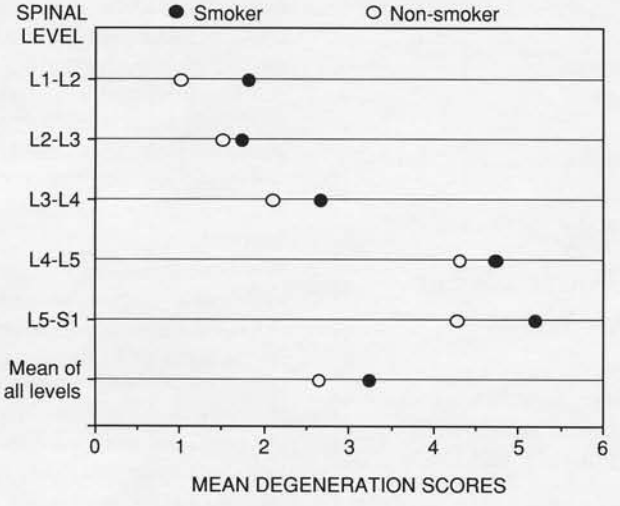


FIGURE: Mean Disc Degeneration Scores of Smokers and Non-Smokers.

How Lax Is the Normal Shoulder?

A Quantitative In-Vivo Assessment

John A. Sidles, Ph.D.
Douglas T. Harryman II, M.D.
Frederick A. Matsen III, M.D.

1991 Charles Neer Award

Dr. Charles S. Neer II generously established an annual award for the most important research presented to the American Shoulder and Elbow Surgeons. The Department shoulder and elbow team was so recognized this year. Team members are Dr. Frederick Matsen (standing), Dr. Douglas Harryman (seated), and Dr. John Sidles, absent from the photo but represented by the computer.

Evaluation of pathologically unstable glenohumeral joints is predicated on knowing the laxity of normal joints. To help define the laxity of normal shoulders, we undertook a quantitative study of eight male volunteers. To our knowledge this is the first time the laxity elicited on standard clinical tests has been quantified *in vivo*.

Methods

We studied normal shoulders of eight male volunteers aged 25 to 45. We used a system for measuring all translations and rotations of the glenohumeral joint via sensors attached to the scapula and humerus via percutaneous steel pins. With this system we measured the translations of the humeral head on the glenoid produced during clinical standard tests of glenohumeral laxity. These tests included the anterior and posterior drawer, the sulcus, the push-pull test and the crank test (also known as the apprehension test). Figure 1 shows computer generated images of the translation of a normal shoulder.

Results

The glenohumeral translations for a given subject were highly reproducible. For example, Figure 2 shows the raw data for a *single* subject for the anterior and posterior drawer test. Notice the consistent end-point for maximum anterior and posterior translation.

By contrast, the results for the magnitude of translation among *different* subjects were highly variable. Shoulders lax on one test were likely to be lax on the others, and shoulders tight on one test were likely to be tight on the others.

For all eight subjects, the average anterior humeral head translation for the anterior drawer test was 7.8 ± 4.0 mm (range: 2 to 13 mm). The average posterior humeral head translation for the posterior drawer test was 7.9 ± 5.6 mm with a range of 3 to 20 mm. The average inferior translation for the inferior sulcus test was 10.6 ± 3.8 mm (range: 5 to 15 mm). The average posterior translation on the push-pull test was 9.0 ± 6.3 mm (range: 3 to 22 mm). The average anterior humeral head translation on the crank test was -0.3 ± 2.5 mm (range: -3 to 5 mm).

Discussion

What is *normal* glenohumeral joint laxity? While clinical tests of shoulder laxity are commonly used to help diagnose shoulder instability and determine the need for and type of surgical repair to be performed, there are no objective criteria that establish whether a given amount of laxity is "normal." Our finding that normal, asymptomatic shoulders show substantial translation on stress testing demonstrates that joint laxity does not equate to clinical instability. This observation is particularly relevant to the common clinical practice of using an examination under anesthesia to determine the repair to be performed.

Clinical methods for measuring glenohumeral translation are limited in accuracy and reproducibility. Radiographic examination during stress testing has been used to evaluate joint laxity, but the analysis depends on accurate orientation of the shoulder to the radiographic beam and film. Our method of *in vivo* three-dimensional measurement of motion provides a unique opportunity to quantitate all translations and rotations accompanying commonly used clinical tests of glenohumeral stability.

Although posterior glenohumeral translation may seem easier to "feel", it is evident from our results that humeral head translation occurs to a similar extent anteriorly, posteriorly, and inferiorly. We were struck by the consistency of average translation on four laxity tests performed in positions where the capsulo-ligamentous restraints are lax (anterior and posterior drawer, sulcus, and push-pull). The mean translation for each of these tests resulted in an average translation of about one centimeter. These data lend support to a global concept of glenohumeral stability for the uninjured shoulder in which similar magnitudes of translation are found in different directions of laxity testing. For the shoulders in our study group, we estimated that the humeral head subluxated up to 35% of its diameter anteriorly and posteriorly from the glenoid fossa with drawer testing. Posterior translation on the push-pull test was estimated at 40% and inferior translation on the sulcus test was estimated at 44% of the humeral head diameter. By contrast, when the capsular ligaments are placed under tension, as in the crank test, minimal translation occurs.

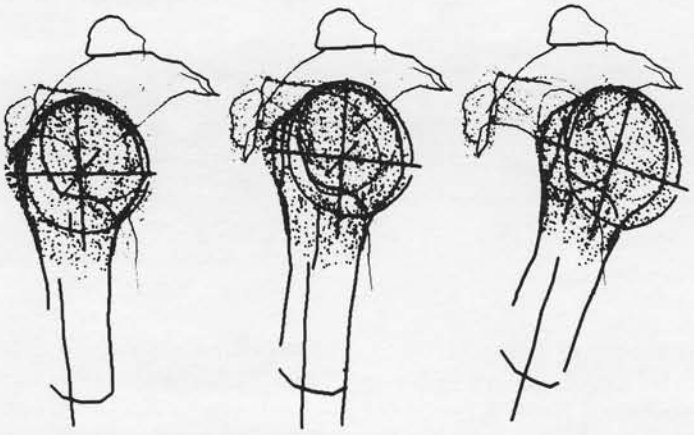


FIGURE 1: Computer reconstruction of the translation of a normal glenohumeral joint from a lateral view. L to R — anterior, neutral, posterior.

Conclusions

Substantial glenohumeral translations occurred in normal shoulders during clinical laxity tests. Translations were reproducible in each subject's shoulder, but showed marked inter-subject variability. The finding that normal glenohumeral joints can show substantial translations suggests that translation on laxity testing is *not* in and of itself a sufficient indication for surgical stabilization. It is critical to differentiate the concepts of mechanical laxity from clinical instability.

Supported by the University of Washington Department of Orthopaedics.

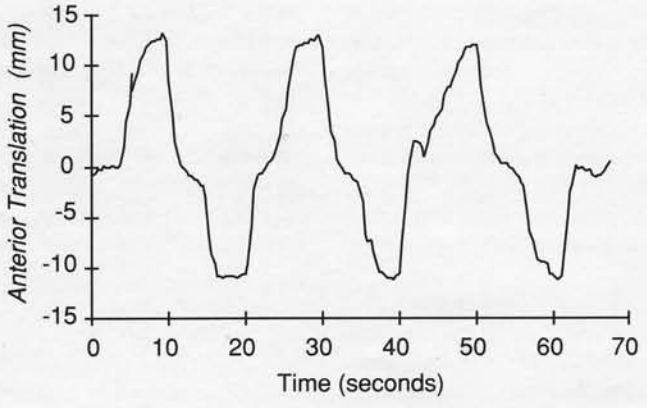


FIGURE 2: Anterior and posterior drawer test for a single subject.

Connective Tissue Biochemistry

David R. Eyre, Ph.D.

Biochemistry of Articular Cartilage and the Intervertebral Disc: Normal and Degenerative States

Co-Investigators: J.J. Wu, P. Woods, P.E. Knigge

The remarkable mechanical integrity of the fibrous collagen framework of articular cartilage, intervertebral disc, and other load-bearing cartilages is crucial for the function of joints. How cartilage collagen is held together at the molecular level, how it differs from collagens of other tissues, and the mechanism of its degradation in osteoarthritis and in disc degeneration are the focus of this project.

Using methods of structural protein analysis, we discovered that the principal type of collagen articular cartilage (genetic type II) does not simply polymerize as a homopolymer to form fibrils, but that an entirely different and unusual form of collagen molecule (type IX) is copolymerized with it. This is an example of a so-called fibril-associated collagen molecule, which has very unusual properties, including a highly charged polysaccharide chain and flexible joints along its length. It appears to act in the matrix of cartilage as a flexible link or tether that is critical for the cohesive strength of the bulk fibril network.

The clinical significance of this work is that these covalent links from type IX collagen to type II collagen are degraded as an early event in osteoarthritis (based on experimental models in animals) by a proteolytic enzyme, stromelysin (Figure). The chondrocytes are switched on to synthesize this protease for tissue remodeling. Thus, the swelling and increased hydration of articular cartilage that has been observed as an early event in laboratory studies of osteoarthritis may well be mediated by a selective degradation of this quantitatively minor collagen ingredient that acts as a matrix glue.

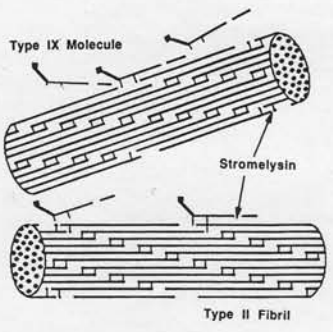


FIGURE: Fibril model showing how stromelysin might remove type IX collagen molecules from the surfaces of type II collagen fibrils. It can act as a telopeptidase on native type II collagen, and bisects native type IX molecules through their NC2 domains. If type IX collagen were able to link adjacent fibrils, then stromelysin could break such links.

Sponsored by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health, and the Ernest M. Burgess Endowed Chair for Orthopaedic Research.

The Role of Metalloproteinases in Bone Remodeling

Co-investigators: C. Niyibizi and A.M. Bollen

When osteoclasts attach to and resorb bone, they excavate the tissue surface first by removing mineral and then by secreting proteolytic enzymes that degrade the collagen matrix. This latter process probably occurs at acid pH outside the osteoclast, leading to the current hypothesis that lysosomal proteases are secreted to do the job rather than the collagenase and other metalloproteinases used in noncalcified tissues at neutral pH.

Extracts of fresh bone tissue, however, do contain significant levels of a metalloproteinase that can degrade bone collagen under certain conditions, notably denatured type I collagen (the main component) and mature type V collagen (a minor component). The significance of this enzymic activity in the metabolism of bone is being investigated. Is it, for example, the principal means by which osteoclasts resorb bone matrix?

Other observations indicate that bone collagen may be degraded in a different fashion, with different peptide bonds being broken, than occurs with the same genetic types of collagen in skin and other soft tissues. If so, this would point to an entirely different regulatory pathway that perhaps could be selectively targeted in future pharmacological therapies for bone disorders.

Sponsored by NIAMS, National Institutes of Health, and the Ernest M. Burgess Endowed Chair for Orthopaedic Research.

Inborn Molecular Defects that Cause Skeletal Disease

Co-investigators: C. Niyibizi, M.A. Weis, R. Bogaert

Research is defining the basic biochemical defects in heritable diseases of connective tissues that affect the skeleton, notably osteogenesis imperfecta (OI), Ehlers-Danlos syndrome, and certain chondrodystrophies. In particular, we are relating underlying mutations in the genes that encode the structural collagens (type I collagen genes in osteogenesis imperfecta and the type II collagen gene in chondrodystrophies) to tissue abnormalities and the clinical pathology.

Investigators have identified at least 50 different mutations in the COLlAl and COLlA2 genes that code for the collagen *al(I)* or *a2(I)* protein chains and that cause brittle bone disease (OI), varying in severity from lethal in utero to mild conditions and disease of late onset. Our goal is to determine the extent to which the bone pathology is caused by mutant protein in the extracellular matrix of bone tissue.

We are using the latest methods in protein microsequence analysis and working with surgical or autopsy tissue specimens from OI subjects with established mutations (e.g., single amino acid substitutions at known sites) to relate the clinical pathology to the degree of mutant protein expression (compared with normal gene expression) in bone tissue. Using similar methods, we also are characterizing mutations in new clinical cases.

Recent studies are beginning to define similar mutations in the COL2Al gene, which codes for type II collagen of cartilage, notably in the spondyloepiphyseal dysplasia (SED) spectrum of inborn disease. This condition also can range from lethal at or before birth to a very mild skeletal dysplasia, or even to no detectable abnormality during skeletal growth but an early onset of systemic osteoarthritis in the third or fourth decade of life. Families with this latter type of disorder highlight the importance of conducting studies on such rare, inherited disease. Evidence is emerging that not-so-rare mutations, and perhaps even fairly common polymorphisms in the human collagen genes, may be an important predisposing factor behind familial forms of osteoporosis (type I collagen) and aortic aneurysms (type III collagen) in addition to osteoarthritis (type II collagen).

Sponsored by NIAMS, National Institutes of Health, and the Ernest M. Burgess Endowed Chair for Orthopaedic Research.

A New Urinary Assay of Bone Resorption

Co-Investigators: D.A. Hanson, M.A. Weiss, S.K. Winfield

Collagen metabolites that result exclusively from bone degradation are excreted in urine and are being investigated as new and highly specific markers of bone resorption rates. They hold promise as useful prognostic indicators of metabolic bone disease and in the monitoring of therapy.

There are no wholly reliable biochemical markers of bone metabolism available to the clinician. Hydroxyproline, an amino acid that is derived from collagen and still frequently used as a urinary marker of bone turnover, is now known to have very little specificity and hence little utility as a bone marker. Our current project is based on the observation that novel peptide fragments of bone collagen are excreted in urine and provide the basis for a highly specific and reliable quantitative index of the rate of bone resorption in any human subject.

When bone tissue is resorbed, as it is continuously in the normal adult skeleton in approximate balance with the rate of new bone formation, both the mineral and the organic components are degraded. The matrix consists of 90% of collagen type I; on osteoclast resorption, most is returned to the metabolic pool as free amino acids. However, the cross-linking domains of the collagen molecules, which contain novel cross-linking amino acids, cannot be used further and are excreted in the urine. Furthermore, both the nature of the cross-linking amino acids and the protein domains they link are distinctive for bone tissue and so are a unique biomarker that can provide a specific urinary index of the rate of bone degradation.

Convenient and accurate methods for measuring these bone collagen metabolites have been developed and are being tested as monitors in diagnostic and therapeutic studies on patients with a diversity of clinical conditions, including Paget's disease, postmenopausal predisposition to osteoporosis, osteolytic tumors, and prostate cancer. Such an assay may be of particular value in monitoring the efficacy of drugs such as estrogen, calcitonin, and the newer bisphosphonates.

Sponsored by Ostex Incorporated, and the Ernest M. Burgess Endowed Chair for Orthopaedic Research.

The Effect of Localized, Controlled Release of Sodium Fluoride on Bone Formation

Allan F. Tencer, Ph.D.
Paul A. Anderson, M.D.

A mechanism for controlling the formation of bone at specific sites would be a most useful tool in the armamentarium of the orthopaedic surgeon. Applications of such a tool might include: stimulating spinal fusions, speeding resolution of delayed unions, increasing the amount of bone in the proximal femur in cases of deficiency, enhancing bone ingrowth in prosthetic arthroplasty, and repairing bone defects. Reported attempts to stimulate local bone formation include electrical stimulation and the application of bone morphogenic protein. These methods attempt to stimulate the biological phenomenon of bone formation and are distinct from attempts to add exogenous materials, such as bone grafting.

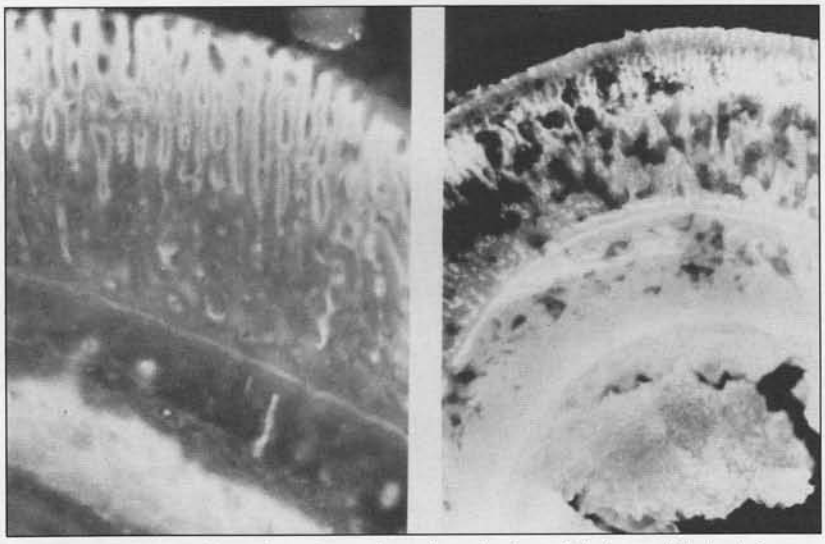


FIGURE 1: Examples of bone formation on the periosteal surface of the femoral diaphysis from two femora exposed to controlled release sodium fluoride.

Recent evidence indicates that sodium fluoride stimulates osteoblasts to form unmineralized matrix and may even cause mesenchyme to differentiate into pre-osteoblasts. Quantitative scanning techniques show that osteoporotic patients receiving oral fluoride have increased spinal trabecular mineral density. Fluoride appears to be effective for enhancing spinal bone density. On the negative side, osteoporotic patients treated with fluoride have a higher risk of fracture of the femoral neck, the tibial metaphysis, and calcaneus. These fractures are thought to be related to the fluoride-induced thinning of the cortex.

Based on these studies, we conclude that: (1) sodium fluoride can stimulate bone formation, and (2) fluoride can have different effects in different regions of the skeleton. The use of locally applied fluoride in orthopaedics is virtually unexplored. Such a topical application may enhance the selectivity of the effect of this agent.

We have studied the local application of fluoride to bone using a biodegradable polymer matrix. This polymer (poly [D,L] lactic acid, or PLA) is commonly used in degradable sutures such as Vicryl and Dexon, which are metabolized in the body to lactic acid and water. This polymer is moldable and easy to handle. Sodium fluoride can be embedded in the matrix as a solid mixture that is released by both diffusion through and erosion of the polymer. The rate of release is controlled by adjusting the molecular weight of the polymer and combining it with other polymers of the same family.

We performed two series of experiments to investigate the effect of fluoride on cortical and cancellous bone. The PLA was formed into a pin approximately 3.5 mm in diameter with a K-wire core for radiographic identification. These pins were implanted in New Zealand white rabbits, which have a demonstrated response to fluoride.

In the initial studies, we compared the effect of a fluoride containing intramedullary PLA pin to that of a control PLA pin containing no fluoride. The control and the experimental pins were inserted through a distal approach into the contralateral femoral canals of rabbits. Examination of femoral cross sections (Figure 1) revealed an increase in periosteal bone of 18% to 20% in the fluoride treated femora, predominantly in the distal areas.

In the second set of experiments, we controlled for the effect of the femoral entry point by comparing the bone formed in response to pins inserted through a proximal femoral hole with contralateral implants inserted through a distal hole. This technique also was used to insert implants containing no fluoride into a control group of rabbits. Again, periosteal bone increased by 18% to 20% adjacent to fluoride implants regardless of entrance hole site. We also found that in the fluoride treated femora, bending strength increased by 25%. No elevation occurred in serum fluoride levels, and neighboring bones were unaffected.

Subsequently, we have investigated the effect of locally applied fluoride on trabecular bone of the greater trochanter, the proximal metaphyseal region of the tibia, and the vertebral body. As compared to controls, fluoride-treated bones had significantly widened trabeculae (Figure 2) and decreased porosity. The number of trabeculae did not change, indicating that fluoride thickens trabeculae but does not cause new ones to form.

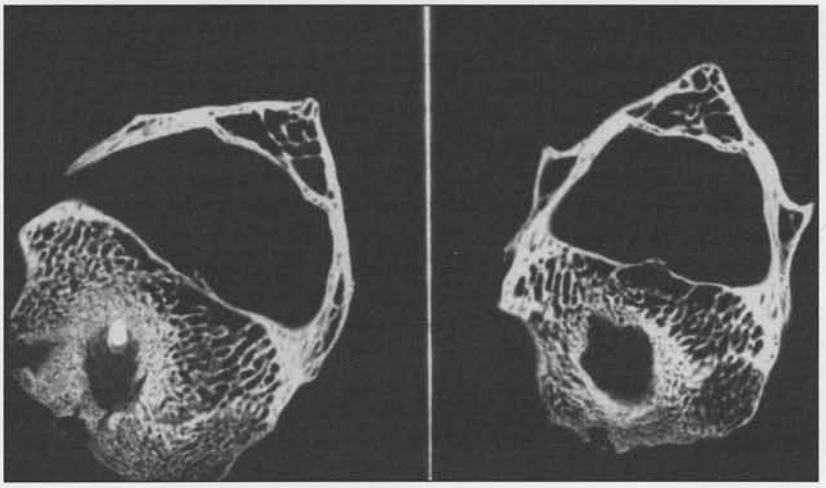


FIGURE 2: A comparison of trabecular density in adjacent vertebrae in which the left had a sham implant and the right contained a fluoride releasing implant.

These results demonstrate that topically applied fluoride can have a substantial effect on local bone metabolism. At present, we do not know the long-term fate of the bone formed in response to the application of fluoride, or whether these same responses would occur in patients in clinical studies. The PLA matrix appears to be well tolerated and may be useful in the topical application of other bioactive agents.

Supported by the University of Washington Department of Orthopaedics.

Measurement of the Outcome of Orthopaedic Trauma Management

Marc F. Swiontkowski, M.D.

Injury is the most common cause of death in the United States for persons under the age of 44. In 1986 injuries were the leading cause of years of potential life lost before age 65. For the noninstitutionalized population, injuries ranked second in direct medical costs, accounting for nearly $17 billion in medical care expenditures. Of all injuries, fractures accounted for the highest direct medical costs, greatest per capita charges, and largest number of restricted activity days based on data from the 1980 National Medical Care Utilization and Expenditures Survey.

The high costs and disabling nature of orthopaedic trauma point to the need for "outcomes" research, which evaluates the effectiveness of treatment from the patient's perspective. Outcomes research is assuming a more prominent role in the nation's health care agenda. In 1989 Congress established the Agency for Health Care Policy and Research (AHCPR) with a mandate to develop, review, and update guidelines to assist health care practitioners in the prevention, diagnosis, and management of clinical conditions. Congress appropriated $37.5 million for effectiveness research and related activities for fiscal year 1990 and $117 million for AHCPR, of which $63 million is earmarked to support medical effectiveness research in 1991. The objective is to help define the efficacy of health care procedures.

Orthopaedists lack good data regarding the effectiveness of treatment for musculoskeletal trauma. Information on long-term outcome is unavailable due to the lack of standardized classifications of injuries and standardized evaluation of the functional end result of treatment.

We established the Harborview Medical Center Orthopaedic Trauma Outcome Database on April 1, 1989, patterned after an initial experience with such a database at Vanderbilt Medical Center. The Harborview database has two essential components: baseline information entered at patient discharge and information entered at one-year follow-up. Baseline data is now available on more than 2,500 injuries of the spine, pelvis, and apendicular skeleton (Figure 1).

At the time of the patient's discharge we enter information on demographics, injury classification, treatment, and complications. At the one-year follow-up, patients are examined by their local orthopaedists, who usually were not involved in the initial care of their injuries. Radiographs are obtained and detailed information is recorded on functional limitations, deformity, range of motion, and any subsequent treatment procedures required during the elapsed year.

We now have follow-up data on approximately 65% of the patients who were treated one year ago. With the help of community physicians, we expect to obtain functional outcomes on 70% of the patients managed at Harborview Medical Center.

Our database is the first of its size and scope dealing with orthopaedic trauma, and already is generating important data regarding the mechanisms of injury. For example, Figure 2 demonstrate the effect of restraining devices on spinal injury patterns in drivers. Additional data

are available on injury level and fracture pattern. Finally, injury-specific outcome data can be used to assess the effect of various treatments, implants, and surgical approaches on function.

The Harborview database forms the cornerstone of efforts by the Orthopaedic Trauma Association to develop a standardized fracture and soft tissue injury classification system. Our Department also has submitted a $1.3 million grant to the AHCPR for the development of a functional outcome scale for upper and lower extremity injuries. The fracture classification system and outcome scale will enable us to deliver detailed functional outcome data for the many simple and complex fractures and dislocations managed at Harborview Medical Center. In the near future this database will help quantify the effect of treatment methods on the functional recovery from musculoskeletal trauma.

Supported by the Centers for Disease Control, the Orthopaedic Trauma Association, and the University of Washington Department of Orthopaedics.

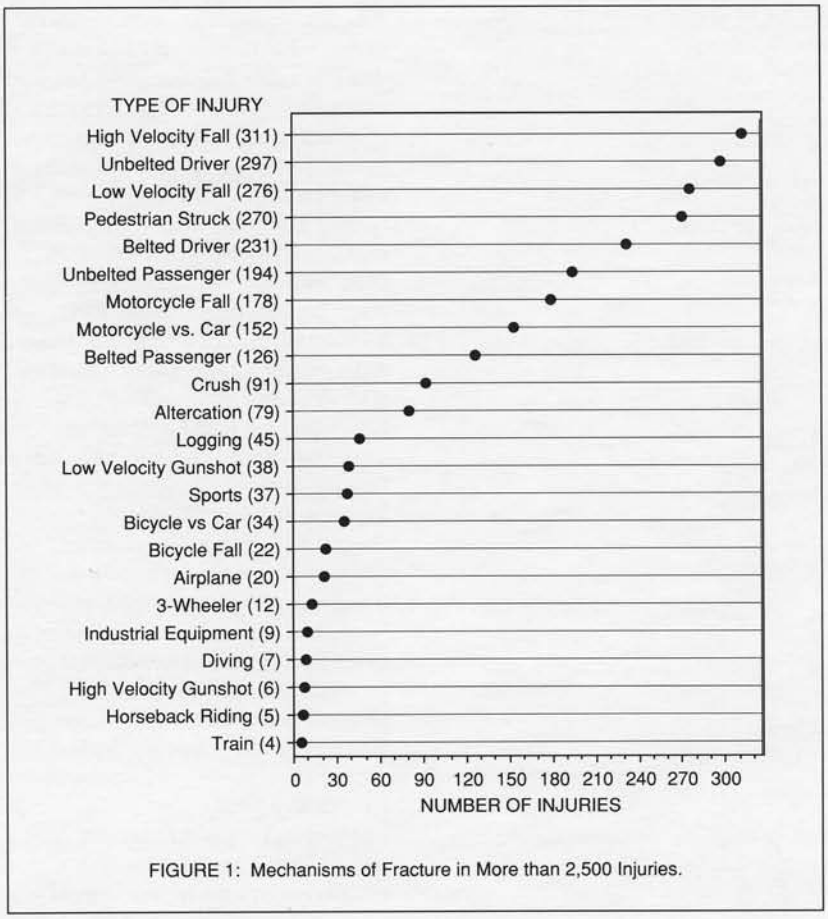


FIGURE 1: Mechanisms of Fracture in More than 2,500 Injuries.

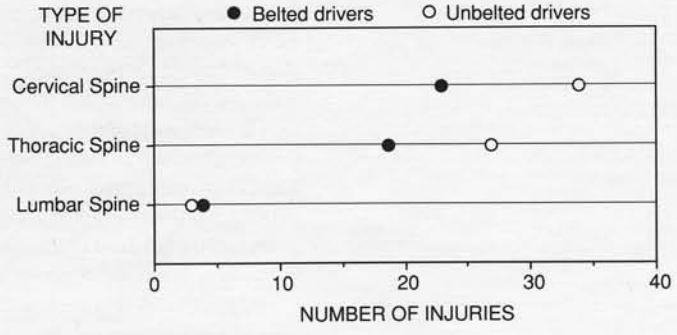


FIGURE 2: Spinal Injury Patterns in Belted and Unbelted drivers.

Tibial-Fibular Fracture Stabilization

M. Bradford Henley, M.D.

Tibial fractures vary according to the pattern, location, and the degree of soft tissue injury. Low-energy fractures with intact skin, minimal displacement, and osseous stability may be treated satisfactorily using casting or bracing. High-energy fractures often require surgical stabilization. Open fractures of the tibia and fibula require surgical care. Some surgeons prefer external fixation for all open tibial fractures, as this technique permits fracture stabilization with minimal additional trauma to the soft tissue envelope. Disadvantages of external fixation center around the potential for bone and soft tissue infection at the pin sites and biomechanical stresses leading to failure of the construct prior to osseous union. These factors contribute to a relatively high incidence of malunion and delayed union and have prompted clinicians to evaluate alternative treatment methods.

Laboratory Study

It has been proposed that the restoration of fibular continuity in association with a tibial external fixator may enhance the security of the external fixator/tibial construct. We designed a study to determine if plating of an associated fibular fracture increased the stiffness of the composite fracture/external fixator construct. Fresh tibiae were removed from donated cadavers and stripped of soft tissue, except for the interosseous membrane (IOM) and the proximal and distal tibio-fibular articulations.

The specimens were mounted upright in a material tester and loaded sequentially in axial compression, posterior to anterior bending, medial to lateral bending, and axial torsion. Each specimen first was tested with both the tibia and fibula intact. Then four 5-mm Schanz pins were drilled transversely through the anterior aspect of the tibial cortices, 5 cm apart in the sagittal plane. Two carbon fiber crossbars were secured to the pins by clamps completing a "double stacked half-pin frame." A 1-cm segment of bone then was removed from the mid-diaphysis of the tibia, leaving the fibula intact. After testing, the fibula was osteotomized obliquely at the same level as the tibia and the tests were repeated. Finally, the fibular osteotomy was stabilized with a six-hole 3.5-mm dynamic compression plate attached with six transverse cortical screws. The testing was repeated.

The data for each loading mode was normalized to the intact tibia to reduce the effects of secondary variables such as frame geometry and different specimen proportions. All constructs ranged from 36% to 44% of intact tibial stiffness in axial loading, but the state of the fibula did not exert a significant effect. In torsion, all constructs ranged from 28% to 29% of intact tibial stiffness, and again the structural state of the fibula — whether intact, osteotomized, or plated — made no difference. All constructs were equivalent in AP bending, both to each other and to the intact tibia, while in ML bending the constructs ranged from 67% to 78% in stiffness compared to the intact tibia. We concluded that there is no structural advantage to plating a fractured fibula in a model of an unstable tibial shaft fracture treated by an external fixator.

Clinical Study

As techniques improve, immediate internal fixation is increasingly being used to manage open fractures. As long as fracture stability is achieved, the incidence of infection and nonunion are similar to or better than with external fixation methods. Interlocking intramedullary nails can be applied to the intramedullary stabilization of comminuted, segmental, and metaphyseal fractures.

In a prospective, randomized clinical study we are comparing the use of small diameter nails (which are inserted without reaming to minimize endosteal vascular injury) to external fixation in the management of open tibial fractures. The purpose of this trial is to compare the safety and efficacy of unreamed IM nails to external fixation of Gustilo grade II and III open tibia-fibular fractures.

From January 1988 to January 1990, we studied 63 skeletally mature patients brought to Harborview Medical Center within 24 hours of injury. We excluded fractures less than 4 cm distal to the tibial tuberosity, less than 5 cm proximal from the tibial plafond, or those with more than a 10-cm segmental bone defect. The series included 32 grade II and 33 grade III (21-A, 12-B) open fractures. For 32 fractures we constructed a 4 half-pin anterior-medial external fixator (AO-Synthes), which was maintained until union or revision was required. Thirty-three patients received unreamed IM nails (32 Russell-Taylor, Richards; one Synthes). Locking was based on fracture pattern. Operative fracture care (emergent debridement, stabilization, and delayed closure) was standardized and comparable for both groups. The two groups also were comparable in age, sex, injury severity score, fracture location, and pattern. Follow-up averaged 14 months, with a range from six to 28 months.

FIGURE: Radiographs of a grade IIIa comminuted open tibia-fibula fracture in a 22-year-old man. The anteroposterior (L) and lateral (R) views show the stabilization with an external fixator. The fibula has been plated to serve as a substrate for planned postero-lateral bone graft.

In the IM nail group, 97% of fractures (32/33) united in an average of 25 weeks (range 12 to 53 weeks). Delayed unions in two fractures (6%) healed after removal of interlocking screws, which permitted dynamization of the fixation construct. A nonunion with IM nail (9 mm) breakage occurred in one fracture and required reamed nail exchange. Superficial infection developed in one patient, but responded to oral antibiotics. No intramedullary sepsis has occurred. Hardware failure occurred in four patients (12%), including IM nail fractures in two (one nonunion) and breakage of interlocking screws in two, all requiring revision surgery. Interlocking screws were removed in two patients and IM nails were removed in three. We performed 44 operative procedures for an average of 1.3 per patient.

In the external fixation group, 76% fractures united at an average of 30 weeks (range 16 to 60 weeks). Five patients remain in the external fixation frame with two requiring bone grafting for delayed union. Six nonunions (18%) required treatment as follows: two IM nailings, two bone grafts, one plating, and one casting. Malunions occurred in nine fractures (27%). Infected pin tracts led to premature external fixator removal at less than three months or before union in six patients (18%) while two others required pin exchange. A deep wound infection required operative debridement in one. We performed 69 operative procedures in this group for an average of 2.1 per patient.

Our study challenges previous published data claiming external fixation as the method of choice in grade II and IIIA open tibial diaphyseal fractures. In our hands, unreamed tibia nails, with or without locking, provided better results.

Supported by the University of Washington Department of Orthopaedics.

Fractures of the Hindfoot

Stephen K. Benirschke, M.D.
Bruce J. Sangeorzan, M.D.

Fractures of the hindfoot are common. Guidelines for optimal treatment of different fracture patterns are unclear, however. We are conducting laboratory and clinical studies to help define the pathomechanics and management of these injuries.

The Effect of Fractures on Joint Contact

Vertical Fractures of the Talar Neck

In collaboration with Allan Tencer, we developed a loading system to apply an axial load through the tibia to the foot simulating the standing position. Pressure-sensitive Fuji film is placed in the subtalar joint and locked into place. After the load is applied, the pattern and density of the joint contact pressure is analyzed by scanning the film with a video analysis system. In a model of a vertical fracture of the talar neck, we found that displacements as little as two millimeters resulted in significant decreases in contact area and increases in contact pressures. Varus displacement and displacements in more than one plane were most likely to adversely affect the loading patterns.

Fractures of the Calcaneus

The same technology was applied to calcaneus fractures. We found that fractures elevating the anterior part of the calcaneus and those producing depression of the posterior part of the calcaneus each altered Bohler's angle. However, fractures producing elevation of the anterior part of the bone produced greater abnormalities of joint contact pressure. We concluded that Bohler's angle alone did not accurately characterize the abnormal mechanics of the joint.

Motion Studies

Using the Orthokine System developed by John Sidles, we have begun studying the kinematics of the ankle and subtalar joint. This system employs a six-degree of freedom space tracker, as well as a six-degree of freedom force and torque transducer to relate applied loads to the resulting movements in three dimensions. Our initial studies of normal cadaver feet indicate that the freedom of motion at the subtalar joint is inversely related to the compressive loads across it. If borne out by subsequent studies, this concept of "load stabilization" may alter our understanding of the function of this important articulation. Preliminary data suggest that the ability of the hindfoot to manage uneven surfaces may depend more on the roundness of the heel than on motion at the subtalar joint.

Treatment of Fractures of the Calcaneus

In the early 1960s, Lapidus advocated early motion for injuries to the foot and ankle, but fear of malunion and nonunion prevented widespread acceptance of the concept. The seventies saw the advent of rigid fixation and early mobilization in the treatment of musculoskeletal injuries. These techniques recently have been applied to the many vexing injuries of the foot and ankle. Secure anatomic internal fixation allows the benefits of early motion without fear of loss of fracture reduction.

Clinical Study

In 1985 we began to approach the treatment of calcaneus fractures using the principles of Letournel, including a lateral approach, reduction of the tuberosity angle and joint surfaces, rigid fixation with a plate, and early postoperative motion. Although we have modified the technique, we have continued to apply uniformly the principles of Letournel. The modifications include a more dramatic curve in the incision to allow the application of a 3.5-mm reconstruction plate. The tuberosity is pulled out to length, and the anterior process and the posterior facet are reduced. Bone graft is placed in the defect, and a lateral plate is applied. Rehabilitation is started on postoperative day four with a therapist supervising range of motion exercises of the ankle and subtalar joint. We have applied this technique to approximately 200 fractures, with no long-term deep infections, no free flaps, and no amputations. Comparison with historical data suggests that accurate reduction of calcaneus fractures leads to a more functional foot.

Supported by the University of Washington Department of Orthopaedics.

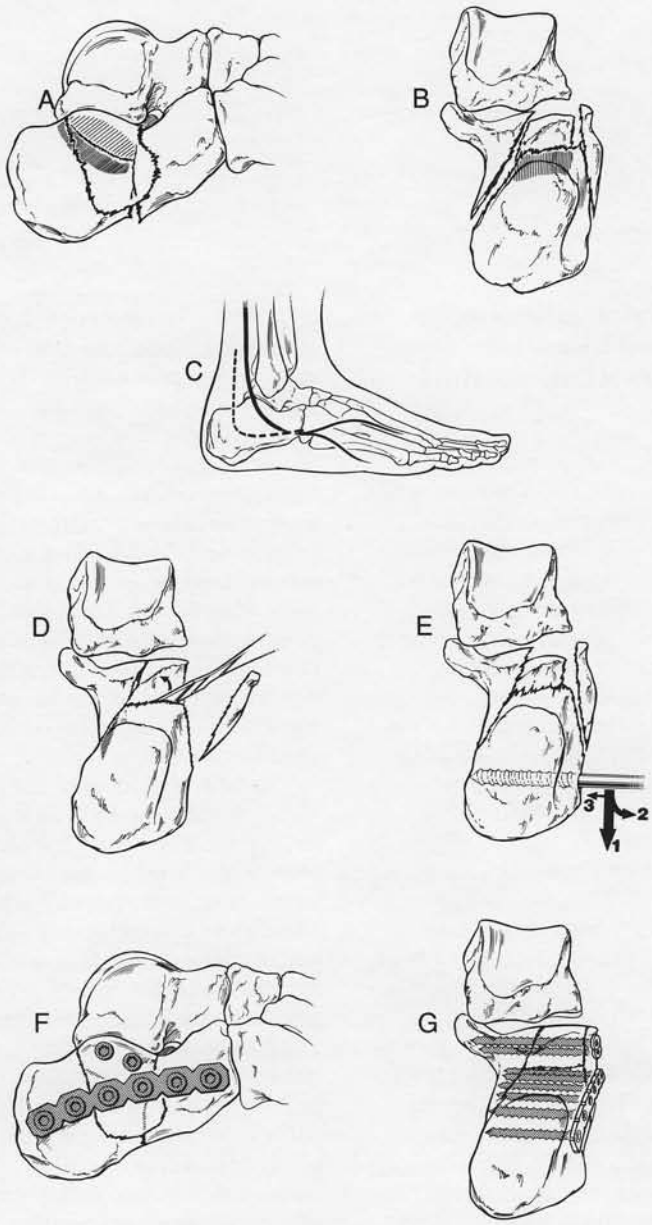


FIGURE: A - fracture pattern, lateral view; B - fracture pattern, superior-posterior view; C - incision; D - use of periosteal elevator to restore posterior facet; E - three-step maneuver to return posterior tubercle to anatomic position; F - fixation, lateral view; G - fixation.

Amputation and Prosthetics

Douglas G. Smith, M.D.

Partial Calcanectomy for Large Heel Ulceration or Calcaneal Osteomyelitis

Patients with large, persistent heel ulcerations present a significant wound healing challenge. Even if these patients meet the criteria for reconstructive surgery or undergo "successful" revascularization, they often must have a below-knee amputation because of failed attempts to obtain durable wound closure. Split thickness skin grafts are too fragile to provide a satisfactory load-bearing surface. Free tissue transfer is often interdicted by the presence of vascular disease or diabetes.

We performed partial calcanectomy in 12 patients who had a large heel ulceration with an exposed calcaneus. Conservative wound treatment had failed, and all patients met the following criteria for distal surgery: ankle-arm index >0.45, $TcPO_2$ >28, albumin >3.0, and total lymphocyte count >1,500. The age range was 22 to 77 years (mean 54 years). The primary diagnosis was diabetes in seven patients, vascular disease in three, quadriplegia in one, and myelomeningocele in one.

We tailored the surgical approach to fit the size and shape of the skin loss. For seven patients with circular ulcers we used a Gaenslens longitudinal approach, occasionally offsetting the proximal and distal limbs of the incision to allow better approximation of the skin. In five patients with ulcers larger in the transverse dimension, we excised the ulcer margins and the posterior process of the calcaneus through this defect, allowing a transverse skin approximation. In all patients the Achilles tendon was released off the calcaneus and allowed to retract. Occasionally a portion of necrotic tendon needed excision. Six wounds had primary closure over suction drains, and six were treated open and allowed to close secondarily.

Follow-up averaged 33 months, with a range of seven to 64 months. In 10 of the 12 patients, the ulcerations healed after partial calcanectomy. Nine of the patients who were ambulatory preoperatively were fit with a custom ankle-foot orthosis. All nine remained at their preoperative Volpacelli ambulatory level. The nonambulatory patient is a quadriplegic who has had no further problem with ulceration. Two patients have experienced episodes of superficial skin breakdown because of failure to wear their protective orthosis when walking, but both have healed with nonoperative wound care. Two patients failed to heal and underwent below-knee amputation.

We conclude that partial calcanectomy can be an excellent salvage technique for the patient with a large heel ulceration provided the limb is a candidate for distal surgery. It can provide a load-bearing foot that tolerates ambulation when fit with a custom ankle-foot orthosis. Under these circumstances the technique is an attractive alternative compared to below-knee amputation.

Development of a Modern Prosthetic Limb System

Lower limb prosthetics have improved dramatically in materials, function, and design. These advances have led to lighter weight prostheses with elastic response or "energy storing" features. However, many amputees, particularly those in Third-World countries, cannot afford or do not have access to these technologically advanced prostheses.

The Department of Orthopaedics, the Seattle Veterans Administation Hospital, and Prosthetic Research Study (E.M. Burgess, PI) have cooperated to pioneer new a new prosthetic limb system. It includes: (1) a socket fit to the residual limb using CAD-CAM technology; (2) an alignment device-socket connector that allows modifications of alignment during the initial and provisional limb stages and is incorporated in the definitive limb; (3) a monolithic shank-ankle component that provides elastic response and 10° of ankle dorsiplantarflexion without the drawback of bearings, moving parts, or multiple piece construction; (4) an elastic response prosthetic foot; and (5) a lightweight and durable ethyl-vinyl alcohol foam cosmetic cover. The components are easy to assemble, adjust, service, and replace.

Three steps are critical to the computer assisted design (CAD) and the computer assisted manufacture (CAM) process: (1) the description of the shape and size of the residual limb in numerical terms, (2) numerical modification or "rectification" of this shape according to accepted prosthetic principles, and (3) rapid manufacture of a customized, modern prosthesis by computerized manufacturing systems. The resulting prosthesis weighs between 2.5 and 3.5 lbs, and combines complex elastic movement and precise socket fit for improved patient comfort and function (Figures 1-4).

Our team evaluated 169 patients during the development of the VA-Seattle limb. One patient developed hyperkeratotic skin reaction and required surgical skin revision. One prototype ankle-shank unit failed structurally at the bolt connector attachment during the development stage. The patient was not injured, and this bolt attachment was strengthened. We are continuing our prospective study of 60 subjects who have been fitted with the final, complete limb system. There have been no major complications at an average of 12 months follow-up.

A traditional below-knee prosthesis costs approximately $3,500 and requires approximately 60 days for fabrication and delivery owing to the hands-on sculpturing and crafting required. Digitization of the residual limbs and numerical rectification provide quantitative tools for improving the efficiency of prosthetic fitting. The CAD-CAM system does not lessen the importance of the prosthetist, but rather simplifies the process of creating a socket and assembling the limb components, allowing the prosthetist more time to evaluate the patient and the fit of the limb. With our system a functional custom prosthesis can be created in two hours at a cost of $325.

We conclude that CAD-CAM technology can be applied successfully to design and manufacture prosthetic limbs with excellent fit and function, and at less cost than conventional methods. A CAD-CAM system such as ours holds promise for improving the fabrication and distribution of high-quality prosthetic limbs at less cost to underserved and Third-World areas.

Supported by Prosthetics Research Study, the Department of Veterans' Affairs Rehabilitation, Research, and Development, and the University of Washington Department of Orthopaedics.

FIGURE 1

FIGURE 2

FIGURE 3

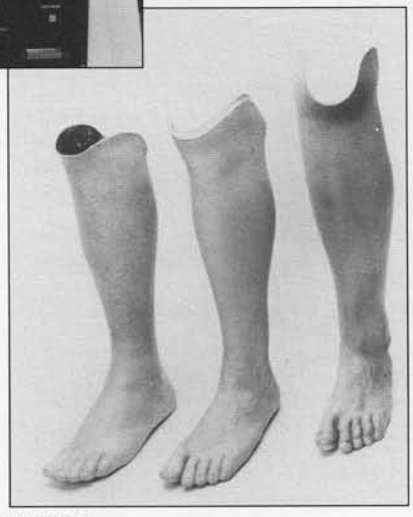


FIGURE 4

FIGURES 1-4: The steps in prosthesis design and manufacture. In Figure 1 (above) the prosthetist wraps a cast to obtain a model for the prosthesis. Through the technique of computer assisted design, the size and shape of the model are automatically translated into numerical terms. Figure 2 shows the prosthetist modifying the prosthesis design by computer. The computer feeds the information to a carver (Figure 3) that forms the final shape of the residual limb. Figure 4 shows several functional prostheses, which are modular, with realistic looking cosmetic covers.

Nerve Transplantation

Thomas E. Trumble, M.D.

Severe musculoskeletal trauma freqently produces nerve injuries with segmental loss in important peripheral nerves. Substantial deficits cannot be closed by primary repair, even with local nerve release or transfer, and patients often have limited recovery. Interpositional nerve grafting is restricted by the limited availability of nerve tissue that can be sacrificed for autograft transplantation. Synthetic nerve tubes and the topical application of growth hormones have been investigated, but have not produced significant return of nerve function.

We have explored the use of nerve transplantation to bridge substantial gaps in peripheral nerves. Optimal nerve regeneration through grafts requires not only hormonal and cytokine regulation, but also viable cells in the nerve grafts, especially the Schwann cells. We have developed techniques for maintaining Schwann cells in tissue culture and have incorporated these cultured Schwann cells in a study of whole nerve transplantation.

Grafts may be obtained from cadaveric donors or composites formulated from substrates such as collagens of laminen that contain cultured Schwann cells. The primary problem in any type of tissue transplantation is host rejection of the graft. This rejection is mediated through recognition of Class I and Class II histocompatibility antigens. We have identified both Class I and Class II antigens in the nerve grafts (Figures 1 and 2). A protein known as S-100 protein is an excellent marker for Schwann cells. Nerve graft rejection can be blocked by using immunosuppressants such as cyclosporin or a newly developed agent, FK506.

Our research has shown that:

1. Excellent nerve regeneration with transplanted grafts is possible when host and donor have a proper histocompatibility match or when immunosuppression is used.
2. Graft rejection can be partially alleviated by techniques causing Wallerian degeneration of the grafts prior to transplantation.
3. Nerve grafts can be successfully stored for prolonged periods at -80° C. This storage technique preserves cell viability.

We have identified the receptor sites for immunosuppressants on the Schwann cells and are evaluating techniques for increasing the receptors so that we can use lower levels of immunosuppressants, avoiding the toxic systemic effects of these agents.

Using electron microscopy and genetic engineering, we are attempting to identify the sites of Class I and Class II antigens on the Schwann cells to evaluate which are most critical in nerve rejection. We propose that the relatively avascular nerve tissue may be less antigenic than more vascularized tissue, such as liver and kidney, since the endothelial cells lining the vessels have the highest concentrations of cell surface markers.

We also hope to determine how standard nerve grafts or the transplanted tissue augment nerve regeneration. Using new fluorescent labels we are monitoring grafts to stage the immunologic response.

Our research is applicable not only to the challenges of nerve transplantation and increasing the availability of tissues for grafting, but also to improving the rate and completeness of nerve healing. The goal is to enhance restoration of motor and sensory function so patients can recover more completely from injuries that once resulted in paralysis and loss of sensation.

Supported by the University of Washington Department of Orthopaedics and a grant from the Orthopaedic Research and Education Foundation.

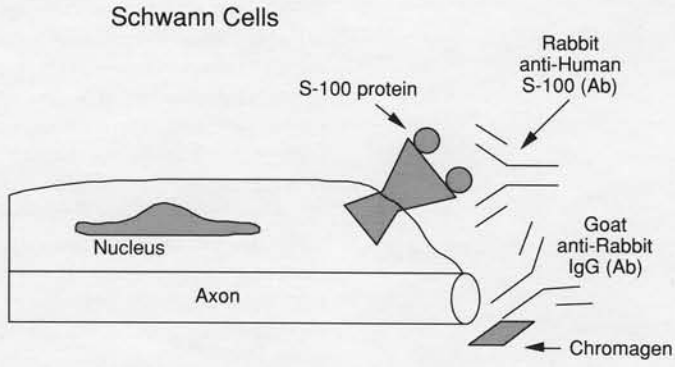


FIGURE 1: Identification of Schwann cells using S-100 marker.

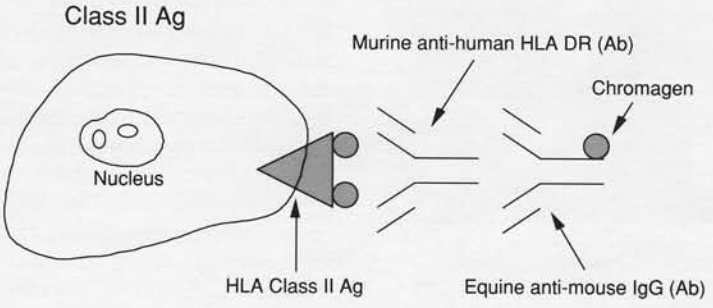


FIGURE 2: Immunohistochemical identification of human leukocyte antigens (HLA).

The Microscopic Architecture of the Collagen Framework in Musculoskeletal Tissues

John M. Clark, M.D., Ph.D.

FIGURE 1: Vertical section through human tibial plateau cartilage produced by freeze-fracture and seen by SEM magnified about 100X. The vertical collagen fibers extend from the tidemark (arrow) to the surface. The surface is rough because the central tibial plateau lacks a tangential layer.

Cartilage reputedly has little capacity for healing. Orthopaedic surgeons commonly encounter injured joint surfaces, and treatment would be much easier if the outcome of such injuries could be predicted. However, we know little about the factors that lead to the degeneration of a joint. One reason is an inadequate picture of the microscopic structure of the articular surface. Without this information we cannot understand lesions in terms of damage to specific elements of the matrix.

By weight, 85% of articular cartilage is a solution of proteoglycans in water. This gel is held together by a complex network of collagen fibers. In the 1920s, a German histologist, Albert Benninghoff, contended that hyaline cartilages derived their shape from an inner fibrous network and discussed a model for their arrangement. This idea was not universally accepted; the term "hyaline" was originally used to distinguish non-fibrous cartilages from the "fibrocartilages." The issue remained unclear until the electron microscope demonstrated the presence of typical collagen fibrils throughout articular cartilage. Electron microscopists, however, rejected the Benninghoff model of fiber organization, claiming instead that the network was predominantly random.

Most of the toughness of articular cartilage derives from the fibrous component. Is the orientation of these fibers random as some have suggested, or are the fibers organized to respond to local mechanical demands? I wanted to find out the extent to which the collagen framework determined the properties of articular cartilage. Early results in our morphology laboratory showed that rabbit knee cartilage seemed to follow the Benninghoff scheme.

I used the scanning electron microscope, an extremely powerful tool for revealing the three-dimensional structure of tissues. For reasons than are not completely clear, it has only rarely been used to study articular cartilage. The magnification of the scanning electron microscope ranges from 24 to 20,000 times, thus we can trace cartilage collagen fibers over large distances and in three dimensions, a marked contrast to the two-dimensional view provided by the transmission electron microscope.

Using special techniques, I was able to improve the view of the tissue. Enzymatic digestion selectively removed various organic components to allow unique views of structures such as the subchondral plate. Decalcification allowed an unimpaired view of the collagen of cartilage and bone. Controlled freeze-fracture enabled the selective view of planes between collagen fiber bundles. Finally, backscatter electron imaging with ions such as silver permitted selective marking of cell nuclei.

Each of these techniques added pieces to the puzzle. They were applied to the hip, knee, and shoulder joints of rabbits, dogs, and humans. All of these specimens had essentially the same pattern of

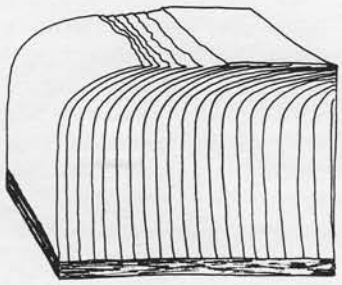


FIGURE 2: This diagram illustrates how collagen fibers turn and flatten at the surface to form the lamellar tangential layer. This configuration is found in all areas except the center of the femoral head, the tibial plateau, and the central patella. In those locations, no tangential layer is found.

collagen fibers. The fibers were anchored in the calcified layer of cartilage, but did not penetrate the bone itself. The fibers ran upward toward the surface and turned to form a layer of tangential fibers. In the lower and middle layers, the fibers were round and separated by vertical columns of cells. In the surface the fibers flattened out and formed thin sheets. Cell groups were found between the sheets in the surface layer as well, but these were flat. The surface layer was thick in the humeral head and acetabulum, but thin in other areas, such as the center of the tibial plateau. The surface layer is distinct at birth, but the vertical fibers seem to form later. Throughout development, the proportion of the vertical to the tangential layer increases.

The depressions known to exist in some joint surfaces correspond to the locations of cell clusters lying just under the surface. The density of cells in the surface decreases with age, and joint centers always contain fewer superficial chondrocytes. These findings explain the observations that these depressions are not found in the centers of adult joints.

The articular cartilage collagen structure revealed by these studies helps us understand many of the previously described biomechanical properties. The horizontal tensile strength of cartilage is always greatest near the surface because the collagen fibers run tangentially only at the surface. The strength of the cartilage at the joint center is less because the tangential layer is thinner there. The difference in tensile strength between the joint surface and deeper layers is less pronounced in younger specimens because the strongly vertical orientation of collagen in the deeper layers does not appear before maturity. These studies give us great respect for the complexity and durability of the normal joint surface as well as the great challenge we undertake when we attempt to replace it.

Tendons and Ligaments

The techniques we initially applied to articular cartilage are equally effective in the study of other dense connective tissues including bone and tendon. The morphology laboratory began to look at the rotator cuff and arterior cruciate ligaments because biomechanical studies of these structures were being performed literally in the same room. We were the first to show that the anterior cruciate ligament (ACL) is actually a collection of fiber bundles separated by chondrocyte-like cells or synovial membrane. These features allow the ligament to twist and bend. The rotator cuff also is more complex and specialized than, say, a flexor tendon. We have been able to trace ligament and tendon fibers into bone and show that they can penetrate much farther than previously believed.

These discoveries about the cuff and ACL may help explain why they are so troublesome clinically. Repair, healing, or reconstruction of such complex anatomy is likely to be slow and unpredictable.

Supported by the University of Washington Department of Orthopaedics and the Orthopaedic Research and Education Foundation.

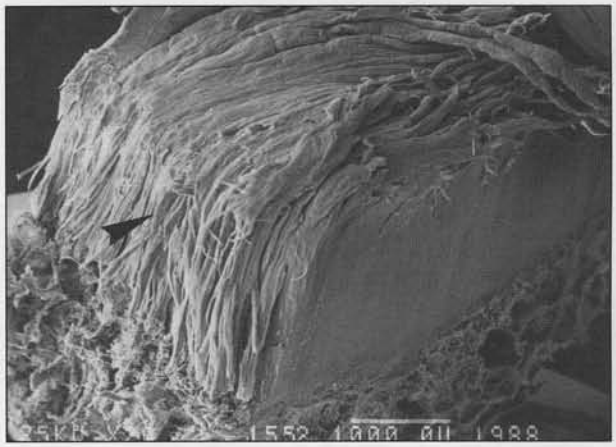


FIGURE 3: This is a cube of mildly degenerative cartilage from a human femoral condyle. The vertical fracture is at the left. The fibers turn at the surface and flatten into sheets. In the early stages of degeneration, the sheets tend to roll up and form fronds, as seen here. These fronds create the apperance of a shaggy fibrillated surface, which is familiar to those who do arthroscopy.

The Rotator Cuff

Douglas T. Harryman II, M.D.

The rotator cuff is a major interest of the Department's Shoulder and Elbow Service. Afflictions of the rotator cuff are among the most common diagnoses in patients with problems of the shoulder. Many questions are unanswered about the rotator cuff: How is it put together? Why does it fail? Can it heal by itself? Why are some patients with substantial cuff tears minimally symptomatic? How can it be best repaired? Do repairs stay intact? What is cuff-tear arthropathy and how can it best be treated? — and many more. This article presents a summary of some of the cuff research we are doing in the Department of Orthopaedics.

John Clark studied 32 shoulders with intact cuffs using advanced morphological techniques. He found previously undescribed interdigitations between the various elements of the cuff tendons. He also found five distinct layers of the cuff. In the deep layers, fibers from the subscapularis anteriorly and the infraspinatus posteriorly interdigitated with those of the supraspinatus. The tendinous portions of the cuff were confluent with the shoulder joint capsule, the coracohumeral ligament, and the glenohumeral ligaments. These studies demonstrate the complex architecture with which the cuff manages the diverse loads applied to it. The extensive intertwining of fibers provides abundant opportunities for load sharing. This arrangement also helps us understand how the cuff can function through the wide range of positions possible at the glenohumeral joint.

The function of the coracohumeral ligament has been an enigma. With John Sidles we characterized the role of this ligament in glenohumeral motion, stability, and obligate translation. The study employed six-degree of freedom force, torque, and position sensors in a cadaver shoulder system. A tightened coracohumeral ligament was found to limit glenohumeral flexion, extension, external rotation, and adduction. Consistent with this experimental observation, we have found that sectioning of the CHL and superior capsule is a valuable adjunct in freeing up tendons for cuff repair and in the surgical management of the limited range of motion in frozen and arthritic shoulders. We also found that a tightened CHL increased the resistance to posterior and inferior translation of the humeral head on the glenoid. Clinically, we are using reconstruction of the CHL and superior glenohumeral ligament complex as components of a global capsulorraphy in the management of multidirectional instability.

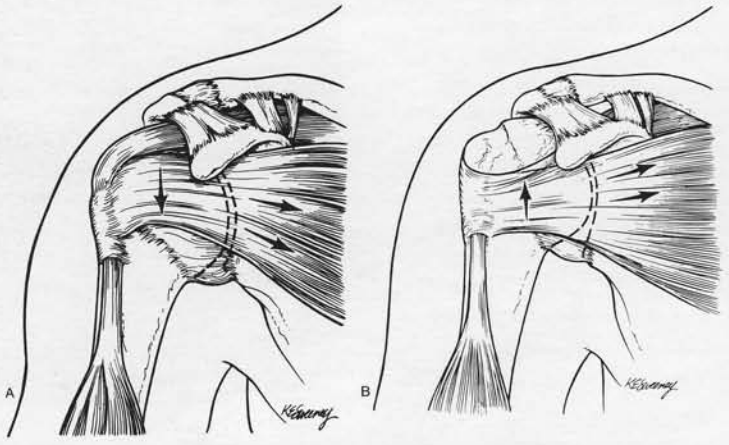


FIGURE 1: A — In the normal shoulder the head is stabilized by compression of the head into the glenoid concavity. B — In massive cuff deficiency a boutonniere deformity can occur in which the head is forced upward.

Recognizing that cuff tears may go unnoticed by some patients, a study was undertaken to identify the prevalence of cuff defects in an unselected group of subjects. Two hundred and fifty volunteers over age 40 were collected by including the entire congregations of two churches. A subset of 112 shoulders in 58 subjects aged 60 to 70 were evaluated by physical exam and ultrasound. Six percent of these shoulders showed cuff tears on ultrasound examination. Half of these tears were entirely asymptomatic.

FIGURE 2: In small rotator cuff tears, radiographs may reveal evidence of chronic impingement such as bony cysts at the normal cuff insertion, subacromial sclerosis, and acromial spurs.

One of the major challenges in cuff repair is the identification of factors influencing the functional outcome of surgery. Along with Sarah Jackins, Larry Mack, Keith Wang, and Mike Richardson, we evaluated 112 cuff repairs using a consistent tendon-to-bone technique. Cuff tears were classified by the number of tendons torn. At an average of five years follow-up, we correlated cuff integrity with shoulder function and the size of the original tear that was repaired. Eighty percent of supraspinatus-only tears were intact at follow-up, while more than 60% of repairs of larger tears were retorn. Older patients also had a statistically higher incidence of recurrent defects at follow-up. Subjects aged 71 to 85 had a 44% incidence of recurrent defects; subjects aged 56 to 70 had a 33% incidence, while those aged 34 to 55 had a 25% incidence of recurrent defects.

Interestingly, it was the cuff integrity at follow-up, as determined by ultrasonography, that was the major determinant of the quality of the functional result. Where ultrasound showed intact cuffs, the shoulders had the greatest active flexion, strength, and function in activities of daily living as well as the highest level of comfort. This was the case even if the tear that was repaired was massive or if the surgery was a second repair for a recurrent cuff defect. Also of significance is the observation that, while intact repairs yielded the best results, more than 75% of persons who had retears of their cuff repairs had less pain than before surgery and were satisfied with their surgery; apparently comfort and patient satisfaction are not reliable indicators of cuff integrity after cuff repair surgery.

Keying off this study, the Shoulder and Elbow Service has joined the national movement to evaluate clinical conditions and treatment methods according to simple functional parameters. We have developed and utilized a "Simple Shoulder Test (SST)" consisting of 12 simple functional "yes-no" questions that can be used to characterize a shoulder in terms everyone can understand. A trial group of normal subjects aged 60 to 70 were able to perform essentially all of these functions. By contrast, patients with cuff tears as well as other conditions such as degenerative joint disease, frozen shoulder, and glenohumeral instability had characteristic patterns of functional compromise. We now have SST results that clearly demonstrate the increment in function from successful treatment of these conditions. It appears that the SST will be a practical tool for orthopaedic surgeons to measure the benefit of treatment. It will also be useful for communicating this information to patients and to those paying for medical care.

Taken together these studies indicate the challenge of the rotator cuff. Its anatomy is complex and difficult to reconstruct by surgical repair. Durability of the repair is the critical determinant of the functional result from the operative management of cuff fiber failure. Finally, we need to continue to investigate the natural history of this common orthopaedic condition, the factors that predispose to cuff failure, the factors determining the symptoms experienced by the patient, the optimal methods of management, and the impact of treatment on the patient's function.

Supported by the University of Washington Department of Orthopaedics.

FIGURE 3: Chronic massive tears result in upward displacement of the humeral head until it articulates with the acromion. Humeral osteophytes result from abnormal glenohumeral articulation. This end stage is called "cuff-tear arthropathy."

Chief Resident Abstracts

Open Fractures of the Tibia in Children

Kit M. Song, M.D.
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Stephen K. Benirschke, M.D.
Keith A. Mayo, M.D.
Sigvard T. Hansen, M.D.

Fractures in children differ markedly from those of adults, with a significant difference in response to injury depending on the state of chondro-osseous maturation. Open fractures of the tibia are reviewed extensively in the adult literature, but these injuries have been considered rare in children, with no reports of clinical series prior to 1983. Reports since then, with a cumulative total of more than 200 patients, suggest an increased incidence of these injuries. However, little information is available on treatment and outcome.

We analyzed the results of treatment of open fractures of the tibia in skeletally immature patients with particular attention to outcome based on age, grade of injury, and type of immobilization. Skeletal immaturity was defined as open growth plates on X-ray examination at the time of injury. Thirty-eight of 48 patients treated between 1979 and 1987 at Harborview Medical Center and Children's Hospital and Medical Center were followed to clinical and radiographic healing and were included in our study group.

Thirty-one of these patients were personally interviewed and examined. The remaining seven had adequate documentation in hospital records to ascertain leg length discrepancy, functional problems, or significant morbidity. Four of these seven were contacted by telephone for additional information.

The 38 patients included 28 boys (74%) and 10 girls (26%), with a mean age of 11 years (range 4 to 15) at time of injury. The mechanism of injury was bicycle versus auto in 17 patients, pedestrian versus auto in 12, motorcycle versus auto in 6, and falls in 2 patients. Eight patients had grade I injuries (21%), 16 had grade II (42%), and 14 had grade III injuries (37%).

Treatment consisted of operative debridement of wounds, the use of parenteral antibiotics, and immobilization by either cast, internal or external fixation, or some combination of limited internal fixation with external fixation. The average follow-up was 34 months (range 9 to 122 months).

Time to healing was defined as the presence of bridging callous on radiographs, absence of tenderness at the fracture site, and ability to bear full weight without aids. Leg-length discrepancy was measured by the use of blocks at final follow-up. Functional outcome was rated as excellent if both child and parents felt the child had returned to full activities. Results were rated as good if limp or pain occurred with sports activities but not with other daily activities. Fair results were defined as presence of limp or pain with daily activities that did not interfere with function, but were noticed by the patient or family. Poor results implied restriction in daily activities due to pain or limp.

All fractures ultimately healed; the mean time to healing was 21 weeks (range 6 to 83 weeks). Clinical ratings showed 33 excellent, 4 good, 1 fair, and no poor outcomes at final follow-up. Patients less than 11 years old had a significantly shorter time to healing, but also had fewer grade III injuries. Both the deep infection rate and nonunion rate were 8%, and occurred only in patients older than 11 years. Pin site infections occurred in 37% of patients treated in external fixators; the average time to infection was 10 weeks. No patients younger than 11 required bone grafting for union. Clinically significant leg length discrepancy was only encountered in patients with ipsilateral femur fracture or with deep infection. No significant overgrowth occurred.

Our findings suggest that open tibia fractures in children older than 11 years will have healing times and complication rates similar to such fractures in adults. With aggressive wound care and stabilization, few complications or sequelae should occur in open tibial shaft fractures in younger patients.

Supported by the University of Washington Department of Orthopaedics.

Effectiveness of Pemberton Pericapsular Osteotomy in the Treatment of Congenital Dislocation of the Hip

Mark C. Remington, M.D., Ph.D
Lynn T. Staheli, M.D.

We reviewed a series of Pemberton pericapsular osteotomies performed for CDH to compare its effectiveness with the Salter innominate osteotomy. Our series included 50 osteotomies in 40 patients. Mean age at surgery was 44 months, and mean length of follow-up was 6.5 years with a range of 2 to 20 years.

Outcome was rated good or excellent by clinical criteria in 64% and by radiographic criteria in 74%. At follow-up, mean improvement in acetabular index was 22 degrees and average C-E angle was 34 degrees. The complication rate was low (5%) and there were no cases of avascular necrosis. Further surgery was required in 20% of the cases.

Overall, results were quite similar to the previously published series of Salter innominate osteotomies from Children's Hospital and Medical Center. Advantages of the Pemberton include the ability to perform bilateral procedures under the same anesthesia, and the avoidance of internal fixation and the additional surgery needed for its removal.

Supported by the University of Washington Department of Orthopaedics.

Biochemical Studies of Calcified Cartilage

Tim P. Lovell, M.D.
David R. Eyre, Ph.D.

Articular cartilage is joined to its underlying subchondral bone by a layer of calcified cartilage. In the normal joint this calcified cartilage layer extends for 100 to 200 microns from the tidemark (the sharply defined junction between calcified and noncalcified cartilage) to the cement line (the calcified cartilage-subchondral bone junction). The calcified zone of articular cartilage seems to play a key role in the joint remodeling that occurs during normal aging and in osteoarthritis. Little had been known about the biochemical structure of this layer because it was difficult to sample. We solved this problem by serially sectioning blocks of frozen tissue for biochemical assays.

Analyses of serial sections for hexosamine and collagen showed that the calcified cartilage layer contained half the amount of hexosamine per weight of collagen compared with the uncalcified cartilage. This finding indicates that proteoglycans, suspected inhibitors of calcification, appear to be lost from the calcified zone compared with the noncalcified zone lying above it.

Collagen typing confirmed that the calcified layer of articular cartilage is indeed basically a cartilaginous matrix that has calcified. However, type X collagen was found exclusively in the calcified cartilage layer. Analysis of the noncollagenous matrix proteins revealed a 45-kilodalton protein present only in the calcified cartilage layer. Sequence data for this protein revealed it to be osteonectin.

The two matrix proteins unique to the calcified zone of articular cartilage, type X collagen and osteonectin, were not present in the immediately adjacent noncalcified cartilage, and are candidates for mediators of matrix calcification. Further characterization of the structure and role of these unique matrix proteins is in progress.

Supported by an OREF Resident Research Grant and the University of Washington Department of Orthopaedics.

Treatment of Triplane Fractures

David H. Bishop, M.D.

Triplane fractures are among the most severe and challenging fractures of the pediatric ankle. To evaluate the factors influencing the final outcome, we studied 11 children with this injury at an average follow-up of 4 years and 5 months. At the time of injury, the average age was 12 years, 3 months for girls and 13 years, 10 months for boys.

We found three fractures involving two fragments, one fracture involving three fragments, and seven that were uncertain. Six fractures entered the weight-bearing surface of the ankle joint. Fractures that did not enter the weight-bearing surface of the joint uniformly healed with good or excellent results with either open or closed reduction. Pain and limited function occurred when intra-articular fractures healed with 2 mm or more of displacement.

Fracture pattern and amount of displacement are very difficult to identify on plain films. In fractures treated by closed methods, we suggest that tomography or CT scan be obtained after reduction to ensure that the displacement of the joint surface is less than 2 mm. If displacement is 2 mm or greater after closed reduction, we recommend open reduction. Two incisions may be necessary to determine whether there are two or three fragments and to reduce the fracture accurately.

Supported by the University of Washington Department of Orthopaedics.

Tibial Nonunion Treated with Reamed Intramedullary Nailing

Mark E. Murphy, M.D.
Gary H. Clancey, M.D.
Sigvard T. Hansen, M.D.
Robert A. Winquist, M.D.

We conducted a retrospective study of the effectiveness of intramedullary nailing in the treatment of established tibial nonunions. The study included 72 patients treated at Harborview Medical Center between 1971 and 1989. Their mean age was 34 years with a range of 18 to 84.

The series included 41 open and 31 closed tibial fractures. Initial methods of treatment included 35 long-leg casts, 11 plates, 7 external fixators, 7 pins in plaster, 4 patellar tendon casts, 4 IM nails, 3 interfragmentary screws, and 1 circlage wire.

Reamed unlocked nails were used to treat the tibial nonunions in 70 patients. One had a proximally locked nail and one had the nail locked at both ends. Twenty-eight patients (39%) underwent open nailings and 44 (61%) had closed nailings. Twenty-three patients had concomitant fibular osteotomy.

Sixty-nine of the nonunions (96%) united uneventfully. Three patients (4%) had persistent nonunions: one required additional bone grafting, one required bone grafting and repeat IM nailing, and one opted for a below-knee amputation after refracture two years post nailing. Average time to union was seven months for closed nailings and ten months for open nailings. Four patients developed postoperative infections, but all cleared with treatment. During the first three weeks after nailing, 82% of patients began to bear full weight.

This series of tibial nonunions shows that reamed IM nailing with unlocked nails and early weight-bearing yields excellent rates of union. Most of the procedures can be accomplished closed; interlocking screws are rarely needed.

Supported by the University of Washington Department of Orthopaedics.

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