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Reports Control Symbol RCS-MEDDH-288 (R1)

ANNUAL PROGRESS REPORT

FISCAL YEAR ~~1982~~ 1983

(1 October ~~1981~~ 1982 - 30 September ~~1982~~ 1983)

1 Oct ~~1982~~ 1983

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UNITED STATES ARMY INSTITUTE OF DENTAL RESEARCH
WALTER REED ARMY MEDICAL CENTER WASHINGTON, D.C., 20307

AD _____

UNITED STATES ARMY INSTITUTE OF DENTAL RESEARCH
WALTER REED ARMY MEDICAL CENTER
WASHINGTON, DC 20307-5300

ANNUAL REPORT
(1 October 1982-30 September 1983)

Thomas P. Sweeney, COL, DC

October 1983

Supported by

US ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21701-5012

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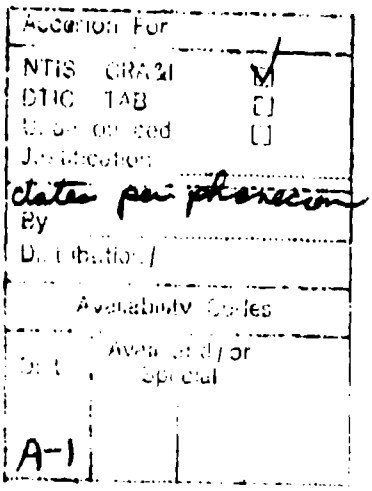

Reports Control Symbol MEDDH-288 (R1)

U.S. ARMY INSTITUTE OF DENTAL RESEARCH
WALTER REED ARMY MEDICAL CENTER
WASHINGTON, DC 20307-5300

ANNUAL PROGRESS REPORT

1 October 1982 - 30 September 1983

DA Project	3A161101A91C	00	In-House Laboratory Research
DA Project	3M161102BS10	Task DA	Management of Dental Injury & Combat Dentistry
DA Project	3S162775A825	Task AA, AB, AC, AD	Combat Maxillofacial Injury
DA Project	3M162734A875	Task AQ	Medical Defense Against Chemical Agents

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
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4. TITLE (and Subtitle) U. S. Army Institute of Dental Research Annual Progress Report FY 83		5. TYPE OF REPORT & PERIOD COVERED Annual 1 Oct 82 - 30 Sep 83 6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) Thomas P. Sweeney, COL, DC		8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS U. S. Army Institute of Dental Research Washington, DC 20307-5300		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS 3M161102BS10 Task DA; 3S162775A825 Task AA, AB; 3M162734A875 Task AQ
11. CONTROLLING OFFICE NAME AND ADDRESS U. S. Army Medical Research & Development Command (SGRD-RMS) Fort Detrick, Frederick, MD 21701		12. REPORT DATE 13. NUMBER OF PAGES
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16. DISTRIBUTION STATEMENT (of this Report)

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17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

None

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

(U) Ancillary Personnel; (U) Antimicrobial Agents; (U) Aphthous Stomatitis; (U) Base Metal Alloys; (U) Biocompatible; (U) Biodegradable; (U) Biodegradable Copolymer; (U) Biopolymers; (U) Bonding Agents; (U) Bone; (U) Bone Stimulating; (U) Casting Accuracy; (U) CD-1 Mice; (U) Cellulose Triacetate;

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

DA Project 3M161102BS10 Management of Dental Injury and Combat Dentistry
Task DA

The objectives are to obtain information by the techniques of clinical and basic research on injuries and diseases, except communicable diseases, commonly seen in soldiers, especially in field operations and overseas. The work is divided according to the major dental specialties. Emphasis is placed on diseases and injuries that are receiving little or no study by →over

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered)

BLOCK 19. Continued:
(U) Ceramic; (U) Ceramic Block; (U) Cidex; (U) Citric Acid; (U) Cold Weather Survey; (U) Composite Restoratives; (U) Controlled Release; (U) Copolymer; (U) Copolymer Bandage; (U) Corrosion of Alloys; (U) Cranio-Mandibulofacial Complex; (U) Crevicular Fluid; (U) Cyclic AMP; (U) Dental Cutting Instrument; (U) Dental Emergencies; (U) Dental Identification; (U) Dental Materials; (U) Dental Porcelain; (U) Dental Radiology; (U) Dental X-ray; (U) Diphosphoinositide-Lysozyme; (U) Dogs; (U) DOT-ELISA; (U) Foreign Bodies; (U) Gentamicin; (U) Gingival Exudates; (U) Gingival Trauma; (U) Granular Tricalcium Phosphate; (U) Guinea Pigs; (U) Health Services Research; (U) Herpetic Lesions; (U) Hydroxyproline; (U) Immunology; (U) Immunopathology; (U) Implant; (U) Impression Materials; (U) Indomethacin; (U) Infection Control; (U) Inflammation; (U) Inhibition; (U) Inhibition of Bone Resorption; (U) Interceptive Methods; (U) Intermaxillary Fixation; (U) Investment Techniques; (U) Isobutyl 2-Cyanoacrylate; (U) Kreb's Cycle Derivatives; (U) Laboratory Animal; (U) Laser Reflectance; (U) Lidocaine; (U) Lip Pathology; (U) Liver Surgery; (U) Logistic Models; (U) Lymphocytes; (U) Lymphokine; (U) Marginal Leakage; (U) Materiel; (U) Medical Materiel; (U) Mice; (U) Microbiology; (U) Microencapsulation; (U) Microencapsulated Antibiotics; (U) Monoclonal Antibodies; (U) Nerve Agent; (U) New Bone Formation; (U) Opaque Porcelain; (U) Operations Research; (U) Oral Health Status; (U) Organ Culture; (U) Osseous; (U) PGE ; (U) PLA/PGA Covering; (U) Polypentapeptide; (U) Porcelain-Metal Bond; (U) Post and Core Restorations; (U) Predictive Methods; (U) Prostaglandin; (U) Rabbits; (U) Radioisotope; (U) Radionuclide X-ray System; (U) RAM IV; (U) Rapid Detection; (U) Rats; (U) Recurrent Aphthous Stomatitis; (U) Recurrent Oral Ulceration; (U) Resin Restorative; (U) Rhesus Monkey; (U) Salivary Amylase; (U) Salivary Enzyme; (U) Salivary Physiology; (U) Segmental Mandibular Defects; (U) Serrated; (U) Shelf-Life; (U) Soldering Base Metals; (U) Sporicidin; (U) Storage Stability; (U) Subtraction Radiography; (U) Sustained Release Antibiotic; (U) Tissue Adhesive; (U) Tooth; (U) Tracheal Grafts; (U) Tricalcium Phosphate; (U) Tumorigenicity Study; (U) Ultrasound; (U) Volunteers; (U) Wound Dressing; (U) Wound Exudate; (U) Wound Healing; (U) Wound Infection; (U) Xerocheiliosis; (U) X-ray Portable

BLOCK 20 Continued:

civilian research groups, and the work is aimed at providing better preventive measures as well as treatment.

DA Project 3S162775A825 Combat Maxillofacial Injury.
Tasks AA, AB

The objectives are to develop simplified procedures for the care of complex maxillofacial wounds and injuries which require long time-consuming procedures for reconstruction; to achieve minimal morbidity rates from oral emergencies, preventable oral disease, and restorative failures; and to develop more efficient, simplified, effective clinical and laboratory techniques which will result in better utilization of manpower and a saving in time and materiel.

DA Project 3M162734A875 Medical Defense Against Chemical Agents.
Task AQ

The objectives and purposes are the development of the basic scientific data required for systems of soldier CW agent antidotes, soldier/patient decontamination, and medical management of CW casualties. Reward; Copolymer;
Gingival trauma; Rhesus monkey;
Military medicine

USAIDR PROJECTS, TASKS, AND WORK UNITS

USAIDR PROJECTS, TASKS, AND WORK UNITS

USAIDR PROJECTS, TASKS, AND WORK UNITS

FOREWORD

IN CONDUCTING THE RESEARCH DESCRIBED IN THIS REPORT, THE INVESTIGATORS ADHERED TO THE "GUIDE FOR THE CARE AND USE OF LABORATORY ANIMALS" AS PREPARED BY THE COMMITTEE ON CARE AND USE OF LABORATORY ANIMALS OF THE INSTITUTE OF LABORATORY ANIMAL RESOURCES, NATIONAL RESEARCH COUNCIL.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

	A. NEW	U	U		NL		A WORK UNIT
10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER	
	611101A	3A161101A91C		00		015	
FORMER							
MOST OBJ.	NONE						

(U) CONTROLLED RELEASE OF ANTIGENS FOR ONE-DOSE IMMUNIZATION

010100 MICROBIOLOGY	012600 PHARMACOLOGY	010300 MISC MAT	
OCT 83	CONT	DA	C. IN-HOUSE

	1983	0.0	$ 0
	1984	0.8	$ 80
F. CUM/TOT:			$ 0

038870	11	
MDRDC INSTITUTE OF DENTAL RSCH USAIDR		
WASHINGTON DC 20307		
SWEENEY, T P		MD 20
202-576-3484		
F.I.C.A.		
MILITARY		

038870	11	
MDRDC INSTITUTE OF DENTAL RSCH USAIDR		
WASHINGTON DC 20307		
SETTERSTROM, J A		DA
202-576-3764		

(U) LAB ANIMALS ;(U) RATS ;(U) MICROENCAPSULATION;(U) CONTROLLED RELEASE;(U) IMMUNIZATION

OBJECTIVE:(U) IT IS THE TECHNICAL OBJECTIVE OF THIS WORK TO DETERMINE THE FEASIBILITY OF APPLYING CONTROLLED RELEASE OF MULTIPLE VACCINE ANTIGENS OF A PREPROGRAMMED MANNER SO THAT A HIGH TITER ANTIBODY RESPONSE IS ELICITED IN THE HOST. SUCCESSFUL DEVELOPMENT OF THE UNIVERSAL VACCINE WOULD RESULT IN A ONE-DOSE, ONE-STEP IMMUNIZATION PROCEDURE FOR SERVICE PERSONNEL.

APPROACH: (U) A BIOCOMPATIBLE, BIODEGRADABLE POLYMER POLY (DL-LACTIDE-CO-GLYCOLIDE), WILL BE USED TO COAT DISPERSED PARTICLES OF DPT VACCINE. MICROSPHERES GREATER THAN 250 M WILL BE FORMULATED SINCE THEY ARE INJECTABLE THROUGH A CONVENTIONAL HYPODERMIC NEEDLE. THE RATE OF ANTIGEN RELEASE WILL BE CONTROLLED BY PROPER CHOICE OF POLYMER AND SYSTEM DESIGN. THE IMMUNE RESPONSE TO THE ENCAPSULATED ANTIGENS WILL BE MONITORED AND COMPARED TO CONVENTIONALLY IMMUNIZED CONTROLS. A SUCCESSFUL IMMUNE RESPONSE TO THE DPT (DIPTHERIA, PERTUSSIS, TETANUS) ANTIGENS WOULD ENCOURAGE INCORPORATION OF ADDITIONAL VACCINE ANTIGENS. IT IS ANTICIPATED THAT THE QUANTITY OF ANTIGEN NEEDED TO STIMULATE THE DESIRED IMMUNE RESPONSE WILL BE CONSIDERABLY LOWER THAN THAT REQUIRED WHEN ADMINISTERED CONVENTIONALLY. IT IS POSSIBLE THAT THE POLYMER WILL HAVE AN ADJUVANT EFFECT THAT MAY ENHANCE THE IMMUNE RESPONSE.

PROGRESS: (U) NONE.

DD 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

DA302938 | 01 OCT 83 | REPORT CONTROL SYMBOL: ZO1708

	A. NEW	U	U		NL	A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
PRIMARY	61101A	3A161101A91C	DD	414
FORMER				
MISC. OBJ.	NONE			

(U) LASER TRANSILLUMINATION AND ULTRASOUND OF TISSUE

002400 BIOENGINEERING | 010300 MISC MAT | 012800 PHYSIOLO

OCT 83	SEP 85	DA	C. IN-HOUSE

PRIOR FISCAL YEAR	1983	0.0	$ 0
CURRENT FISCAL YEAR	1984	0.2	$ 20

F. CUM/TOT: $ 0

PERFORMING ORGANIZATION			
NAME	MORDC INSTITUTE OF DENTAL RSCH USAIDR	038870	11
ADDRESS	WASHINGTON DC 20307		

PRINCIPAL INVESTIGATOR		
NAME	VANORE, R H	DA
TELEPHONE	415-561-2206	
ASSOCIATE INVESTIGATORS		
NAME	LORTON, L	
NAME	GROVER, P S	

RESPONSIBLE INDIVIDUAL	
NAME	SWEENEY, T P
TELEPHONE	202-576-3484
ADDRESS	WASHINGTON DC 20307

GENERAL USE: F.I.C.A.

MILITARY APPLICATION: MILITARY

(U) RAM IV;(U) LASER REFLECTANCE ;(U) ULTRASOUND ;(U) FOREIGN BODIES ;(U) GINGIVAL TRAUMA

OBJECTIVE:(U) THE OBJECTIVE IS TO DEVELOP A TECHNIQUE AND APPARATUS FOR LOOKING THROUGH GINGIVAL TISSUES TO QUICKLY IDENTIFY ALL EMBEDDED FOREIGN BODIES AND PRODUCE A USEFUL IMAGE OF TEETH AND BONE. THIS TECHNIQUE WOULD BE USED TO MINIMIZE EXPLORATORY TRAUMA TO THE SOLDIER. THE GOAL IS THE SLLECTIVE REPLACEMENT OF X-RAY USAGE AND THE NEED FOR LAYING OF PERIODONTAL FLAPS WHEN SEARCHING FOR FOREIGN OBJECTS IN THE GINGIVA.

APPROACH: (U) LASER TRANSILLUMINATION AND ULTRASOUND TECHNIQUES WILL BE EXPLORED. VARIOUS FREQUENCIES OF LASER LIGHT WILL BE EVALUATED TO DETERMINE IF LASER LIGHT HAS THE ABILITY TO PASS THROUGH GINGIVAL TISSUE WITH MINIMUM DISPERSION. ULTRASOUND TECHNIQUES WILL BE IDENTIFIED CONCURRENTLY. ULTRASOUND OFFERS A SIMILAR ABILITY TO LOOK THROUGH TISSUE USING SOUND WAVES. ULTRA-HIGH-FREQUENCY SOUND EQUIPMENT WITH A RESOLUTION OF 0.1 MM WILL ALSC BE ASSESSED.

PROGRESS: (U) NONE.

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

Field	Value
1. Agency Accession	DA OB 6027
2. Date of Summary	83 10 01
Report Control Symbol	DD-DR&E(AR)636
3. Date Prev Sum'ry	82 10 01
4. Kind of Summary	H. TERM
5. Summary Scty	U
6. Work Security	U
8. Dissem Instr'n	NL
8b. Specific Data-Contractor Access	☒ Yes ☐ No
9. Level of Sum	A. Work Unit

10. No./Codes	Program Element	Project Number	Task Area Number	Work Unit Number
a. Primary	61102A	3M161102BS10	DA	009
b. Contributing				
c. Contributing		STOG: 82/83-6.2/4		

11. Title (Precede with Security Classification Code): (U) Acceleration of Wound Healing

12. Scientific and Technological Areas: 002300 Biochemistry; 012900 Physiology

13. Start Date: 66 07

14. Estimated Completion Date: CONT

15. Funding Agency: DA

16. Performance Method: C. IN-HOUSE

17. Contract/Grant

a. Dates/Effective: Expiration:

b. Number:

c. Type: d. Amount:

e. Kind of Award: f. Cum. Amt.

18. Resources Estimate

Fiscal Year		a. Professional Man Yrs	b. Funds (In thousands)
Preceding	83	3.0	195
Current			

19. Responsible DOD Organization

Name: U.S. Army Institute of Dental Research

Address: Washington, DC 20307

Responsible Individual

Name: SWEENEY, T.P.

Telephone: (202) 576-3484

20. Performing Organization

Name: U.S. Army Institute of Dental Research

Address: Washington, DC 20307

Principal Investigator (Furnish SSAN if U.S. Academic Institution)

Name: HOLLINGER, J.O.

Telephone: (202) 576-3764

Social Security Account Number: POC:DA

Associate Investigators

Name: WOODYARD, S.

Name: HEATH, J. & MILLER, R.

21. General Use

Foreign Intelligence Considered

22. Keywords (Precede each with Security Classification Code): (U) Diphosphoinositide-Lysozyme; (U) Citric Acid; (U) Laboratory Animal (U) Prostaglandin; (U) Copolymer; (U) Inhibition of Bone Resorption (U) Cyclic AMP

23. Technical Objective, 24. Approach, 25. Progress (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) Recent studies show that 10-12% of combat wounds involved the maxillofacial apparatus. Furthermore, 7% of noncombat injuries requiring hospital care involve the maxillofacial region. This results in the loss of approximately 1,000,000 man-hours per year.

24. (U) Studies on the effects of biochemical and physical factors to include chelate complexes, cyclic AMP, prostaglandins, and in vivo growth factors on the rate of healing in soft tissue and bone will be done. The mechanism of any beneficial alteration in healing effected will be investigated and pursued to human usage.

25. (U) Exogenous PGE was found to increase the rate of bone resorption in mouse calvaria while indomethacin inhibited spontaneous bone resorption in vitro. Fifty-fifty PLA:PGA plus DPI-L was found to promote osseous healing to a greater extent than 50:50 PLA:PGA. Diphenylhydantoin-sodium in conjuction with 50:50 PLA:PGA did not produce a statistical difference. A powerful inhibitor of osteolysis with a molecular weight of 6000 daltons has been identified. Hybridomas are ready for assay to determine the extent to which Osteoclast Activating Factor (OAF) can be inhibited. Citric acid application significantly enhanced wound repair, indicating this treatment offers substantial benefit. Adhesion of tissue allowed nearly complete repair of exposed root surfaces to be accompished, unlike control surfaces where repair was unsatisfactory.

*Available to contractors upon originator's approval

DD Form 1498, Mar 68 — Previous editions of this form are obsolete.

PROJECT: 3M161102BS10

WORK UNIT TITLE: (U) Acceleration of Wound Healing

PRINCIPAL INVESTIGATOR: LTC Jeffrey O. Hollinger, DC

A Study on the Behavior of Bone in Organ Culture with Special Emphasis on PGE_2 and Indomethacin

PROBLEM: It has been demonstrated that PGE_2 administered to bone implants results in an increase in osteoclasts and decrease in total bone volume. Cyclic AMP (cAMP) has been described in relation to prostaglandins (PG) and bone resorption (Yu et al., 1979). Cyclic GMP (cGMP) has been mentioned as a possible antagonist of cAMP (El-Attar, 1978). It is fundamentally important to understand the principles of bone resorptive processes and agents that control or buffer those activities so that osteolysis can be controlled and bone morbidity can be decreased.

APPROACH: Calvaria were removed aseptically from CD-1, 5-7 day old neonatal mice and were placed into tissue culture wells containing enriched BGJ$_b$ medium. Calvaria were divided equally into control and treatment groups of 4 calvaria per group. The treatment groups had either a known or putative PGE_2 inhibitor added to the medium (i.e., indomethacin, phenylbutazone). All calvaria were incubated at 37°C in 5% CO_2 and air. Specimens were retrieved at 24, 48, and 72 hours and were assayed by ^{125}I-RIA for PGE_2, c-AMP, and c-GMP; and by atomic absorption spectroscopy for Ca++ concentration.

RESULTS: The per cent PGE_2 and Ca++ differences between treatment and control groups were used as bench marks for comparisons. The indomethacin (100ng/ml) displayed several levels of prostaglandin E_2 inhibition during the 72 hour test period. Maximum levels for indomethacin and niflumic acid were 98% and 80%, respectively. Phenylbutazone levels must be reconfirmed, as they were variable. Cyclic AMP levels of experimental calvaria were greater than control. The greatest increase (5 times control) occurred in PGE_2 supplemental media. The smallest increase (1 1/2 times control) took place in the niflumic acid supplemental media. Cyclic GMP levels, however, varied in their relation to control and experimental. The ratio of c-AMP/c-GMP ranged from 6/1 (24 hours) to 67/1 (72 hours) for PGE_2 medium. Other experimentally supplemented media exhibited temporal variations of c-AMP/c-GMP which were less drastic. Cyclic AMP increased in approximately a parabolic fashion and c-GMP decreased in approximately linear fashion in the PGE_2 medium. Relationships between c-AMP and c-GMP displayed an approximately non-sloping, linear relationship with all other experimental media. Results may be summarized by stating that known and probable inhibitors that were evaluated affected PGE_2 synthesis in vitro; however, certain inhibitors (i.e., indomethacin) caused almost complete PGE_2 inhibition and may, therefore, prove to be useful in controlling osteolysis in vivo. Furthermore, in vitro the presence of PGE_2 is associated positively

with c-AMP and inversely with c-GMP. Similar associations between cAMP, cGMP, and PG inhibitors were not demonstrated.

PROJECT: 3M161102BS10

WORK UNIT TITLE: (U) Acceleration of Wound Healing

PRINCIPAL INVESTIGATOR: LTC Jeffrey O. Hollinger, DC

A Study on 50:50 PLA:PGA Plus Diphosphoinositide-Lysozyme (DPI-L)

for the Promotion of Calcification in Osseous Healing

PROBLEM: To determine if a biodegradable, biocompatible copolymer of PLA and PGA in combination with a diphosphoinositide inositol-lysozyme complex could induce osteogenesis in experimental wounds created in endochondral and intramembranous bones.

APPROACH: A material was formulated that consisted of a combination of a proteolipid and biodegradable, biocompatible copolymer. The proteolipid was prepared by combining a lysozyme and phosphatidyl inositol 4, 5 - diphosphate in a 1:1 weight ratio. A raw polymer of 50:50 poly (L(-) lactide-co-glycolide) was solubilized in methylene chloride, reprecipitated with anhydrous methanol, and blended with the proteolipid at a 1% w/w ratio of proteolipid to copolymer. The combined material was formed into cylindrical implant plugs (1.95mm X 2.05mm) in a teflon mold and placed into a lyophilizer chamber for 48 hours at 40°C. The implants recovered were then sterilized with ethylene oxide for 6 hours and degassed. Implants were also prepared that consisted of only a plain copolymer of 50:50 poly (L(-) lactide-co-glycolide), and these were managed in a fashion identical to the copolymer plus proteolipid. One hundred and eighty rats were randomly divided into three groups and wound sites were prepared in the tibias using a bone trephine (1.95mm O.D.). One group(A) received copolymer - proteolipid implants; the second group(B) received plain copolymer; the third group(C) served as controls. At 3, 7, 14, 21, 28, and 42 days animals from each group were sacrificed and implant sites were retrieved, processed for plastic embedding, stained by Goldner-trichrome, and 3.5 m sections were evaluated histomorphometrically using an image analysis system. In addition to the tissue histomorphometry, serum and bone alkaline and acid phosphatases were assayed; protein and hydroxyproline determinations were performed; and atomic absorption spectrophotometric evaluations were done to quantify calcium and phosphate molar ratios in host bone. Isoelectric focusing was also applied for isoenzyme identification.

RESULTS: The copolymer-proteolipid implant group demonstrated overall increases in the total volumetric density of bone formation, trabecular diameter, osteoid thickness, and number of osteoblasts that exceeded the healing response in wounds of groups B and C. Similarly, the plain copolymer group results exceeded those of the control group. Overall trends between treatment groups displayed an ascending, predominantly linear difference over time; however, towards the latter stages a quadratic component of that trend was evident. Based soley upon histomorphometric data, therefore, it appears that the copolymer-proteolipid implant may be useful

for stimulating the important early phase of bone repair. Biochemical enzyme assays were an unpredictable indicator of osseous repair. In contrast, histochemical assays were considerably more representative and essentially the data on these analyses ran parallel to the histomorphometric variables. Atomic absorption spectrophotometry and isoelectric focusing proved to be of only marginal value in evaluating bone repair.

PROJECT: 3M161102BS10

WORK UNIT TITLE: (U) Acceleration of Wound Healing

PRINCIPAL INVESTIGATOR: LTC Jeffrey O. Hollinger, DC

Enhanced Healing of Soft Tissue Wounds Using Diphenylhydantoin Sodium Incorporated into a Meshwork of Biodegradable Copolymer (50:50 poly L-(-) lactide-co-glycolide)

PROBLEM: To develop an agent that could be applied topically to a skin wound to hasten primary closure. To develop an agent that could "bulk-up" atrophic soft tissue morphology.

APPROACH: A fibrous mesh consisting of 50:50 poly L-(-) lactide-co-glycolide incorporating diphenylhydantoin-sodium (DPH) was prepared. An unembellished mesh (pure copolymer) was also prepared. Excisional wounds 3X5cm were made to the panniculus carnosus in backs of rats. Treatment consisted of either one or the other types of fibrous mesh dressing, IP - DPH, or no treatment. Wound sites were evaluated histologically, histomorphometrically, by total protein and hydroxyproline assays, by tensile testing, and by RIA (^{125}I) for DPH.

RESULTS: The 1-28 day evaluation period analyses revealed little or no difference between treatments for the excisional wounds. Subtle differences were occasionally displayed by animals receiving IP-DPH. This group displayed a greater amount of collagen and a higher density of fibroblasts than the other treatment groups. The primary reason for the lack of a positive healing response may be explained as a consequence of the "wicking" action that was engendered by the fibrous nature of the copolymer mesh. This condition militated against an intimate tissue-dressing interface, obviating suitable DPH dissemination into the healing wound bed. A second generation "film-type" dressing has been prepared; however, continuation of this project can no longer be anticipated.

PROJECT: 3M161102BS10

WORK UNIT TITLE: Acceleration of Wound Healing

PRINCIPAL INVESTIGATOR: James R. Heath III

Identification of Leukocyte Populations Responsible

for Production of OAF and Their Role in Bone Resorption

PROBLEM: Studies have shown 10-12% of all combat wounds involve the maxillofacial apparatus. Many of these result in contaminated osseous wounds. The lymphokine, Osteoclast Activating Factor (OAF), is one of the mediators of the delayed bone healing seen in contaminated osseous wounds. OAF is produced by white blood cells in response to bacterial products and stimulates local osteoclasts leading to bone resorption instead of bone growth. A better understanding of the mechanisms of action of OAF and of its chemical nature could lead to an abrogation of the detrimental effects of OAF and thus an acceleration of wound healing.

APPROACH: 1. Production of OAF: OAF is produced *in vitro* by stimulating human small lymphocytes with the mitogen phytohemagglutinin (PHA) in large volume cell culture. The culture supernatants are filter sterilized then passed through an ultrafiltration membrane with a 10,000 molecular weight cut-off. The retentate is made 1 molar with NaCl and filter dialyzed with phosphate buffered saline (PBS) on the same membrane. The ultrafiltrate and dialysate are combined and subjected to a second ultrafiltration on a 1,000 molecular weight cut-off membrane followed by filter dialysis with PBS. The retentate is fractioned on a Sephadex G-25 packed column with PBS as the mobile phase.
2.Bioassays: (a) The presence of osteolytic activity in gelfiltration fractions, culture supernatants, ultrafiltration retentates and filtrates is measured by the standard bone resorption bioassay. Briefly, rats in the 18th day of gestation are injected i.p. with ^{45}Ca. The following day, the fetuses are removed aseptically and the radial and ulnar bones of each fetus are dissected free of muscle, connective tissue and cartilagenous epiphyses and placed individually in 4 wells of a 24-well culture plate containing 0.23ml BGJ_b in each well. After an 18hr preculture, the culture medium is removed and replaced with 0.125ml test solution and the other pair receives control solution. The bones are incubated for 120 hrs. at 37°C in 5% CO_2 and 100% humidity. The bones and culture supernatants are separated and placed in individual scintillation vials. The bones are decalcified with 5% CCl_3COOH and then the amount of ^{45}Ca in both bones and culture supernatants is determined. The per cent $^{45}Ca^{++}$ released from experimental and control bones is computed. A test/control (T/C) ratio is computed. T/C ratios >1 indicate increased bone recorption. However, ratios <1 are ambiguous since they could indicate either decreased bone resorption, increased calcium uptake or toxicity of the test solution to the bone cuiture. (b) To resolve the ambiguity seen when ratios >1 are encountered, we have developed the following modification of the standard

bioassay. The bones are not prelabeled with ^{45}Ca prior to dissection. Instead, an equal amount of ^{45}Ca is added to every well at the same time the test and control solutions are added. The incubation time is shortened to 6 hrs. The percent of calcium uptake is computed and a T/C per cent uptake determined. Thus, this modification is essentially a reversal of the standard bone resorption assay.

RESULTS: We have reported identifying a substance in the PHA stimulated human mononuclear cell culture supernatants which causes a highly significant inhibition of osteolysis in the bone resorptipn bioassay. Further studies in the past year have shown that this subetance, in nanogram quantities can block the activity of the known osteolytic agents prostaglandin (PGE_2) and OAF. Using the new modification of the bone assay, we have found that this substance causes a significant ($p<.0001$) increase in calcium uptake. This accounts for the antiosteolytic activity of the substance and suggests that it may be a stimulator of osteogenesis.

PROJECT: 3M161102BS10

WORK UNIT TITLE: (U) Acceleration of Wound Healing

PRINCIPAL INVESTIGATOR: COL Stephen G. Woodyard

Citric Acid Enhancement of Oral Soft Tissue Healing

PROBLEM: Citric acid application to uncontaminated root surfaces apparently enhances soft tissue healing. Soft tissue pedicle flaps do not heal satisfactorily when placed against contaminated tooth root surfaces as evidenced by a failure of such tissues to reattach. This investigation was designed to determine if citric acid applications might enhance soft tissue healing (adhesions) to contaminated root surfaces as might occur following oral wounding.

APPROACH: Single surface root recession defects were created in six monkeys followed by six weeks of exposure to oral fluids. Surgical repair utilizing soft tissue flaps placed against citric acid treated and untreated root surfaces followed. Histologic evidence of repair was evaluated.

RESULTS: Citric acid application significantly enhanced wound repair, indicating this treatment offers substantial benefit. Adhesion of tissue allowed nearly complete repair of exposed root surfaces to be accomplished, unlike control surfaces where repair was unsatisfactory.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION: DA OD 6021	2. DATE OF SUMMARY: 83 10 01	REPORT CONTROL SYMBOL: DD-DRAR(AR)636					
3. DATE PREV SUMMARY: 82 10 01	4. KIND OF SUMMARY: M. TERM	5. SUMMARY SCTY: U	6. WORK SECURITY: U	7. REGRADE:	8. CLASS CONTR: NL	9. SPECIAL DATA: CONTRACTOR ACCESS: YES NO	10. LEVEL OF SUM: A. WORK UNIT
11. NO./CODES: PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER	
a. PRIMARY	61102A	3M161102BS10		DA		010	
b. CONTRIBUTING							
c. EFFECTIVE	////////////	STOG 82/83-6.2/4					

12. TITLE (Procede with security classification code): (U) Problems Involved in Military Oral Health Care Delivery Related to Therapeutic Agents and Materials

13. SCIENTIFIC AND TECHNOLOGICAL AREAS: 012600 Pharmacology 002300 Biochemistry 010100 Microbiology

14. START DATE	15. ESTIMATED COMPLETION DATE	16. FUNDING AGENCY	17. PERFORMANCE METHOD
68 09	CONT	DA	C. IN-HOUSE

18. RESOURCES ESTIMATE

FISCAL YEAR	a. PROFESSIONAL MAN YRS	b. FUNDS (In Thousands)
PREVIOUS 83	2.5	175
CURRENT		

19. CONTRACT/GRANT: a. DATE/EFFECTIVE: ; DURATION: ; b. NUMBER: ; c. TYPE: ; d. AMOUNT: ; e. KIND OF AWARD: ; f. CUM. AMT.:

20. RESPONSIBLE DOD ORGANIZATION

NAME: USA Institute of Dental Research

ADDRESS: Washington, DC 20307

RESPONSIBLE INDIVIDUAL

NAME: SWEENEY, T.P.

TELEPHONE: 202 576-3484

21. GENERAL USE: Foreign Intelligence Considered

22. PERFORMING ORGANIZATION

NAME: USA Institute of Dental Research

ADDRESS: Washington, DC 20307

PRINCIPAL INVESTIGATOR (Provide Name and U.S. Academic Institution)

NAME: Setterstrom, J.A.

TELEPHONE: 202 576-3662

SOCIAL SECURITY ACCOUNT NUMBER: POC:DA

ASSOCIATE INVESTIGATORS

NAME: Vincent, J., Miller, R.A.

NAME: Heath, J.

23. KEYWORDS (Provide Key Technical Terms): (U) Microencapsulated Antibiotics; (U) Infection Control; (U) Wound Healing; (U) Sustained Release Antibiotic; (U) Laboratory Animals

24. TECHNICAL OBJECTIVE, 25. APPROACH, 26. PROGRESS (Provide individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) To evaluate the special military problems of drug storage, heat susceptibility, long-term drug potency, sterility of bulk items, lack of refrigeration in combat zones and delivery to the patient. To investigate drug hazards. To investigate the use of biodegradable polymers for the long-term, slow release of drugs.

24. (U) Improved means of drug delivery in the field using microencapsulated medicaments will be studied. The hazards in the use of various drugs and the use of biodegradable, biocompatible materials for surgical repair of combat wounds will be studied.

25. (U) 8209-8309 Ampicillin anhydrate microcapsules have been formulated using a 50:50 PL-PLGA excipient. The goal was achieved when highly loaded microcapsules with desired in vivo release kinetics were obtained in very good yields. The microcapsules were effective in vivo. Problems remain in the formulation of gentamicin sulfate microcapsules. Although release kinetics are not optional, the drug has been encapsulated in 50:50 DL-PLG.

(Continued on reverse side)

DD FORM 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498A AND 1498B, 1 MAR 80 FOR ARMY USE ARE OBSOLETE.

PROJECT: 3M161102BS10

WORK UNIT TITLE: (U) Problems Involved in Military Oral Health Care Delivery Related to Therapeutic Agents and Materials

PRINCIPAL INVESTIGATOR: JEAN A. SETTERSTROM, Ph.D.

Development of Encapsulated Antibiotics for Topical Administration to Wounds

Problem: Combat wounds are characterized by a high incidence of infection primarily because of the inevitable presence of devitalized tissue and foreign body contaminants from missile fragments that carry dirt and debris into the wound. During evacuation, the wound may be exposed to further contamination and delay before initial treatment. Wound healing in the combat casualty, therefore, must overcome adversities not seen in the highway victim or civilian counterpart. Among soldiers, infections have remained a major cause of morbidity that results in lengthened hospitalization and combat ineffectiveness.

Approach: Improved methods to deliver antibiotics to contaminated tissue following traumatic injury are needed in order that sustained and effective tissue levels of antibiotics can be maintained at the wound site despite the inadequate perfusion of blood resulting from shock or the destruction of blood vessels to devitalized areas. The improved method should be easily applied in a single dose to the wound site as soon as possible after injury when infection is most likely to be suppressed. Such a novel antibiotic delivery system is being developed in which ampicillin anhydrate and gentamicin sulfate are being incorporated individually into microspheres of biocompatible, biodegradable, copolymer that are formulated to slowly release the drug over a sustained period (14 days). These microspheres, which will completely biodegrade once all drug is released, exist as a free-flowing powder that can be easily dusted onto wounds under field conditions.

Results: Experiments were performed to evaluate the efficacy of prototype microcapsules in artificially induced infections. Wounds 2.5-3.0cm long and 1cm deep were made in the thigh muscle of albino rats. The muscles were traumatized by uniformly pinching with tissue forceps, and inoculated with known quantities of Staphylococcus aureus and Streptococcus pyogenes. Sterile dirt was placed in each wound to serve as in infection potentiating factor. The wounds were then treated within one hour by sprinkling sterile, preweighed amounts of microencapsulated antibiotic directly in the wound. Control groups consisted of animals with wounds receiving no therapy, unloaded microcapsules, or topically applied, free ampicillin anhydrate. All

wounds were sutured closed with 3-0 black silk.

The ampicillin anhydrate microcapsules effectively reduced bacterial counts in the contaminated wounds. S. pyogenes was present in 90% of the untreated wounds at 14 days, but was eliminated from microcapsule treated wounds within 48 hours. Although S. aureus remained in all microcapsule treated wounds at 7 days, compared with untreated controls, the bacterial count decreased ($\geq$2 log $_{10}$/gram of tissue) between day 2 and 7. This reduction was not observed in untreated controls. Wounds treated with unloaded DL-PGL microcapsules, or topically applied free ampicillin anhydrate remained infected at 14 days with $\geq 10^8$ organisms per gram of tissue. Whereas, 60% of the wounds treated with microencapsulated ampicillin anhydrate were sterile.

Successful controlled release of bioactive ampicillin anhydrate was achieved in vitro and in vivo. The system developed provides a successful model that encourages efforts to encapsulate additional antibiotics. Often, it may be desirable for broad spectrum control to combine two or more antibiotics in treating wounds. It is anticipated that mixtures of different antibiotic-containing microcapsules may be blended and packaged together to increase the versatility of the product.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA OF6024	831001	DD-DR&E(AR)636

3. DATE PREV SUMRY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8. DOD/N INSTR'N	8a. SPECIFIC DATA FOR CONTRACTOR ACCESS	9. LEVEL OF SUM
821001	H. TERM	U	U		NL	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61102A	3M161102BS10	DA	012
b. CONTRIBUTING				
c. CONTRIBUTING	/ / / / /	STOG 82/83-6.2:4		

11. TITLE (Procede with Security Classification Code)

(U) Identification and Control of Oral Infections

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

010100 Microbiology; 002300 Biochemistry; 012600 Pharmacology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
6607	CONT	DA	C. IN-HOUSE

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION:

b. NUMBER:

c. TYPE: d. AMOUNT:

e. KIND OF AWARD f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR: PRECEDING 83	2.0	154
FISCAL YEAR: CURRENT		

19. RESPONSIBLE DOD ORGANIZATION

NAME: U S Army Institute of Dental Research

ADDRESS: Washington, DC 20307

RESPONSIBLE INDIVIDUAL

NAME: SWEENEY, T.P.

TELEPHONE: (202) 576-3484

20. PERFORMING ORGANIZATION

NAME: U S Army Institute of Dental Research

ADDRESS: Washington, DC 20307

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)

NAME: SETTERSTROM, J.A.

TELEPHONE: (202) 576-2290/3062

SOCIAL SECURITY ACCOUNT NUMBER: POC:DA

ASSOCIATE INVESTIGATORS

NAME: Woodyard, S.

NAME: Vincent, J., Heath, J.

21. GENERAL USE

Foreign Intelligence Considered

22. KEYWORDS (Provide each with Security Classification Code)

(U) Oral Health Status; (U) Gingival Exudates; (U) Crevicular Fluid; (U) Sporicidin; (U) Cidex; (U) Monoclonal Antibodies

23. TECHNICAL OBJECTIVE; 24. APPROACH; 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) To investigate the source and treatment of orofacial infections encountered in field conditions, foreign countries and diverse climates. To evaluate the special agents, instruments and chemicals necessary under military conditions.

24. (U) Orofacial infections of significance in the diverse military environment will be studied by microbiological, immunological, and electron microscopy methods. Possible sources of oral infections will be evaluated and the effectiveness of commercially available as well as in-house designs will be studied for their ability to control or prevent oral infections.

25. (U) Several in vivo evaluations of wound dressings containing povidone iodine and benzalkonium chloride have been performed. To date, all experiments have suggested that while these antiseptic agents can decrease somewhat the bacterial counts in the wound, they do not reach an acceptable level at 72 hours. An in vitro evaluation of the effectiveness of nitrofurazone resulted in similar findings. At present, steps are underway to evaluate clindamycin, ampicillin, and chlorhexidine diphosphanilate in the same wound dressing material. Studies have begun on the production and use of monoclonal antibodies for the rapid identification of maxillofacial infections. The similarity of cellular protein patterns has been determined by polyacrylamide gel electrophoresis. Hybridoma cells producing antibody reactive with Fusobacterium nucleatum have been cloned and antibody produced and purified from mouse ascites fluid. Steps are underway to accomplish this for the five other anaerobic microorganisms selected for study.

* Available in contractor's own originator's format

DD FORM 1 MAR 88 1498

PROJECT: 3M161102BS10

WORK UNIT TITLE: (U) Identification and Control of Oral Infections

PRINCIPAL INVESTIGATOR: COL Jack W. Vincent, DC

In Vivo Evaluation of a Dressing Containing Poly-L(-) Lactide and Povidone Iodine

PROBLEM: In a battlefield environment, the feasibility of immediate evacuation of a patient may not exist. Wounds which are contaminated or which run the risk of contamination will require an effective means of therapy for extended periods. Antimicrobial agents presently must be administered on a continuing basis which may not be advantageous in a hostile environment. If wound infection is not prevented or controlled, the detrimental effects which hinder the healing process may become life threatening or, at the least prolong recovery time before the soldier can return to duty.

APPROACH: A wound dressing of a non-woven poly-L(-) lactide has been developed. This material has been shown to be able to incorporate both povidone iodine and bensalkonium chloride and once incorporated, to release this material in a controlled fashion over a 72 hour period *in vitro*. This determination involved release into a reservoir of buffer. This study was designed to evaluate these materials *in vivo* to determine if the release kinetics were the same and, if so, were these preparations effective in treating an infected wound. The guinea pigs were selected as the animal model due to the anatomical similarity of the subcutaneous tissue of the paravertebral area in relation to that of a humans. A controlled size full thickness wound created in this area would receive a known quantity of a known pathogen. This area would then be covered with a wound dressing containing the antimicrobial agent to be tested. An identical wound receiving the same inoculum will be covered with the same wound dressing without the antimicrobial agent and thus serve as a control. Following application, the wound dressing will be secured in place with tissue adhesive. After 72 hours all wounds will be assayed for viable micro-organisms from the initial inoculum. Tissue biopsies can be removed, homogenized and resulting supernatant assayed for cfu/mg tissue weight. An alternate means of assay will be to isolate the wound surface with a sterile wash-basin and scrubing the surface with a mild detergent solution. This solution can then be evaluated by serially diluting and plating on culture medium to determine cfu/ml which can be converted to cfu/surface area. Bacterial counts of 10^5 cfu (or greater)/cm^2 is indicative of an infected wound.

RESULTS: During this period, several *in vivo* experiments have been accomplished in order to evaluate these antimicrobial agents. Initially thirty guinea pigs (twenty experimental and ten control) were wounded by full thickness dissection in the paravertebral area inoculated with

approximately 10^9/ml of Stephylococcus aureus following which they were covered with the appropriate wound dressings: ten controls, ten containing povidone iodine and ten containing benzalkonium chloride. Following 72 hours incubation, tissue biopsies were removed, homogenized and assayed. Counts from both experimental groups were low ($0-10^5$ cfu/gm) however, counts were also low in the control group animals ($0-10^7$ cfu/gm). The possibility of absorption of the inoculum into the non-woven dressing was a destinct possibility which although possibly a good characteristic for a wound dressing did little to allow evaluation of the efficency of the antimicrobial agent involved. This experiment was repeated and at the time of assay, the wound dressing material was also evaluated for viable S. aureus. Both the experimental and control dressing demonstrated high counts of S. aureus indicating the inability of povidone iodine to control this organism. Pure povidone iodine (22mgcm^2 wound) also proved ineffective in the management of this wound model. At this time by a standard tube dilution method for its ability to inhibit the growth of S. aureus in vitro. A concentration of 6.2 g/ml inhibited visable growth of S. aureus however, when this material was plated, high counts were obtained even from samples containing 50 g/ml of nitrofurazone. These results suggest that nitrofurazone would not be effective in this model system. Efforts are presently being directed toward characterization of non-woven dressing powders and microcapsules containing clindamycin, ampicillin, and chlorhexidine diphosphanilate.

PROJECT: 3M161102BS10

WORK UNIT TITLE: (U) Identification and Control of Oral Infections

PRINCIPAL INVESTIGATOR: COL Jack W. Vincent, DC

Production and Utilization of Monoclonal Antibodies in the Rapid Identification of Anaerobic Microorganisms Associated With Maxillofacial Infections

PROBLEM: There is currently no rapid method for the identification of microorganisms present in a wound exudate. Conventional techniques require approximately 2 to 3 days for this procedure. Such a delay in evaluating contaminated maxillofacial wounds and in selecting appropriate antibiotic therapy could result in severe sequelae. A method of rapid detection would appear to be ideal for the prevention of such a delay and may serve as a model for the detection of biological agents which might be utilized in a biological warfare environment.

APPROACH: The technique of monoclonal antibodies will be used to develop a system for the rapid identification of anaerobic microorganisms. A 2% suspension of whole cells of bacteria will be used to immunize BALB/c BYJ mice by an intraperitoneal injection (0.25ml) weekly for five weeks. At three days before the cell fusion a final injection will be given to each mouse. After anesthesia, the spleen will be removed aseptically and minced to a single cell suspension and residual red blood cells lysed by the addition of 0.17m ammonium chloride. Approxmately 10^8 splenocytes will be combined with either 10^8 P-3 mouse myeloma cells or 10^8 P-3 Ag 8.653 mouse myeloma cells in the presence of 35% polyethylene glycol to allow for fusion and then plated in a selective medium which will inhibit the growth of all but successfully fused hybrid cells. These hybrids will be screened by serological methods so as to identify clones of cells which carry the genetic information enabling synthesis and secretion of monoclonal antibody and, also, the ability to survive in cells culture. Appropriate hybrid clones will be isolated by limiting dilution and grown in sufficient volume so as to be preserved in cryoprotective media. Following isolation, these clones can be injected (10^6 viable cells) intraperitoneally into BALB/c mice which have been previously primed with pristane. The ascites fluid produced by the resulting tumors should contain 25-75mg/ml of antibody. When isolated this monoclonal antibody will be used to develop a system for rapid (2-3 hours) detection of wound contaminants. Such a system (most probably the ELISA) must display extreme sensitivity and specificity which should be provided by these techniques.

RESULTS: BALB/c BYJ mice have been immunized with the following anaerobic microorganisms: Fusobacterium nucleatum, Bacteroides gingivalis, Bacteroides fragilis, Peptococcus magnus, Peptostreptococcus micros and Peptostreptococcus anaerobius. Both the cell lines P-3 and P-3 Ag 8.653 have

been used for fusion procedures. To date several fusion attempts have been destroyed by fungal growth or by failure of the selective medium to inhibit the growth of unfused cells. To date, a hybrid cell line containing nuclear material from splenocytes sensitized to F. nucleatum and P-3 mouse myeloma cells has been cloned and shown to be positive for anti - F. nucleatum antibody by ELISA. Additional fusions have been performed using other splenocytes and P-3 Ag 8.653 mouse myeloma cells. Preliminary results suggest hybrid cells have resulted which are producing antibody reactive with Peptococcus magnus and Becteroides fragilis. Work is presently ongoing to accomplish these same procedures with the remaining anaerobic microorganisms selected for study.

PROJECT: 3M161102BS10

WORK UNIT TITLE: (U) Identification and Control of Oral Infections

PRINCIPAL INVESTIGATOR: COL Jack W. Vincent, DC

Use of Monoclonal Antibodies for the Isolation and Identification of Osteoclast Activating Factor (OAF) and a Recently Identified Inhibitor of Osteolysis

PROBLEM: The study of OAF presently requires a prolonged procedure in order to obtain the material from the culture supernatant of stimulated human leukocyte. Once obtained in the form of 105, 5ml fractions, each fraction must be tested in a bone bioassay system in order to identify OAF activity. A maximum of 15 fractions/week can be tested. In addition, there is presently no technique which can be used to identify OAF in tissue specimens or to determine its site of activity. When available, monoclonal antibodies could be utilized in vivo to block OAF activity much in the same way as they are presently used to block graft vs host reactions in bone marrow transplants.

APPROACH: The technology of monoclonal antibodies can be utilized due to their specificity or ability to recognize and react with a single antigenic determinant when present in a vast mixture of substances. Mice which have been immunized with the antigen of interest provide sensitized lymphoblasts which, in the presence of polyethylene glycol, can be fused with an established mouse myeloma cell line. Resulting hybrid cell lines carry nuclear material from both cells thus are coded for synthesis and secretion of monospecific antibodies and the capability of survival in continuous culture. Although OAF is a small molecule (molecular weight 1500 daltons) for an effective immunogen, other small molecules can be detected by antibody reactions. If it is possible to develop monoclonal antibodies to OAF, such antibodies could be used to extract OAF from crude culture supernatants by affinity chromatography. Such a capability could be accomplished in days rather than the months now required to fractionate and test culture supernatants acquired from phytohemagglutinin (PHA) stimulated human leukocyte populations. These antibodies could also be used to identify the specific active site of OAF in tissue specimens. Lastly, as anti-T-cell monoclonal antibodies vs host responses with bone marrow transplants in immuno-deficient hosts, anti-OAF antibodies could be used to control or eliminate OAF activity in vivo. An additional substance whose biological activity appears to be one of inducing osteogenesis has also been identified in these same culture supernatants of stimulated human leukocytes. The activity of this substance is such that it can apparently block OAF activity and the activity of other known osteolytic agents when evaluated with a molecular weight of 6000 daltons requires the identical, lengthy procedures for isolation and identification as does OAF. Monoclonal antibodies reactive with this substance would provide the same advantages as

those previously described for OAF.

RESULTS: A crude culture supernatant from a PHA stimulated human leukocyte culture was tested to verify both OAF and the osteolytic inhibitor activity. The crude form was utilized in the hopes that these substances might be present in a complex form which might prove to be more immunogenic. An additional sample of culture supernatant was mixed with bovine serum albumin (BSA) (1mg/ml) because of the known tendency of OAF to complex with BSA and thus take advantage of a more complex and more immunogenic substance. On a weekly basis for five weeks two BALB/c BYJ mice were infected intraperitonealy with 0.25ml of this complex. Fusion of splenocytes obtained from these mice was performed three days following the final immunization. Approximately 10^8 splenocytes and 10^7 P-3 mouse myeloma cells were exposed to 35% polyethylene glycol and then plated in a selective medium which would inhibit the growth of all but hybrid cells. Following twenty-one days of inbucation, twenty-four hybrid clone were detected and tranfered to larger volume culture. When viability counting identified the presence of at lease $5X10^6$ cells, the clones were transfered to a cryoprotective medium and frozen for preservaton in liquid nitrogen at a concentration of $5X10^6$ cells per ml. Testing for specificity was accomplished by an inhibition assay combined with the bone bioassay. Due to technical problems, only samples of the osteolytic inhibitors were available. This 6000 molecular weight fraction would also contain some OAF as this 1500 molecular weight substance is known to exist in complexed forms in the mol. wt. range of 1500 to 18,000 daltons. The inhibition assay involved incubation of the osteolytic inhibitors with the culture supernatant from hybrid clones prior to the bone bioassay with the same osteolytic inhibitors incubated with uninoculated culture medium served as appropriate controls. Of the hybrids tested, none appeared to inhibit the activity of the osteolytic inhibitor but four hybrid clones appeared to enhance the osteogenic effect. It is speculated that this phenomenon may represent an inactivation of residual OAF in this fraction. These hybrid clones are preserved and available for testing against OAF at this time.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

				DA302908	Q1 OCT 83		Z01708
	A NEW	U	U		NL		A WORK UNIT
TO NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER	
	61102A	3M161102BS10		DA		081	
FORMER							
MCSS: ORV	8T00	82/83-M.2/B					

(U) IDENTIFICATION OF LEUKOCYTE POPULATIONS RESPONSIBLE FOR PRODUCTION OF OSTEOCLAST ACTIVATING FACTOR AND THEIR ROLE IN BONE RESPORTION

002300 BIOCHEMISTRY	002800 BIOLOGY	010200 MINING E

OCT 83	CONT	DA	C. IN-HOUSE

		1983	0.0	$ 0
		1984	0.8	$ 82

F. CUM/TOT: $ 0

038870	11	038870	11

MORDC INSTITUTE OF DENTAL RSCH USAIDR

WASHINGTON DC 20307

SWEENEY, T P MD 2C

202-576-3484

F.I.C.A.

MILITARY

MORDC INSTITUTE OF DENTAL RSCH USAIDR

WASHINGTON DC 20307

HEATH, J R, III DA

202-576-3092

(U) WOUND HEALING ;(U) OSTEOCLAST ACTIVATING FACTOR ;(U) LYMPHOKINE ;(U) BONE RESORPTION ;(U) LAB ANIMALS ;(U) RATS ;(U) RAM IV;

OBJECTIVE:(U) MAXILLOFACIAL WOUNDS ACCOUNT FOR 10-12 PERCENT OF ALL COMBAT WOUNDS. MANY OF THESE RESULT IN CONTAMINATED OSSEOUS WOUNDS. THE LYMPHOKINE OSTEOCLAST ACTIVATING FACTOR (OAF) IS ONE OF THE AGENTS THAT CAUSES THE DELAYED BONE HEALING SEEN IN THIS TYPE OF WOUND. A BETTER UNDERSTANDING OF THE ACTION AND CHEMICAL NATURE OF OAF COULD LEAD TO AN ABROGATION OF ITS DETRIMENTAL EFFECTS ON BONE HEALING AND THUS LEAD TO AN ACCELERATION OF BONE HEALING.

APPROACH: (U) OAF IS PRODUCED BY STIMULATING HUMAN LEUKOCYTES WITH THE MITROGEN PHYTOHEMAGGLUTININ (PHA) IN LARGE VOLUME CELL CULTURE. THE CULTURE SUPERNATANTS, WHICH CONTAIN OAF IN NANOGRAM QUANTITES, ARE FIRST SUBJECTED TO AN ULTRAFILTRATION PROTOCOL WHICH CONCENTRATES AND ISOLATES COMPOUNDS WITH MOLECULAR WEIGHTS BETWEEN 1,000 AND 10,000 DALTONS. THIS IS FOLLOWED BY GELFILTRATION ON A STANDARDIZED COLUMN. OAF IS DETECTED IN CULTURE SUPERNATANTS AND PURIFICATION FRACTIONS BY A STANDARD BONE RESORPTION BIOASSAY WHICH INVOLVES THE RELEASE OF SUPERSCRIPT 45CA FROM FETAL RAT LONG BONES IN VITRO. THIS PROJECT WAS STARTED AS DA088037.

PROGRESS: (U) NONE.

DD 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY	DA302911	01 OCT 83	REPORT CONTROL SYMBOL Z01708

	A. NEW	U	U		NL	☒ ☐	A WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
PRIMARY	61102A	3M161102BS10	DA	302
FORMER				
STRAT. OBJ. STOG : 82/83-8.2/6 :				

(U) A COMPARISON OF HYDROXYPROLINE LEVELS OF GINIVAL TISSUE EXUDATES TO CLINICALLY GRADED LEVELS OF INFLAMMATION

010100 MICROBIOLOGY 002300 BIOCHEMISTRY 012600 PHARMACO

START DATE	ESTIMATED COMPLETION DATE	FUNDING AGENCY	PERFORMANCE METHOD
OCT 83	CONT	DA	C. IN-HOUSE

CONTRACT/GRANT		RESOURCES ESTIMATE	PROFESSIONAL MAN YRS	FUNDS (In Thousands)
DATES EFFECTIVE / EXPIRATION	FISCAL YEAR	1983	0.0	$ 0
NUMBER / TYPE / AMOUNT	CURRENT	1984	0.2	$ 20
KIND OF AWARD / F. CUM/TOT: $ 0				

RESPONSIBLE DOD ORGANIZATION 038870 11	PERFORMING ORGANIZATION 038870 11
NAME: HQRDC INSTITUTE OF DENTAL RSCH USAIDR	NAME: HQRDC INSTITUTE OF DENTAL RSCH USAIDR
ADDRESS: WASHINGTON DC 20307	ADDRESS: WASHINGTON DC 20307
RESPONSIBLE INDIVIDUAL	PRINCIPAL INVESTIGATOR
NAME: SWEENEY, T P MD 20	NAME: WOODYARD, S G DA
TELEPHONE: 202-576-3484	TELEPHONE: 202-576-3393
GENERAL USE: F.I.C.A.	ASSOCIATE INVESTIGATORS
MILITARY/CIVILIAN APPLICATION: MILITARY	NAME: MILLER, R A

(U) INFLAMMATION;(U) WOUND EXUDATE ;(U) HYDROXYPROLINE ;(U) RAM IV;

OBJECTIVE:(U) HYDROXYPROLINE (HYP) IS A UNIQUE COMPONENT OF CONNECTIVE TISSUE, ITS PRESENCE IN TISSUE EXUDATES INDICATING SOME DEGREE OF COLLAGEN DESTRUCTION. EXUDATES ORIGINATING IN INFECTED WOUNDS MIGHT REASONABLY BE EXPECTED TO DEMONSTRATE INCREASING LEVELS OF INFECTION AND COLLAGEN DEGRADATION, WHILE THE OPPOSITE WOULD OCCUR IN HEALING WOUNDS. USING PERIODONATAL POCKETS AS A CONVENIENT MODEL REPRESENTING CHRONIC INTRAORAL INFECTIONS, EXUDATES ARE TO BE COLLECTED, EVALUATED FOR HYP AND COMPARISONS MADE BETWEEN SUCH LEVELS AND CLINICALLY GRADED LEVELS OF INFLAMMATION. THE GOAL IS TO DEVELOP AN OBJECTIVE, NONINVASIVE MEANS FOR EVALUATING THE EFFECTS OF THERAPY AND DEGREE OF INFLAMMATION EXISTING IN ORAL WOUNDS AND INFECTIONS.

APPROACH: (U) FOLLOWING CLINICAL GRADING OF TISSUE INFLAMMATION, SAMPLES OF TISSUE EXUDATE ARE COLLECTED. SAMPLES ARE HYDROLYZED AND PROCESSED TO ALLOW MEASUREMENT OF HYP CONTENT USING HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY. CONVENTIONAL MEANS OF TREATMENT WHICH REDUCE OR ELIMINATE INFLAMMATION AND INFECTION FOLLOW, WITH SUBSEQUENT TISSUE EXUDATES BEING COLLECTED. HYP LEVELS SHOULD DECREASE IF THIS IS TO BE A USEFUL INDICATOR. THIS PROJECT WAS STARTED UNDER DAOF8024.

PROGRESS: (U) NONE.

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				DA302925	01 OCT 83	REPORT CONTROL SYMBOL Z01708
	A. NEW	U	U		NL	A. WORK UNIT
10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER	WORK UNIT NUMBER	
a. PRIMARY	61102A	3M161102BS10		DA	083	
b. CONTRIBUTING						
c. CONTRIBUTING	MIPS, OBJ. STOG. 82/83-8.2/8					

(U) IN VIVO EVALUATION OF A WOUND DRESSING CONTAINING POLY-L(-) LACTIDE AND VARIOUS MEDICAMENTS

010100 MICROBIOLOGY 002300 BIOCHEMISTRY 012900 PHARMACO

START DATE	ESTIMATED COMPLETION DATE	FUNDING AGENCY	PERFORMANCE METHOD
OCT 83	CONT	DA	C. IN-HOUSE

CONTRACT/GRANT: a. DATES/EFFECTIVE: EXPIRATION: b. NUMBER: c. TYPE: d. AMOUNT: e. KIND OF AWARD: f. CUM/TOT: $ 0

RESOURCES ESTIMATE		PROFESSIONAL MAN YRS	FUNDS (In thousands)
PRECEDING	1983	0.0	$ 0
CURRENT	1984	0.5	$ 32

RESPONSIBLE DOD ORGANIZATION: 038870 11
NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR
ADDRESS: WASHINGTON DC 20307
RESPONSIBLE INDIVIDUAL
NAME: SWEENEY, T P MD 20
TELEPHONE: 202-576-3484
GENERAL USE: F.I.C.A.
MILITARY/CIVILIAN APPLICATION: MILITARY

PERFORMING ORGANIZATION: 038870 11
NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR
ADDRESS: WASHINGTON DC 20307
PRINCIPAL INVESTIGATOR
NAME: VINCENT, J W DA
TELEPHONE: 202-576-3092
ASSOCIATE INVESTIGATORS
NAME: SETTERSTROM, J A
NAME: HOLLINGER, J O

KEYWORDS: (U) WOUND INFECTIONS ;(U) MICROBIOLOGY;(U) CONTROLLED RELEASE;(U) ANTIMICROBIAL AGENTS ;(U) LAB ANIMALS ;(U) GUINEA PIGS ;(U) RAM IV;

OBJECTIVE:(U) THE ABILITY TO CONTROL OR PREVENT WOUND INFECTIONS IN A FIELD ENVIRONMENT PROVE ADVANTAGEOUS IN THE EARLY RETURN OF THE SOLDIER TO EFFECTIVE DUTY. THE CONCEPT OF CONTROLLED RELEASE OF ANTIMICROBIAL AGENTS PROVIDES THE TECHNOLOGY OF SUPPLYING AN EFFECTIVE LEVEL OF AGENT TO A GIVEN SITE FOR A PROLONGED PERIOD OF TIME WITHOUT REQUIRING MULTIPLE APPLICATIONS. THE CONCEPT OF TOPICAL APPLICATION WOULD ALLOW AN EFFECTIVE DOSE TO BE MAINTAINED LOCALLY WITHOUT OBTAINING HIGH LEVELS SYSTEMATICALLY WHICH MIGHT RESULT IN TOXICITY OR OTHER DETRIMENTAL EFFECTS.

APPROACH: (U) IN VITRO EVALUATIONS OF A NON WOVEN FABRIC OF POLY-L(-) LACTIDE HAS BEEN DONE WITH RESULTS INDICATING CONTROLLED RELEASE OF ANTIMICROBIAL AGENTS. THIS STUDY PROVIDES A METHOD WHEREBY THE EFFICACY OF THIS DRESSING MATERIAL CAN BE EVALUATED IN A CONTROLLED INFECTED WOUND MODEL SYSTEM. A STANDARDIZED FULL-THICKNESS WOUND IS PREPARED IN THE PARAVERTEBRAL AREA OF A GUINEA PIG AND INFECTED WITH A KNOWN INOCULUM OF STAPHYLOCOCCUS AUREUS AND THE WOUND COVERED WITH THE WOUND DRESSING CONTAINING THE ANTIMICROBIAL AGENT. AFTER 72 HOURS, THE WOUND IS ASSAYED TO DETERMINE THE ABILITY OF THE DRESSING TO CONTROL OR, PREFERABLY, ELIMINATE THE MICROORGANISMS. THIS PROJECT WAS STARTED UNDER DAOF8024.

PROGRESS: (U) NONE.

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

DA302928 | 01 OCT 83 | REPORT CONTROL NUMBER VE0208

A. NEW | U | U | CX | A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
PRIMARY	61102A	3M161102BS10	DA	084
SECONDARY				
SECONDARY				

(U) MONOCLONAL ANTIBODIES FOR THE ISOLATION AND IDENTIFICATION OF OSTEOCLASTIC ACTIVATING FACTOR (OAF) & A RECENTLY IDENTIFIED INHIBITOR OF OSTEOLYSIS

0818 PHYSIOLOGY 0813 MICROBIOLOGY

OCT 83 | CONT | DA | C. IN-HOUSE

FISCAL YEARS	PROFESSIONAL MANYEARS	FUNDS
1983	0.0	$ 0
1984	0.8	$ 24

F. CUM/TOT: $ 0

038870 1100 | 038870 H100

NAME MDRDC INSTITUTE OF DENTAL RSCH USAIOR

ADDRESS WASHINGTON DC 20307

RESPONSIBLE INDIVIDUAL
NAME SWEENEY, T P
TELEPHONE 202-576-3484

GENERAL USE
MILITARY

NAME MDRDC INSTITUTE OF DENTAL RSCH USAIOR

ADDRESS WASHINGTON DC 20307

PRINCIPAL INVESTIGATOR
NAME VINCENT, J W
TELEPHONE 202-576-3082

ASSOCIATE INVESTIGATORS
NAME HEATH, J R, III
NAME WOODYARD, S G

(U) IMMUNOLOGY ;(U) MONOCLONAL ANTIBODIES ;(U) LYMPHOKINES ;(U) LAB ANIMALS ;(U) MICE ;(U) RAM IV

OBJECTIVE:(U) CONTAMINATION OF AN OSSEOUS WOUND OF THE MAXILLOFACIAL COMPLEX WOULD RESULT IN NITROGENIC STIMULATION OF THE HOST'S IMMUNE SYSTEM. ONE OF THE RESULTANT BIOLOGICALLY ACTIVE SUBSTANCES PRODUCED WOULD BE OAF WHOSE ACTION RESULTS IN ENHANCED OSTEOCLASTIC ACTIVITY AND INCREASED OSSEOUS RESORPTION. THE UNDERSTANDING OF THE MODE OF ACTIVITY AND SITE OF ACTION OF OAF WILL GREATLY ENHANCE THE ABILITY TO CONTROL BONE LOSS ASSOCIATED WITH SUCH WOUNDS.

APPROACH: (U) MONOCLONAL ANTIBODIES ARE RECOGNIZED FOR THEIR EXQUISITE SPECIFICITY IN THE ABILITY TO RECOGNIZE A SINGLE ANTIGENIC DETERMINANT. THIS TECHNOLOGY WILL BE UTILIZED TO DEVELOP A SYSTEM WHICH CAN BE USED TO EXTRACT PURE OAF FROM CULTURE SUPERNATANTS. SUCH MONOCLONAL ANTIBODIES COULD BE USED TO IDENTIFY THE PRESENCE OF OAF IN TISSUE SPECIMENS AND IDENTIFY THE ACTIVE SITE. BY REACTING OAF WITH MONOCLONAL ANTIBODIES IT CAN BE EXPECTED THAT OAF ACTIVITY COULD BE BLOCK IN VIVO. THIS PROJECT WAS STARTED UNDER DA086037.

PROGRESS: (U) NONE.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY | 0A302927 | 01 OCT 83 | REPORT CONTROL NUMBER VE0208

	A. NEW	U	U		CX	A. WORK UNIT

TO NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
	61102A	3M161102BS10	DA	083

(U) PRODUCTION AND UTILIZATION OF MONOCLONAL ANTIBODIES IN THE RAPID IDENTIFICATION OF ANAEROBIC MICROORGANISMS ASSOCIATED WITH MAXILLOFACIAL INFECTIONS

0902 BIOENGINEERING 0813 MICROBIOLOGY 0806 ENVIR SI

OCT 83 | CONT | DA | C. IN-HOUSE

	FISCAL YEARS	PROFESSIONAL MAN-YEARS	FUNDS IN THOUSANDS
	1983	0.0	$ 0
	1984	2.0	$ 132

F. CUM/TOT: $ 0

038870 1100

MORDC INSTITUTE OF DENTAL RSCH USAIOR

WASHINGTON DC 20307

SWRENEY, T P
202-576-3484

MILITARY

038870 11100

MORDC INSTITUTE OF DENTAL RSCH USAIOR

WASHINGTON DC 20307

VINCENT, J W
202-576-3082

SETTERSTROM, J A

(U) MICROBIOLOGY;(U) WOUND INFECTIONS ;(U) MONOCLONAL ANTIBODIES ;(U) RAPID DETECTION ;(U) LAB ANIMALS ;(U) MICE ;(U) RAM IV;

OBJECTIVE:(U) MICROBIAL CONTAMINATION OF TRAUMATIC INJURIES TO THE MAXILLOFACIAL COMPLEX RESULTS IN DELAYED HEALING AND OTHER SEQUELAE WHICH HINDER RETURN OF THE PATIENT TO DUTY. A METHOD WHICH WILL RAPIDLY AND SPECIFICALLY IDENTIFY THE OFFENDING MICROORGANISMS WOULD BE MILITARILY RELEVANT IN ENHANCING WOUND HEALING IN MAXILLOFACIAL WAR WOUNDS. SUCH A SYSTEM COULD SERVE AS A USABLE MODEL IN THE RAPID DETECTION OF BIOLOGICAL WARFARE AGENTS.

APPROACH:. (U) THE REMARKABLE SPECIFICITY AND AVAILABILITY OF MONOCLONAL ANTIBODIES TO SELECTED MICROORGANISMS WILL BE UTILIZED TO DEVELOP A RAPID ASSAY SYSTEM ONCE THE ANTIBODIES CAN BE PRODUCED AND ISOLATED. THE SELECTION OF AN ASSAY SYSTEM WILL BE DEPENDENT ON SIMPLICITY, SPECIFICITY, SENSITIVITY, AND FIELD ADAPTABILITY. THIS PROJECT WAS STARTED UNDER DAOF8024.

PROGRESS: (U) NONE.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				DA302928	01 OCT 83	REPORT CONTROL SYMBOL 201708	
	A. NEW	U	U		NL		A. WORK UNIT
10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER	WORK UNIT NUMBER		
	61102A	3M161102BS10		DA	088		
FORMER							
MISS. OBJ. BTDG : 83/83-01.2/8 ;							

(U) A STUDY ON 50:50 PLA:PGA PLUS DIPHOSPHOINSITIDE-LYSOZYME (DPI-L) FOR THE PROMOTION OF CALCIFICATION IN OSSEOUS DEFECTS

002300 BIOCHEMISTRY 012900 PHYSIOLOGY

OCT 83	CONT	DA	C. IN-HOUSE

		PROFESSIONAL MAN YRS	FUNDS (IN THOUSANDS)
FISCAL YEAR	1983	0.0	$ 0
	1984	0.3	$ 40

F. CUM/TOT: $ 0

RESPONSIBLE DOD ORGANIZATION: 038870 11
NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR
ADDRESS: WASHINGTON DC 20307
RESPONSIBLE INDIVIDUAL
NAME: SWEENEY, T P MO 20
TELEPHONE: 202-576-3484
F.I.C.A.
MILITARY

PERFORMING ORGANIZATION: 038870 11
NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR
ADDRESS: WASHINGTON DC 20307
PRINCIPAL INVESTIGATOR
NAME: HOLLINGER, J O DA
TELEPHONE: 202-576-3764
ASSOCIATE INVESTIGATORS
NAME
NAME

(U) LAB ANIMALS ;(U) RATS ;(U) DIPHOSPOINOSITIDE-LYSOZYME ;(U) BIOCOMPATABLE ;(U) BIODEGRADABLE ;(U) IMPLANT ;(U) BONE STIMULATING ;(U) RAM IV;

OBJECTIVE:(U) THE TECHNICAL OBJECTIVE WAS TO DETERMINE IF A BIODEGRADABLE, BIOCOMPATIBLE COPOLYMER OF POLYACTIC ACID AND POLYGLYCOLIC ACID, IN COMBINATION WITH A DIPHOSPHOINOSITIDE INOSITOL-LYSOZYME COMPLEX, COULD INDUCE OSTEOGENESIS IN EXPERIMENTAL WOUNDS CREATED IN ENDOCHONDRAL AND INTRAMEMBRANOUS BONES. THE APPLICATIONS OF SUCH A MATERIAL WILL BE FOR FIXATION DEVICES AND AS IMPLANTS FOR OSSEOUS INDUCTION IN THE MAXILLOMANDIBULOFACIAL COMPLEX WHEN BONE IS LOST DUE TO TRAUMA, PATHOLOGY, OR ABLATION. BECAUSE APPROXIMATELY 10 PERCENT OF ALL COMBAT INJURIES ARE IN THE MALLIOMANDIBULOFACIAL REGION, DEVELOPMENT OF A BONE INDUCING AGENT IS HIGHLY IMPORTANT.

APPROACH: (U) AFTER INSERTION OF THE IMPLANT MATERIALS, TISSUE COMPATIBILITY AND BONE INDUCTION TESTS WERE PERFORMED IN RABBITS AND RATS. SERUM AND HARD AND SOFT TISSUE PHOSPHATASES (ACID AND ALKALINE) WERE ASSAYED, HISTOMORPHOMETRY WAS PERFORMED ON PLASTIC EMBEDDED UNDECALCIFIED BONE, PROTEIN AND HYDROXYPROLINE ASSAYS WERE DONE, AND ATOMIC ABSORPTION SPECTROPHOTOMETRY WAS USED TO DETERMINE CALCIUM TO PHOSPHATE MOLAR RATIOS IN HOST BONE. ISOELECTRIC FOCUSING WAS ALSO FOR ISOENZYME IDENTIFICATION. THIS PROJECT WAS STARTED UNDER DA088037.

PROGRESS: (U) NONE.

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY		DA302930	01 OCT 83	REPORT CONTROL SYMBOL
				Z01708

	A. NEW	U	U		NL	[X] [ ]	A. WORK UNIT

10. NO./CODES:*	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
PRIMARY	61102A	3M161102BS10	DA	287
FORMER				
MTEP, OBJ, STOG : 82/83-6.2/8 :				

(U) A STUDY OF THE BEHAVIOR OF BONE IN ORGAN CULTURE WITH SPECIAL EMPHASIS ON PGE2 AND INDOMETHACIN

002300 BIOCHEMISTRY 012900 PHYSIOLOGY

START DATE	ESTIMATED COMPLETION DATE	FUNDING AGENCY	PERFORMANCE METHOD
OCT 83	CONT	DA	C. IN-HOUSE

CONTRACT/GRANT		RESOURCES ESTIMATE			
a. DATES EFFECTIVE	EXPIRATION			a. PROFESSIONAL MAN YRS	b. FUNDS (In Thousands)
b. NUMBER *		FISCAL YEAR	PREVIOUS 1983	0.0	$ 0
c. TYPE	d. AMOUNT		CURRENT 1984	0.4	$ 15
e. KIND OF AWARD	f. CUM/TOT: $ 0				

RESPONSIBLE DOD ORGANIZATION 038870 11

NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR

ADDRESS: WASHINGTON DC 20307

RESPONSIBLE INDIVIDUAL

NAME: SWEENEY, T P MD 20

TELEPHONE: 202-576-3484

GENERAL USE: F.I.C.A.

MILITARY/CIVILIAN APPLICATION: MILITARY

PERFORMING ORGANIZATION 038870 11

NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR

ADDRESS: WASHINGTON DC 20307

PRINCIPAL INVESTIGATOR

NAME: HOLLINGER, J O DA

TELEPHONE: 202-576-3764

SOCIAL SECURITY ACCOUNT NUMBER

ASSOCIATE INVESTIGATORS

NAME

NAME

KEYWORDS: (U) CD-1 MICE ;(U) LAB ANIMALS ;(U) ORGAN CULTURE ;(U) BONE ;(U) PGE2 ;(U) INHIBITION ;(U) INDOMETHACIN;(U) RAM IV

OBJECTIVE:(U) THE TECHNICAL OBJECTIVE WAS TO DETERMINE IF A NONSTEROIDAL, ANTI-INFLAMMATORY AGENT, INDOMETHACIN, COULD INHIBIT PROSTAGLANDIN SYNTHESIS IN BONE ORGAN CULTURE. COMBAT INJURIES CAN PRODUCE MECHANICAL STRESS TO PERIOSTEUM AND ENDOSTEUM, CAUSING THE SYNTHESIS AND RELEASE OF PROSTAGLANDINS OF THE E SERIES. THE CONSEQUENCES ARE BONE LOSS AND BONE MORBIDITY. SURGICAL REPAIR AND HEALING OF OSSEOUS WOUNDS WOULD HAVE A MORE PREDICTABLE AND RELIABLE INCIDENCE OF REPAIR IF THE ENDOGENOUS PROSTAGLANDINS OF THE E SERIES COULD BE INHIBITED EFFECTIVELY.

APPROACH: (U) A TOTAL OF 192 NEONATAL MICE CALVARIA WERE DIVIDED INTO FOUR TREATMENT GROUPS: (1) CONTROL; NO EXOGENOUS AGENTS; (2) INDOMETHACIN: 200 NG/ML OF MEDIUM; (3) PGE2: 100 NG/ML OF MEDIUM; AND (4) COMBINATION: 200 NG/ML OF INDOMETHACIN PLUS 100 NG/ML OF PGE2. CALVARIA WERE HARVESTED AT 24, 48, AND 72 HOURS AND EVALUATED HISTOMORPHOMETRICALLY BY RIA'S FOR PGE2, CGMP, CAMP, AND BY ATOMIC ABSORPTION FOR CALCIUM AND PHOSPHATE. THIS PROCEDURE WAS REPEATED ONCE EACH MONTH AND VARIABLES (2)-(4) WERE ALTERED. THIS PROJECT WAS STARTED UNDER DA086037.

PROGRESS: (U) NONE.

*Available to contractors upon originator's approval

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

			0A3029S3	01 OCT 83		REPORT CONTROL NUMBER	VE0208
	A. NEW	U	U		CX		A. WORK UNIT
TD NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER	
	61102A	3M161102BS10		DA		060	

(U) A STUDY TO EVALUATE COPOLYMER OF PLA:PGA & DIPHOSPHOINSITIDE-LYSOZYME FOR BRIDGING A SURGICALLY PREPARED BONE DISCONTINUITY DEFECT IN DOGS

0801 BIOCHEMISTRY 0816 PHYSIOLOGY

OCT 83	CONT	DA	C. IN-HOUSE

		1983	0.0 / $ 0
		1984	0.5 / $ 45

P. CUM/TOT: $ 0

031670	H100	031670 H100

MDRDC INSTITUTE OF DENTAL RSCH USAIDR

WASHINGTON DC 20307

SWEENEY, T P
202-576-3484

MILITARY

MDRDC INSTITUTE OF DENTAL RSCH USAIDR

WASHINGTON DC 20307

HOLLINGER, J O
202-576-3764

(U) LAB ANIMALS ;(U) DOGS ;(U) RAM IV;(U) DIPHOSPHOINOSITIDE-LYSOZYME ;(U) BIOCOMPATIBLE ;(U) IMPLANT ;(U) COPOLYMER ;(U) BONE

OBJECTIVE:(U) THE TECHNICAL OBJECTIVE WAS TO DETERMINE IF A BIOCOMPATIBLE, BIODEGRADABLE COPOLYMER OF PLA AND PGA, IN COMBINATION WITH A DIPHOSPHOINOSITIDE-LYSOZYME COMPLEX, COULD INDUCE BONE FORMATION IN A MANDIBULAR DISCONTINUITY DEFECT IN THE MANDIBLE OF A DOG. SUCH A MATERIAL WOULD BE FOR MANDIBULAR FIXATION AND AN IMPLANT FOR OSSEOUS INDUCTION WHEN PART OF THE MANDIBLE IS MISSING. DEVELOPMENT OF BONE STIMULATING SUBSTANCE FOR MANDIBULAR REPAIR IS MILITARILY SIGNIFICANT; APPROXIMATELY 10 PERCENT OF ALL COMBAT INJURIES INVOLVE THE MAXILLO MANDIBULOFACIAL REGION.

APPROACH: (U) INITIAL PREPARATION OF THE HOST BONE WILL INVOLVE SELECTIVE EXTRACTION OF MAXILLARY AND MANDIBULAR TEETH. IMPLANT BLOCKS WILL BE PREPARED BY SOLUBILIZING 50:50 POLY L(-) LACTIDE-CO-GLYCOLIDE IN METHYLENE CHLORIDE, REPRECIPITATING IN ANHYDROUS METHANOL, AND ADDING A COMPLEX CONSISTING OF DPH-L. BONE COMPATIBILITY AND INDUCTION TEST WILL BE PERFORMED USING PREPARED 2CM DEFECTS IN THE DOG MANDIBLE. AT SELECTED TIME PERIODS, EXPERIMENTAL SITES WILL BE CLINICALLY EVALUATED AND RADIOGRAPHED; SERUM AND BONE ACID AND ALKALINE PHOSPHATASES WILL BE ASSAYED; HISTOCHEMISTRY AND HISTOMORPHOMETRY WILL BE PERFORMED ON PLASTIC EMBEDDED UNDECALCIFIED SPECIMENS; PROTEIN AND HYDROXYPROLINE ASSAYS WILL BE ACCOMPLISHED; RIA'S FOR CYCLIC NUCLEOTIDES WILL BE ATTEMPTED; AND ATOMIC ABSORPTION SPECTROPHOTOMETRY WILL BE USED TO DETERMINE CALCIUM TO PHOSPHATE MOLAR RATIOS. THIS PROJECT WAS STARTED UNDER DA086037.

PROGRESS: (U) NONE.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY | DA302938 | 01 OCT 83 | REPORT CONTROL SYMBOL 201708

A. NEW | U | U | NL | A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
PRIMARY	61102A	3M161102BS10	DA	070
CONTRIBUTING				
FORMER				
CONTRIBUTING	CARDS: OBJ. STOG : 82/83-6.2/8 ;			

11. TITLE: (U) IN VIVO EVALUATION OF ULTRAMICROPOROUS CELLULOSE TRIACETATE WOUND DRESSINGS AS SLOW-RELEASE SYSTEM FOR ANTIBIOTICS

12. SCIENTIFIC AND TECHNOLOGICAL AREAS: 002300 BIOLOGY 003500 CLIN MEDICINE 010100 MICROBIO

13. START DATE: OCT 83 | 14. ESTIMATED COMPLETION DATE: CONT | 15. FUNDING AGENCY: DA | 16. PERFORMANCE METHOD: C. IN-HOUSE

17. CONTRACT/GRANT: a. DATES/EFFECTIVE: EXPIRATION: b. NUMBER: c. TYPE: d. AMOUNT: e. KIND OF AWARD: f. CUM/TOT: $ 0

18. RESOURCES ESTIMATE		a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR	PRECEDING 1983	0.0	$ 0
	CURRENT 1984	0.5	$ 75

19. RESPONSIBLE DOD ORGANIZATION: 038870 11
NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR
ADDRESS: WASHINGTON DC 20307
RESPONSIBLE INDIVIDUAL
NAME: SWEENEY, T P MD 20
TELEPHONE: 202-576-3484

20. PERFORMING ORGANIZATION: 038870 11
NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR
ADDRESS: WASHINGTON DC 20307
PRINCIPAL INVESTIGATOR
NAME: SETTERSTROM, J A DA
TELEPHONE: 202-576-3784
SOCIAL SECURITY ACCOUNT NUMBER:
ASSOCIATE INVESTIGATORS
NAME: VINCENT, J W
NAME:

21. GENERAL USE: F.I.C.A.
MILITARY/CIVILIAN APPLICATION: MILITARY

22. KEYWORDS: (U) LAB ANIMALS ;(U) GUINEA PIGS ;(U) RAM IV;(U) WOUND DRESSING ;(U) SUSTAINED ANTIBIOTIC RELEASE ;

23. TECHNICAL OBJECTIVE, 24. APPROACH, 25. PROGRESS

OBJECTIVE:(U) UNTIL RECENTLY, AVAILABLE ARTIFICIAL WOUND DRESSINGS WERE MADE OF COTTON GAUZE. THESE DRESSINGS PROTECT WOUNDS FROM THE EXTERNAL ENVIRONMENT, BUT LITTLE ELSE. AN IMPROVED WOUND DRESSING THAT CLINGS TO WOUNDS WITHOUT ADHERING, KEEPS THE WOUND MOIST WITHOUT ALLOWING FLUID ACCUMULATION, ALLOWS OXYGEN EXCHANGE, AND PREVENTS INFECTION IS REQUIRED. IT IS THE OBJECTIVE OF THIS WORK TO DEVELOP A MATERIAL WITH THESE CHARACTERISTICS THAT IS EASILY APPLICABLE, WILL PROTECT THE WOUND, DECREASE INFECTION, AND ENHANCE WOUND HEALING.

APPROACH: (U) AN ULTRAMICROPOROUS CELLULOSE TRIACETATE MATERIAL (POROPLASTIC) WHICH POSSESSES MANY INHERENT CHARACTERISTICS THAT ARE THEORETICALLY DESIRABLE IN A WOUND DRESSING IS BEING EVALUATED IN VIVO. EFFORTS ARE DIRECTED TOWARD DEVELOPING THE MATERIAL AS A CONTROLLED RELEASE VEHICLE FOR ANTIBIOTICS. THIS PROJECT WAS STARTED UNDER DA068878.

PROGRESS: (U) NONE.

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

Agency accession	DA302936
Date of summary	01 OCT 83
Report control symbol	Z01708
Kind of summary	A. NEW
Summary security	U
Work security	U
Distribution	NL
Level of sum	A WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
Primary	61102A	3M161102BS10	DA	301
Contributing				
Contributing	FORMER			
	MISC. OBJ. STOG : 82/83-6.2/5 ;			

Title: (U) BIOLOGICAL ACTIVITY VERIFICATION OF SPECIFIED MICROENCAPSULATED ANTIBIOTICS IN VIVO

Scientific and technological areas: 010100 MICROBIOLOGY 012600 PHARMACOLOGY 003500 CLIN MED

Start date: OCT 83 — Estimated completion date: CONT — Funding agency: DA — Performance method: C. IN-HOUSE

Contract/grant: F. CUM/TOT: $ 0

Resources estimate		Professional man yrs	Funds (in thousands)
Fiscal year	1983	0.0	$ 0
	1984	0.5	$ 80

Responsible DOD organization: 038870 11
NAME: MDRDC INSTITUTE OF DENTAL RSCH USAIDR
ADDRESS: WASHINGTON DC 20307
Responsible individual
NAME: SWEENEY, T P MD 20
TELEPHONE: 202-576-3484
General use: F.I.C.A.
Domestic/Foreign application: MILITARY

Performing organization: 038870 11
NAME: MDRDC INSTITUTE OF DENTAL RSCH USAIDR
ADDRESS: WASHINGTON DC 20307
Principal investigator
NAME: ZETTERSTROM, J A DA
TELEPHONE: 202-576-3764

Keywords: (U) LAB ANIMALS ;(U) RATS ;(U) GUINEA PIGS ;(U) RAM IV (U) MICROENCAPSULATED ANTIBIOTICS ;(U) INFECTION CONTROL ;(U) SUSTAINED ANTIBIOTIC RELEASE

OBJECTIVE:(U) COMBAT WOUNDS ARE CHARACTERIZED BY HIGH INFECTION RATES DUE TO THE PRESENCE OF DEVITALIZED TISSUE AND FOREIGN BODIES CARRIED BY MISSLE FRAGMENTS. EVACUATION EXPOSES WOUNDS TO FURTHER CONTAMINATION AND DELAY BEFORE TREATMENT. IMPROVED METHODS TO DELIVER ANTIBIOTICS TO CONTAMINATED TISSUE FOLLOWING TRAUMATIC INJURY ARE NEEDED IN ORDER THAT SUSTAINED AND EFFECTIVE TISSUE LEVELS CAN BE MAINTAINED DESPITE REDUCTED BLOOD PERFUSION FROM SHOCK OR DESTROYED BLOOD VESSELS. IT IS THE OBJECTIVE OF THIS WORK TO DEVELOP MICROSPHERES THAT SLOWLY RELEASE ANTIBIOTICS INTO CONTAMINATED WOUNDED TISSUE IN A THERAPEUTIC DOSE FOR AN EXTENDED TIME (14 DAYS). THE MICROSPHERES ARE APPLICABLE IN A SINGLE DOSE VIA AN AEROSOL SPRAY OR SHAKER-TYPE DISPENSER.

APPROACH: (U) AMPICILLIN ANHYDRATE AND GENTAMICIN SULFATE ARE BEING INCORPORATED INDIVIDUALLY INTO MICROSPHERES OF BIOCOMPATIBLE, BIODEGRADABLE PLA:PGA COPOLYMER. THE MICROSPHERES ARE BEING ENGINEERED TO SLOWLY RELEASE THE ANTIBIOTIC OVER A KNOWN PERIOD, AFTER WHICH TIME THEY WILL COMPLETELY BIODEGRADED WITHIN THE WOUND SITE. THIS PROJECT WAS STARTED UNDER DAOA6021.

PROGRESS: (U) NONE.

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				DA302967	01 OCT 83		REPORT CONTROL SYMBOL Z01708
	A. NEW	U	U		NL		A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	61102A	3M161102BS10	DA	503
b. CONTRIBUTING FORMER				
c. CONTRIBUTING	MIXS, OBJ, STOG : 82/83-6.2/5 ;			

(U) A STUDY ON THE IMMUNOGENICITY OF THE COPOLYMER PLA:PGA USING A DOT ELISA METHOD

002300 BIOCHEMISTRY 012900 PHYSIOLOGY

START DATE	ESTIMATED COMPLETION DATE	FUNDING AGENCY	PERFORMANCE METHOD
DEC 83	CONT	DA	C. IN-HOUSE

		PROFESSIONAL MAN YRS	FUNDS (In Thousands)
FISCAL YEAR	PRECEDING 1983	0.0	$ 0
	CURRENT 1984	0.3	$ 20

F. CUM/TOT: $ 0

RESPONSIBLE DOD ORGANIZATION	PERFORMING ORGANIZATION
038670 11	038670 11
NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR	NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR
ADDRESS: WASHINGTON DC 20307	ADDRESS: WASHINGTON DC 20307
RESPONSIBLE INDIVIDUAL	PRINCIPAL INVESTIGATOR
NAME: SWEENEY, T P MD 20	NAME: HOLLINGER, J O DA
TELEPHONE: 202-576-3484	TELEPHONE: 202-576-3764
GENERAL USE: F.I.C.A.	ASSOCIATE INVESTIGATORS
MILITARY/CIVILIAN APPLICATION: MILITARY	NAME:

(U) LAB ANIMALS ;(U) RABBITS ;(U) RAM IV;(U) KREBS CYCLE DERIVATIVES ;(U) IMMUNOLOGY ;(U) BIOPOLYMERS ;(U) DOT-ELISA ;

OBJECTIVE:(U) STUDIES HAVE DEMONSTRATED THAT BOTH HOMOPOLYMERS AND COPOLYMERS OF CERTAIN KREBS CYCLE DERIVATIVES CAN BE EFFECTIVELY EMPLOYED AS WOUND REPAIR MATERIALS. THESE MATERIALS HAVE BEEN SHOWN TO BE TISSUE TOLERANT, BASED UPON CELLULAR EVALUATION. A RECENT ADVANCE IN THE FIELD OF IMMUNOLOGY HAS MADE IT POSSIBLE TO DETERMINE IF THE KREBS CYCLE BIOPOLYMERS ARE AS INNOCUOUS HUMORALLY AS THEY HAVE BEEN SHOWN TO BE CELLULARLY.

APPROACH: (U) ANTISERUM REACTIVE WITH THE COPOLYMER PLA:PGA WILL BE PREPARED. THE COPOLYMER WILL ALSO BE PREPARED IN 1MG/ML AND 2MG/ML CONCENTRATIONS AND EMULSIFIED IN AN EQUAL VOLUME OF COMPLETE FREUND'S ADJUVANT. PLAIN COPOLYMER AND COPOLYMER PLUS ADJUVANT WILL SERVE AS THE IMMUNOGENS FOR IMMUNIZATION OF 2 EQUAL GROUPS OF RABBITS (5 ANIMALS/GROUP). THE DOT-ELISA METHOD WILL BE USED TO DETECT THE PRESENCE OF REACTIVE QUANTITIES (GREATER THAN NANOGRAM LEVELS) OF ANTIBODY IN THE RABBIT SERA RECOVERED AT WEEKLY INTERVALS FOR 8 WEEKS.

PROGRESS: (U) NONE.

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

DA302988 | 01 OCT 83 | REPORT CONTROL SYMBOL Z01706

A. NEW | U | U | NL | A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
	61102A	3M161102BS10	DA	302
FORMER				

MISS. OBJ. STOG : 82/83-6.2/6 :

(U) A STUDY TO EVALUATE A SYNTHETICALLY PRODUCED POLYPENTAPEPTIDE TO INDUCE OSTEOGENESIS

002300 BIOCHEMISTRY 012900 PHYSIOLOGY

OCT 83 | CONT | DA | C. IN-HOUSE

FISCAL YEAR	1983	0.0	$ 0
	1984	0.3	$ 15

F. CUM/TOT: $ 0

038870 11 | 038870 11

NAME: NMRDC INSTITUTE OF DENTAL RSCH USAIDR
ADDRESS: WASHINGTON DC 20307

RESPONSIBLE INDIVIDUAL
NAME: SWEENEY, T P MD 20
TELEPHONE: 202-576-3484

F.I.C.A.

MILITARY

NAME: NMRDC INSTITUTE OF DENTAL RSCH USAIDR
ADDRESS: WASHINGTON DC 20307

PRINCIPAL INVESTIGATOR
NAME: HOLLINGER, J O DA
TELEPHONE: 202-576-3784

(U) LAB ANIMALS ;(U) RATS ;(U) RAM IV;(U) IMPLANT ;(U) CRANIO-MANDIBULOFACIAL COMPLEX;(U) POLYPENTAPEPTIDE ;(U) NEW BONE FORMATION

OBJECTIVE:(U) NUMEROUS INVESTIGATIONS HAVE BEEN CONDUCTED USING A VARIETY OF IMPLANT MATERIALS TO SUPPORT AND TO PROMOTE OSSEOUS WOUND REPAIR OF THE CRANIO-MANDIBULOFACIAL COMPLEX. THE PURPOSE OF THE PROPOSED INVESTIGATION IS TO DETERMINE IF A SYNTHETICALLY DERIVED POLYPENTAPEPTIDE CAN INDUCE NEW BONE FORMATION IN ENDOCHONDRAL WOUNDS IN THE DIAPHYSES OF THE TIBIAS OF RATS.

APPROACH: (U) THE AREA OVERLYING THE ANTERIO MEDIAL ASPECTS OF THE RIGHT TIBIAS OF 70 ADULT WALTER REED RATS WILL BE PREPARED FOR INSERTION OF A POLYPENTAPEPTIDE IMPLANT. THE LEFT DIAPHYSEAL AREA WILL SERVE AS A CONTROL. AT 3, 7, 14, 21, 28, AND 42 DAY INTERVALS TEN ANIMALS WILL BE EUTHANITIZED AND BONE HOST-IMPLANT AND CONTROL SITES WILL BE RECOVERED AND TISSUES WILL BE PROCESSED FOR PLASTIC EMBEDDING, HISTOCHEMISTRY, AND HISTOMORPHOMETRY. THE HETEROTOPIC SITES FOR POLYPENTAPEPTIDE EVALUATION WILL BE THE RIGHT GLUTEAL MUSCLE MASS. AFTER INSERTION OF THE IMPLANT, SPECIMENS WILL BE RECOVERED AT 7, 21, AND 42 DAYS AND WILL BE PROCESSED FOR HISTOLOGIC EXAMINATION.

PROGRESS: (U) NONE.

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA OE6022	831001	DD-DR&E(AR)636

3. DATE PREV SUMRY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8a. GRADE MONTH	8b. SPECIFIC DATA - CONTRACTOR ACCESS	9. LEVEL OF SUM
821001	H. TERM	U	U		NL	YES ☒ NO ☐	A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62775A	3S162775A825	AB	014
b. CONTRIBUTING				
c. CONTRIBUTING		STOG 82/82-6.2:4		

11. TITLE (Include with Security Classification Code)

(U) Preventive Dentistry Measures of Military Significance

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

012900 Physiology 002400 Bioengineering 003500 Clinical Medicine

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
7101	CONT	DA	C. IN-HOUSE

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION:
b. NUMBER:
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	b. PROFESSIONAL MAN YRS	c. FUNDS (In thousands)
FISCAL YEAR — PREVIOUS	83	0.2	50
FISCAL YEAR — CURRENT			

19a. RESPONSIBLE DOD ORGANIZATION

NAME: U.S. Army Institute of Dental Research

ADDRESS: Washington, DC 20307

RESPONSIBLE INDIVIDUAL
NAME: SWEENEY, T. P.
TELEPHONE: (202) 576-3484

20a. PERFORMING ORGANIZATION

NAME: U.S. Army Institute of Dental Research

ADDRESS: Washington, DC 20307

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME: LORTON, L.
TELEPHONE: (415) 561-4845
SOCIAL SECURITY ACCOUNT NUMBER: POC:DA

ASSOCIATE INVESTIGATORS
NAME: MADER, C.
NAME: GROVER, P.

21. GENERAL USE

Foreign Intelligence Considered

22. KEYWORDS (Include KWIC Security Classification Code)

(U) Marginal Leakage; (U) Resin Restorative; (U) Post and Core Restorations; (U) Dental Emergencies

23. TECHNICAL OBJECTIVE, 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) To develop new and simplified methods of preventing disease related dental emergencies in the field. To assess new methods of (1) improving the biologic management of militarily relevant oral conditions and (2) improving the cost-effectiveness factors of preventive dental therapy in the military.

24. (U) Studies will be conducted which will (1) develop and evaluate improved methods of dental care which will prevent dental emergencies in the field; (2) develop more rapid and effective means of identifying and treating soldiers with at-risk-profiles for field dental emergencies.

25. (U) (8210-8310) Records of emergency and routine visits to two of three dental clinics are being collected in order to determine factors in dental status that contribute to emergency visits. The data gathering phase is 75% complete. All data collection will be completed by 15 November. Final analysis of the data will begin as soon as the data base can be compiled. Study of a simplified method for restoring endodontically treated teeth using composite resins has appeared to be promising as a field expedient, but was terminated due to personnel losses.

*Available to contractors upon originator's approval

DD FORM 1 MAR 88 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498A 1 MAY 87 AND 1498-1 1 MAR 88 (FOR ARMY USE) ARE OBSOLETE.

PROJECT: 3S16277A825

WORK UNIT TITLE: (U) Preventive Dentistry Measures of Military Significance

PRINCIPAL INVESTIGATOR: LTC Lewis Lorton, DC

Evaluation of a New Restorative Procedure for Resin Restorations Designed to Prevent Dental Emergencies on the Battlefield

Problem: Marginal leakage, at the tooth/restoration interface, is a weakness shared by all restorations done with traditional restorative materials and operative techniques. Marginal leakage of restorations may cause or contribute to several undesirable consequences to include: recurrent caries, staining, postoperative pain, chronic hypersensitivity, and pulpal pathosis. Any one, or combination of these conditions, may lead to premature failure of the restoration and/or the production of a dental emergency on the battlefield, necessitating removal of the soldier from combat. The development of techniques to decrease or eliminate marginal leakage around restorations is thus highly desirable.

Approach: Extracted human teeth will be used in the study. Cavity preparations with traditional and experimental cavosurface margin designs will be prepared. The cavity preparations will be restored with several commercial dental resins and the teeth dissolved with nitric acid. The remaining resin restorations will be prepared for scanning electron microscopic evaluation. The scanning electron microscope will be used to evaluate the adaptation of the various resins to the traditional and experimental cavity designs. If the adaptation is good, then leakage studies will be done followed by clinical testing.

Results: It was determined from scanning electron microscopic evaluation that all of the commercial dental resins adapted well to both the traditional and experimental cavosurface margin designs. Tooth harvest, literature review, and discussions are currently taking place so that the leakage studies can be done as the next planned step.

PROJECT: 3S162775A825

WORK UNIT TITLE: (U) Preventive Dentistry Measures of Military Significance

PRINCIPAL INVESTIGATOR: COL Carmon L. Mader, DC

Evaluation of a New Restorative Procedure for Post and Core Restorations Designed to be More Economical and to Prevent Dental Emergencies on the Battlefield

PROBLEM: Post and core restorations are involved in the restoration of teeth that have been endodontically treated. The traditional techniques used to fabricate post and core restorations are very time consuming and expensive as these techniques require substantial amounts of time from the doctor, the dental assistant, the laboratory technician, and the patient. In addition, relatively large amounts of precious metals (usually gold) are required. Also, the exacting various steps to be redone. In addition, trauma to anterior teeth that have been treated with traditional cast metal post and core restorations frequently results in a fracture of the root and subsequent loss of the tooth. These teeth must then be replaced requiring additional time (by the dentist, dental assistant, dental laboratory, and patient) and expense (precious metal framework for a fixed or removable prosthesis). The development of new, simplified, more economical techniques for post and core fabrication, that require less personnal time and do not utilize precious metals, is highly desireable. Composite resins adapt well to etched tooth surfaces and have reasonable compression strength. This material may be satisfactory for use in new, simplified, more economical techniques for post and core fabrication.

APPROACH: Extracted, single-rooted, human teeth will be used in the research. Routine endodontic therapy will be performed in their canals. The canals will then be etched with acid to remove the smeared layer produced by instrumentation. Next, the canals will be filled with a low viscosity resin. The teeth will be longitudinally split in half and processed for scanning electron microscopic evaluation. The scanning electron microscope will be used to evaluate how well the resin adapted to the dentinal tubules. If the resin adaption is good, then additional studies will be done to evaluate leakage and shear strength. If these studies are promising, then clinical testing of the technnique is planned.

RESULTS: It was determined from scanning electron microscopic evaluation that the low viscosity resin reliably penetrated the dentinal tubules and adapted well to them. Tooth harvest, literature review and discussions are currently taking place so that the leakage and shear strength studies can be done as the next planned step.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

				DA0G8033	01 OCT 83	REPORT CONTROL NUMBER VEJOSA	
01 OCT 83	D. CHANGE	U	U		CX		A. WORK UNIT
10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER	WORK UNIT NUMBER		
	62770A	3S162770A82B		AB	002		

(U) DEVELOPMENT AND EVALUATION OF DENTAL MATERIALS AND MATERIEL FOR ARMY USE.

1107 MISC MAT	0704 PHYS CHEM	0702 INORG CH	
JAN 89	CONT	DA	C. IN-HOUSE

FISCAL YEARS	PROFESSIONAL MAN-YEARS	FUNDS (In Thousands)
1983	1.8	$ 85
1984	1.5	$ 135

F. CUM/TOT $ 0

038670	1100	038670 H100

NDRDC INSTITUTE OF DENTAL RSCH USAIDR

WASHINGTON DC 20012

SWEENEY, T P
202-576-2484

NDRDC DENTAL MATERIALS DIVISION USAIDR

WASHINGTON DC 20012

WOOLSEY, G
415-752-8343

MOFFA, J

(U) STORAGE STABILITY ;(U) COMPOSITE RESTORATIVES ;(U) IMPRESSION MATERIALS ;(U) CORROSION OF ALLOYS ;(U) PORCELAIN-METAL BOND ;(U) RAM IV

OBJECTIVE:(U) TO EVALUATE NEW MATERIALS AND MATERIEL OF SPECIAL INTEREST TO THE ARMY DENTIST. CRITERIA FOR SELECTION OF MATERIALS, DEVICES OR TECHNIQUES FOR EVALUATION ARE BASED ON ANTICIPATED HIGH POTENTIALS FOR- (1) SAVINGS OF FISCAL AND/OR MANPOWER RESOURCES- (2) WORK SIMPLIFICATION- (3) IMPROVED HEALTH CARE DELIVERY IN COMBAT AREAS- AND (4) ENHANCED SAFETY WITH RESPECT TO PROFESSIONAL AND ANCILLARY PERSONNEL AS WELL AS TO THE PATIENT.

APPROACH: (U) NEW MATERIALS WILL BE EVALUATED ON THE BASIS OF THE FOLLOWING PARAMETERS- COMPOSITION, MICROSTRUCTURE, PHYSICAL AND MECHANICAL PROPERTIES, CYTOTOXICITY, AND CLINICAL PERFORMANCE. STORAGE STABILITY OF MATERIALS FOR FIELD USE WILL BE EVALUATED.

PROGRESS: (U) THE INTERACTION BETWEEN OPAQUE LIQUIDS AND CERAMIC METALS HAS BEEN DEMONSTRATED. VITA LIQUID DEMONSTRATED THE LOWEST CONTACT ANGLES FOLLOWED BY NEY, CERAMIC, WILL-CREAM, AND BIO BOND LIQUIDS. SURFACE ROUGHNESS PREPARATION WAS FOUND TO HAVE STATISTICALLY SIGNIFICANT EFFECTS ON CONTACT ANGLE MEASUREMENTS ON OPTION, BAKE-ON N/P, AND TRIUMPH METALS. SITE VISITS TO THE SIXTH U.S. ARMY LOGISTICS COMMAND AND LETTERMAN ARMY MEDICAL CENTER LOGISTICS DIVISION PROVIDED SUFFICIENT DATA ON WHICH TO BASE RECOMMENDATIONS FOR THE DELETION OF GROUPS OF SUPPLIES FROM CONSIDERATION FOR STORAGE STABILITY EVALUATION INASMUCH AS THEY ARE NOT PROJECTED FOR FIELD USE. ADDITIONAL WORK DONE UNDER AGENCY ACCESSION NUMBER DA3021889 AND DA3021808.

PROJECT: 3M162775A825

WORK UNIT TITLE: (U) Development and Evaluation of Dental Materials and Materiel for Army Use

PRINCIPAL INVESTIGATOR: LTC G. D. Woolsey, DC

Surface Phenomenon of Opaque Porcelain on Oxidized Metal

PROBLEM: The ease of manipulation of porcelain and metal systems is of paramount importance in the modern military dental laboratory. Knowledge of handling characteristics of porcelain opaque suspensions on oxidized metal surfaces can improve the fabrication time of restorations and benefit the military dental laboratory in training and utilizing constantly rotating personnel.

APPROACH: The wetting mediums for five dental opaque porcelains were evaluated by sessile drop contact angle measurements technique on five dental ceramic alloys. Eight replications on both smooth and sandblasted metal surfaces were evaluated in a fully randomized design.

RESULTS: Statistically significant interactions of opaque liquids on specific ceramic metals were observed in this study, indicating that broad generalizations of the wetting characteristics of opaque liquids on oxidized metals cannot be made. Even though a trend did develop with Vita liquid demonstrating the lowest contact angles, followed by Ney, Ceramco, Will-Ceram, and Biobond; the statistical significance of this ranking varied with each of the five metals and two surfaces evaluated. Surface roughness preparation was found to have statistically significant effects on contact angle measurements on Option, Bake-on N/P, and Triumph metals.

PROJECT: 3S162775A825

WORK UNIT TITLE: (U) Development and Evaluation of Dental Materials and Materiel for Army Use

PRINCIPAL INVESTIGATOR: LTC G. D. Woolsey, DC

Storage Stability of Medical and Dental Materiel

PROBLEM: Dental and medical materiel currently used by the U.S. Army Medical Department is stored in 6 major depots (2-in CONUS, 2-in Asia, and 2-in Europe). The monitoring of the serviceability of these supplies is outlined in "Appendix M" of the "Quality Control Depot Serviceability Standards". The standards outlined in "Appendix M" are those derived from manufacturers and are usually tests of no more than 60°C for one week. Dental and Medical teams must be able to depend upon supplies which will function after prolonged storage in areas of varying temperature and humidity.

APPROACH: The initial phase of this work will be the collection of background information on the Army medical supply storage system, how materials and supplies are stored, types of material stored and the storage environments within the major medical supply depots. The basis of this investigation will be information within AR 40-61, site visits to Tracy Army Depot, the Defense Procurement Support Command (where some limited materials testing is conducted on materials in the Army supply system), and the U.S. Army Medical Materiel Agency (source of world-wide deployment of medical and dental supplies). The second phase of this study will be the laboratory testing of those dental and medical supplies found in medical depots and determined potentially sensitive to adverse environmental storage conditions. It is imperative that the temperature and humidity within each major storage facility be determined to properly design a laboratory study of storage stability. Knowledge of perishable supplies currently stored in the major depots (as outlined in Appendix "E" of AR 40-61) will yield a study design more relevant to the modern mobile Army. An environmental chamber model LR-386-C-MP will be used to evaluate environmental effects on dental and medical materiel.

RESULTS: The identification of major military depots where major and minor medical assemblages are stored has been accomplished through site visits to the Sixth U.S. Army Logistics Command and the Letterman Army Medical Center Logistics Division. The evaluation of "Appendix M" of "Quality Control Depot Serviceability Standards" and AR 40-61 have formed the reference basis for the initial work on this project. Through the initial phase of this work, groups of materials have been identified which are not stored and can be deleted from consideration for this study.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA OG 6034	83 10 01	DD-DR&E(AR)636

3. DATE PREV SUMRY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8a. GROUP INTERVAL	8b. SPECIFIC DATA CONTRACTOR ACCESS	9. LEVEL OF SUM
82 10 01	H. TERM	U	U		NL	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62775A	3S162775A825	AB	002
b. CONTRIBUTING	62775A	3S162775A825	AC	003
c. CONTRIBUTING	////////////	STOG: 80-7.2:5		

11. TITLE (Procede with security classification Code)

(U) Development and Improvement of Metallic Restorative Materials

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

009900 Metallurgy and Metallography; 008300 Inorganic Chemistry; 002400 Bioengineering

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
69 01	CONT	DA	C. IN-HOUSE

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION:

b. NUMBER:

c. TYPE: d. AMOUNT:

e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR 83 PREVIOUSLY	0.3	65
FISCAL YEAR 84 CURRENTLY	0	0

19a. RESPONSIBLE SUBORGANIZATION

NAME: U.S. Army Institute of Dental Research

ADDRESS: Washington, DC 20307

RESPONSIBLE INDIVIDUAL

NAME: SWEENEY, T.P.

TELEPHONE: (202) 576-3484

19b. PERFORMING ORGANIZATION

NAME: U.S. Army Institute of Dental Research

ADDRESS: Washington, DC 20307

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic institution)

NAME: VERMILYEA, S.

TELEPHONE: (415) 752-8343

SOCIAL SECURITY ACCOUNT NUMBER: POC:DA

ASSOCIATE INVESTIGATORS

NAME: WOOLSEY, G.

NAME:

20. GENERAL USE

Foreign Intelligence Considered

21. KEYWORDS (Provide each with security classification Code)

(U) Base Metal Alloys; (U) Casting Accuracy; (U) Soldering Base Metals; (U) Investment Techniques

22a. TECHNICAL OBJECTIVE, 22b APPROACH, 22c PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with security classification Code.)

23. (U) Annual Army expenditures for precious metals utilized in the fabrication of fixed dental prostheses are in the vicinity of $1,000,000. The cost of an equal volume of base metal alloy is $30,000. Properties of base metal alloys indicate however, that these alloys cannot be utilized for small castings without drastic metallurgical modifications. This work is therefore being conducted to (1) develop heat treatment methods for controlling properties of nickel-chromium based casting alloys; (2) evaluate nickel-chromium based alloys for use in operative dentistry.

24. (U) The properties of nickel-chromium based alloys will be studied in detail by various physical methods available in order to devise procedures which will optimize their usefulness. Any improvement obtained will be evaluated clinically.

25. (U) Loss of the principal investigator prevented significant progress on this work unit. Continued efforts to develop reliable techniques for soldering base metal alloys have not been successful.

*Available in computer listing upon originator's approval

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA OG6679	831001	DD-DR&E(AR)636

3. DATE PREV SUMRY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8A. GROUP MGT'N	8B. SPECIFIC DATA - CONTRACTOR ACCESS	9. LEVEL OF SUM
821001	H. TERM	U	U		NL	YES NO	A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62775A	3S162775A825	AB	010
b. CONTRIBUTING				
c. CONTRIBUTING	/ / / / / /	STOG 80-7.2:5		

11. TITLE: (U) The Initial Treatment of Combat Wounds

12. SCIENTIFIC AND TECHNOLOGICAL AREAS: 012600 Pharmacology 012900 Physiology 002300 Biochemistry

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
8101	CONT	DA	C. IN-HOUSE

17. CONTRACT/GRANT
a. DATES/EFFECTIVE: EXPIRATION:
b. NUMBER:
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR PRECEDING 83	1.0	99
FISCAL YEAR CURRENT		

19. RESPONSIBLE DOD ORGANIZATION
NAME: U S Army Institute of Dental Research
ADDRESS: Washington, DC 20307
RESPONSIBLE INDIVIDUAL
NAME: SWEENEY, T. P.
TELEPHONE: (202) 576-3484

20. PERFORMING ORGANIZATION
NAME: U S Army Institute of Dental Research
ADDRESS: Washington, DC 20307
PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME: SETTERSTROM, J. A.
TELEPHONE: (202) 576-2290/3662
SOCIAL SECURITY ACCOUNT NUMBER: POC:DA
ASSOCIATE INVESTIGATORS
NAME: VINCENT, J.
NAME:

21. GENERAL USE
Foreign Intelligence Considered

22. KEYWORDS: (U) Cellulose Triacetate; (U) Gentamicin; (U) Copolymer Bandage; (U) Lidocaine; (U) Laboratory Animals

23. TECHNICAL OBJECTIVE. 24. APPROACH. 25. PROGRESS (Furnish individual paragraphs identified by number. Precede text of each with Security Classification Code.)

23. (U) To develop a multipurpose wound dressing which will provide anesthesia, antisepsis and hemostasis so that, where appropriate, the result will be rapid return of the wounded soldier to duty as well as reduction of the morbidity occasioned by delayed definitive treatment and secondary complications.

24. (U) Contract developed drug release systems will be evaluated in animal models developed specifically for that purpose. Various methods and materials for maintaining contact over a variety of maxillofacial contours will be evaluated for their utility of application and use in the combat situation.

25. (U) 8209-8309 Wounds infected with Staphylococcus aureus ($\geq 10^5$ organisms/cm^2) when covered with POROPLASTIC® impregnated with gentamicin (6.0 - 8.0% w/w) were freed of infection. The POROPLASTIC® appears to provide an excellent vehicle for sustained topical delivery of antibiotics and shows promise as an improved wound dressing. In future studies additional antibiotics will be incorporated and efforts will be directed toward improving its ability to cling to the wound surface.

* Available to contractors upon originator's approval.

DD FORM 1 MAR 88 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE (DD FORMS 1498A 1 NOV 68 AND 1498 1 MAR 88 (FOR ARMY USE) ARE OBSOLETE

PROJECT: 3S162775A825

WORK UNIT TITLE: (U) The Initial Treatment of Combat Wounds

PRINCIPAL INVESTIGATOR: Jean A. Setterstrom, Ph.D.

In Vivo Evaluation of POROPLASTIC® Wound Dressings

Problem: Until recently, available artificial wound dressings were made of cotton gauze. These dressings are unable to prevent wound surface dehydration and due to wound adherence, they are difficult to remove without disrupting the healing process. Research has confirmed that epithelialization proceeds most rapidly in a moist environment. Easily applied wound dressings are needed which will provide a moist environment, are permeable to oxygen, resist bacterial permeation, are bactericidal, and promote wound healing.

Approach: PORPLASTIC® a material made of cellulose triacetate, is available for development of a new wound dressing. It is ultramicroporous and easily impregnated with drugs which release slowly into aqueous solutions. The material is supple, resilient, comformable to wound topography, and transparent, which allows for continuous observation of wounds. Moisture vapor transmission, oxygen permeability, biocompatibility, and toxicity tests must be performed to evaluate its applicability as an optimal wound dressing. Its ability to release drugs into tissue has been investigated. Gentamicin-impregnated POROPLASTIC® has been overlaid on wound infected with gentamicin-sensitive Staphylococcus aureus. Wash solutions obtained by repeated scrubbing of the wound surface were subjected to bacterial plate counts to ascertain the quantity of viable bacteria/cm^2. The bacterial counts obtained for treated and untreated wounds were compared.

Results: A comparison was made of the effectiveness of celullose triacetate wound dressings which were either unloaded or loaded with gentamicin (4.0-6.4 wt%). All wound dressings had been applied to animal wounds infected with 4.5×10^9 cfu of S. aureus. After three days, all control wounds yielded an average of 5.59×10^7 S. aureus, while the gentamicin-treated group yielded an average of 7.21×10. Those animals that had received a wound dressing of $\geq$6 wt% gentamicin (n=4) had sterile wounds. When wound dressings were placed on freshly reinfected, established wounds, control animals displayed 3.76×10 S. aureus while the gentamicin-treated group ($\geq$6.2 wt%) yielded an average of 8.6×10 S. aureus. Results to date indicate the the POROPLASTIC® impregnated with $\geq$6 wt% gentamicin provides an effective means of treatment for both acute and established infections of S. aureus.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL
DA OG 8670	831001	DD-DR&E(AR)636

3. DATE PREV SUM'RY	4. KIND OF SUMMARY	5. SUMMARY SCTY	6. WORK SECURITY	7. REGRADING	8. GVT'S INTR'N	8a. SPECIFIC DATA CONTRACTOR ACCESS	9. LEVEL OF SUM
821001	H. TERM	U	U		NL	☒ YES ☐ NO	A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62775A	3S162775A825	AB	013
b. CONTRIBUTING				
c. CONTRIBUTING	/ / / / / / /	STOG 82/83-6.2/4		

11. TITLE (Precede with security classification code)

(U) Development and Evaluation of Dental Material for Field Use

12. SCIENTIFIC AND TECHNOLOGICAL AREAS

002400 Bioengineering; 010300 Miscellaneous Materials; 008500 Isotopes

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY			16. PERFORMANCE METHOD
8110	CONT	DA			C. IN-HOUSE

17. CONTRACT/GRANT

a. DATES/EFFECTIVE: EXPIRATION:
b. NUMBER:
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE	a. PROFESSIONAL MAN YRS	b. FUNDS (In thousands)
FISCAL YEAR PREVIOUS 83	2.0	165
FISCAL YEAR CURRENT		

19a. RESPONSIBLE DOD ORGANIZATION

NAME: U.S. Army Institute of Dental Research

ADDRESS: Washington, DC 20307

RESPONSIBLE INDIVIDUAL
NAME: SWEENEY, T.P.
TELEPHONE: (202) 576-3484

20a. PERFORMING ORGANIZATION

NAME: U. S. Army Institute of Dental Research

ADDRESS: Washington, DC 20307

PRINCIPAL INVESTIGATOR (Furnish SSAN if U.S. Academic Institution)
NAME: VANDRE, R.
TELEPHONE: (415) 561-3162
SOCIAL SECURITY ACCOUNT NUMBER: POC:DA

ASSOCIATE INVESTIGATORS
NAME: LORTON, L.
NAME: GROVER, P.

21. GENERAL USE

Foreign Intelligence Considered

22. KEYWORDS (Precede each with security classification code)

(U) Dental X-ray; (U) Dental Cutting Instrument; (U) Subtraction Radiography; (U) Radionuclide X-ray System; (U) Laboratory Animals

23. TECHNICAL OBJECTIVE, 24. APPROACH, 25. PROGRESS (Furnish individual paragraphs identified by number. Precede each with security classification code.)

23. (U) To assist in the development of dental equipment capable of reliable performance and easy maintenance under all field operational conditions. Included are the development of concepts for field dental equipment which is miniaturized, lightweight, energy efficient and low cost.

24. (U) Conceptual and basic engineering requirements for a field dental x-ray system and a field dental cutting instrument will be studied. Current technology will be reviewed for its ability to produce the needed design criteria and advanced technology requirements will be identified. Experimental devices will be constructed.

25. (U) A prototype dental x-ray camera has been designed and fabricated which is the size of a pack of cigarettes, weighs eight ounces, requires no electrical power, and is nearly indestructable. This unit uses radioactive Gadolinium as its x-ray source with a half-life of nearly one year. Equipment allowing standardization of radiographs has been developed and a comparison between conventionally viewed and computer subtraction processes radiographs has been completed. Diagnostic accuracy is greatly enhanced using computer subtraction techniques. Very small changes in bone apposition following arrest of disease were successfully documented in the monkey, but histologic correlation has not been completed. No results are yet available from the implant studies.

*Available to contractors upon originator's approval

DD FORM 1 MAR 88 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE AND 1498-1, 1 MAR 88 (FOR ARMY USE) ARE OBSOLETE

PROJECT: 3S162775A825

WORK UNIT TITLE: (U) Development and Evaluation of Dental Material for Field Use

PRINCIPAL INVESTIGATOR: MAJ Robert H. Vandre, DC

Design and Evaluation of a Combat Field X-Ray Unit

Using a Radiographic Source

PROBLEM: The present dental X-ray unit is a cumbersome, relatively delicate instrument. It is nothing more than an office X-ray unit that fits into a carrying case. It requires two men to transport it and needs 100 volts AC to power it. This unit also requires a darkroom and processing equipment which also tend to reduce the portability of the system.

APPROACH: In concert with the Dental Radiology Department, University of California at San Francisco, an extremely portable dental X-ray unit is being developed which will use a radioactive source to generate x-rays. The use of Polaroid® film with image-intensifying screens is being explored to remove the need for a darkroom and developer.

RESULTS: A contract for the joint development and testing of the above system was drawn with the Dental Radiology Department, University of California at San Francisco. A prototype dental X-ray camera has been designed and fabricated. It is the size of a pack of cigarettes, weighs eight ounces, requires no electrical power, and is nearly indestructible. This unit uses radioactive Gadolinium as its x-ray source with a half-life of nearly one year. Preliminary data shows that x-ray exposure levels to the patient will be 200 times less than those taken with conventional dental X-ray units. Radiographs of the skull taken using this system show details with clarity at least as good as conventional Panorex radiographs.

PROJECT: 3S162775A825

WORK UNIT TITLE: (U) Development and Evaluation of Dental Material for Field Use

PRINCIPAL INVESTIGATOR: MAJ Michael P. Rethman, DC

Subtraction Radiography for the Diagnosis of

Bone Lesions in Dogs

PROBLEM: A computer program has been developed at NIH to allow processing of sequential standardized radiographs by digital computer. Structured noise (unchanged imagery) is eliminated by subtraction, leaving only images of that which has changed. Such radiographs would be extremely useful for monitoring osseous healing in experimental animals if correlation could be made with demonstrated histological and established wound healing parameters. Equipment allowing standardization of radiographs in a live animal model was to be developed. Following development of such equipment, the usefulness of computer subtracted images for location of osseous wounds was to be determined. If preliminary data was promising, documentation of osseous wound healing was to be evaluated.

APPROACH: Radiographic cones were manufactured which keyed directly into custom splints which held the film in a reproducible relationship. Small intraosseous wounds were placed in the mandibles of anesthetized dogs and sequential healing radiographs were secured. One monkey which had naturally progressive periodontal disease was documented following nonsurgical treatment designed to arrest that disease. Current implant studies were documented using the same radiographic equipment.

RESULTS: The equipment allowing standardization of radiographs has been developed and a comparison between conventionally viewed and computer subtraction processed radiographs has been completed. Diagnostic accuracy is greatly enhanced using computer subtraction techniques. Very small changes in bone apposition following arrest of disease were successfully documented in the monkey, but histologic correlation has not been completed. No results are yet available from the implant studies.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

				DA OG 8672	83 10 01		
82 10 01	H. TERM	U	U		NL	☒ YES ☐ NO	

	62775A	3S162775A825	AB	019
		STOG 82783=6.274		

(U) Epidemiological Investigation of Dental Emergencies

012900 Physiology; 012600 Pharmacology; 003500 Clinical Medicine

81 10	CONT	DA	C. IN-HOUSE

	PREVIOUS		
FISCAL YEAR	83	1.2	75
	CURRENT		

U.S. Army Institute of Dental Research

Washington, DC 20307

U.S. Army Institute of Dental Research

Washington, DC 20307

SWEENEY, T.P.

TELEPHONE: (202) 576-3484

CARPENTER, W.M.

TELEPHONE: (202) 576-3258

SOCIAL SECURITY ACCOUNT NUMBER: POC:DA

ASSOCIATE INVESTIGATORS

NAME: SHULMAN, J.

NAME: GROVER, P.

Foreign Intelligence Considered

(U) Lip Pathology; (U) Herpetic Lesions; (U) Cold Weather Survey; (U) Xerocheiliosis

23. (U) To determine the causes of dental emergencies in a population of soldiers receiving regular dental care and to determine "at-risk-profiles" for those soldiers in critical occupation specialties so as to minimize problems with dental casualties during deployment.

24. (U) Studies will be conducted among soldier populations to pinpoint the causes of dental emergencies, their frequency and diagnostic strategies which will permit the prediction of the potential of each soldier for such emergencies. The goal is to select out the "at-risk" group for dental treatment and thus minimize dental casualties during deployment.

25. (U) (8210 - 8310) Analysis of data from the cold weather survey indicates that while actinic exposure is a risk factor in acute lip injury, relative humidity is even more significant. The modifying effects of complexion were also significant; in cold weather dark complexion is a risk factor, while it is a protective factor in hot weather. Based on these findings, the use of emollient preparations is recommended to protect the lips from dessication in a dry climate.

DD FORM 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE

PROJECT: 3S162775A825

WORK UNIT TITLE: (U) Epidemiological Investigation of Dental Emergencies

PRINCIPAL INVESTIGATOR: COL William M. Carpenter, DC

The Prevalence of Lip Injury During U. S. Army Cold Weather Exercises

PROBLEM: It is commonly assumed that extended outdoor exposure to extreme climates is a contributory cause of lip pathology, since the facial area is poorly protected from the environment. Soldiers on military operations are exposed to adverse climates to a greater degree than are civilians living in similar environments. They are often subjected to extreme physical exertion or long periods of minimal activity while exposed to an extremely cold environment. In cold weather for example, civilians spend, on the average, less than 5 to 10% of the day outdoors, while soldiers in the field spend 30% or more of the day outdoors. While acute lip problems are not medical emergencies, they are a morale problem for the troops. The prevalence and nature of cold weather lip damage has never been studied in a systematic manner. It was the purpose of this study to observe active duty soldiers engaged in cold-weather training and to document the prevalence of acute lip injury.

APPROACH: The studies were conducted at Fort Drum, New York. The first study occurred in January, 1980 during the "Empire Glacier" exercise. Participants were 763 personnel from Fort Bragg, North Carolina. The second study was conducted in January, 1982 during the "Snow Eagle" exercise. The participants were 659 personnel from Fort Campbell, Kentucky. Each survey was conducted during the third week of a four-week exercise. The subjects were interviewed and examined while they were waiting in mess hall lines. Each examination/interview for the purposes of this study took approximately 10-15 seconds. If lesions were found, a more thorough examination was performed.
Data on the percentage of time devoted to outdoor duties were obtained by interview and were categorized as (a) more than 50% of time outdoors, (b) less than 50% outdoors, or (c) equal time outdoors and indoors. Age by decade and lip protectant use (Army issue; comercial, none) were elicited from the subjects. The presence of acute lip damage and type of complexion were also recorded during the examination. All examination data were agreed upon by both the examiner and the recorder.

RESULTS: Fifteen subjects (1.1%) exhibited severe acute lip damage; 743 (52.3%) exhibited moderate changes, and 664 (46.7%) had normal lips. Herpetic lesions were found in 32 (2.4%) of the 1331 soldiers included in the survey. The data on the frequency of acute lip injury during two field exercises were analyzed by age, use of lip protectant, complexion, amount of exposure, and weather. The association

between acute lip damage and age was not statistically significant in the sample. Eighty-five per cent of the study population was in the 17-29 age range. Dealing with a relatively small age range and recording age by decades, however, may have reduced the sensitivity of our study with regard to age as a risk factor. The hot-weather study dealt with a similar population. The prevalence of chronic lip damage was found to increase with age, but no information on age and frequency of acute lip damage was presented. The small number of females in our survey population (1.8%) did not justify stratification of the variables by sex. The association of acute lip injury with complexion was significant. Higher rates of acute lip damage were found in darker complected individuals. This finding was in conflict with the hot-weather survey. In dealing with a similar complexion distribution, both acute and chronic lip damage were found to vary significantly with complexion; with darker complexions having lower prevalence rates. A possible explanation for the conflicting results is that during the cold-weather surveys, the amount of actinic exposure was much less than that during the hot-weather survey. The amount of duty time spent outdoors was not significantly associated with the prevalence of lip injury. When the frequencies of acute lip damage in the two cold-weather surveys were compared (23% in 1982 and 12% in 1980), the differences were found to be significant. The weather during the second survey was colder, had less sun exposure, and resulted in an increased problem of lip damage. The relative humidity did not vary substantially during the two surveys. The modifying effects of complexion were significant; in cold weather, dark complexion is a risk factor, while it is a protective factor in hot weather. Age and amount of time spent outdoors are not significant risk factors in acute cold-weather lip injury.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY	DA0H6030	01 OCT 83	REPORT CONTROL NUMBER VEJOSA

01 OCT 83	D. CHANGE	U	U		CX		A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
	62775A	3S162775A825	AA	004

(U) NATURAL HISTORY OF ORAL LESIONS ENCOUNTERED IN THE SOLDIER

0616 PHYSIOLOGY 0605 CLIN MEDICINE 0613 MICROBIO

JUL 69	CONT	DA	C. IN-HOUSE

FISCAL YEARS	PROFESSIONAL WORKYEARS	FUNDS (In Thousands)
1983	0.7	$ 59
1984	0.7	$ 65

F. CUM/TOT: $ 0

Responsible DOD organization: 038870 1100
Name: MORDC INSTITUTE OF DENTAL RSCH USAIDR
Address: WASHINGTON DC 20012
Responsible individual
Name: SWEENEY, T P
Telephone: 202-576-3444

Performing organization: C38870 1100
Name: MORDC PATHOLOGY DIVISION USAIDR
Address: WASHINGTON DC 20012
Principal investigator
Name: BURNETT, P
Telephone: 202-576-3080
Associate investigators
Name:
Name:

(U) APHTHOUS STOMATITIS ;(U) WOUND HEALING ;(U) RECURRENT APHTHOUS STOMATITIS ;(U) LYMPHOCYTES ;(U) VOLUNTEERS ;(U) RAM IV;

OBJECTIVE:(U) TO RECOGNIZE, CHARACTERIZE AND DEVELOP EFFECTIVE THERAPEUTIC MEASURES FOR THOSE LESIONS AND CONDITIONS WHICH EFFECT THE SOLDIER DUE TO MILITARY DUTY. THE RECOGNITION OF ENVIRONMENTAL AND OTHER FACTORS WHICH PARTICIPATE IN THE ETIOLOGY OF LESIONS AND CONDITIONS UNIQUE TO THE MILITARY OR ARE CASUALLY RELATED TO MILITARY DUTY WILL ENABLE THE DEVELOPMENT OF INTERCEPTIVE OR THERAPEUTIC MEASURES.

APPROACH: (U) TO DETECT THROUGH CLINICAL AND/OR MICROSCOPIC OBSERVATION ORAL LESIONS OR A CONDITION UNIQUE TO THE MILITARY POPULATION. TO IDENTIFY ORAL LESIONS OR CONDITIONS WHICH, THOUGH NOT UNIQUE TO THE SOLDIER, ARE ETIOLOGICALLY RELATED TO THE PERFORMANCE OF DUTY. ONCE IDENTIFIED THE NATURAL HISTORY INCLUDING ETIOLOGY, THERAPY, AND PROGNOSIS WILL BE ESTABLISHED UTILIZING APPROPRIATE METHODS SUCH AS SURVEYS, ANIMAL, AND HUMAN INVESTIGATIONS.

PROGRESS: (U) 8210-8310. WITH APPROXIMATELY HALF OF THE NECESSARY DATA GATHERED, THE FOLLOWING TRENDS ARE APPARENT: (1) CYTOTOXIC ACTIVITY OF FRESH RAS SERA EXCEEDS THAT OF MATCHED CONTROL SERA; (2) CYTOTOXIC ACTIVITY OF RAS MONONUCLEAR LEUKOCYTES IS NOT SIGNIFICANTLY GREATER THAN MATCHED CONTROLS; (2) IN SOME CASES, HEAT-ACTIVATED RAS SERA SHOW SIGNIFICANTLY GREATER CYTOTOXIC ACTIVITY WHEN COMBINED WITH RAS MONONUCLEAR LEUKOCYTES (DURING EARLY STAGE OF ACTIVE DISEASE, ONLY). BOTH COMPLEMENT-MEDIATED AND CELL-MEDIATED ANTIBODY-DEPENDENT CYTOTOXICITY ARE IMPLICATED IN THIS SYSTEM.

PROJECT: 3S162775A825

WORK UNIT TITLE: (U) Natural History of Oral Lesions Encountered in the Soldier

PRINCIPAL INVESTIGATOR: LTC Paul R. Burnett, DC

In Vitro Cytolytic Effects of Serum and Mononuclear Leukocytes From RAS Patients

PROBLEM: Recurrent aphthous stomatitis (RAS), a stress-related condition prevalent in military populations, significantly impairs performance of duty of duty (in its more severe forms) and reportedly retards oral soft tissue wound healing. The objective of this research is to elucidate pathophysiological mechanisms responsible for the destruction of tissue and prolongation of healing associated with RAS.

APPROACH: A radioisotope-release assay utilizing trypsinized, ^{51}Cr-labeled, allogeneic, nonkeratinizing oral epithelial cells has been developed to quantify immune cytotoxic activity in the serum and mononuclear leukocytes of RAS patients.

RESULTS: With approximately half of the necessary data gathered, the following trends are apparent:

1. Cytotoxic activity of fresh RAS sera exceeds that of matched control sera.

2. Cytotoxic activity of RAS mononuclear leukocytes is not significantly greater than matched controls.

3. In some cases, heat-inactivated RAS sera show significantly greater cytotoxic activity when combined with RAS (autologous) mononuclear leukocytes than with control leukocytes (during early stage of active disease, only).

Both complemented-mediated and cell-mediated antibody-dependent cytotoxicity are implicated in this system.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION: DA 011 6037	2. DATE OF SUMMARY: 83 10 01		REPORT CONTROL SYMBOL: DD-DR&E(AN)635
3. DATE PREV SUM'RY: 82 10 01	4. KIND OF SUMMARY: D CHANGE	5. SUMM'RY SCTY: U	6. WORK SECURITY: U	7. REGRADING:	8a. ORG'N INSTR'N: NL	8b. SPECIFIC DATA-CONTRACTOR ACCESS: ☒ YES ☐ NO	9. LEVEL OF SUM: A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62775A	3S162775A825	AA	007
b. CONTRIBUTING				
c. [illegible]	////////////	STOG 82/83-6.2/4		

11. TITLE (Possible with Security Classification Code): (U) New and Improved Techniques for Grafts and Bone Regeneration in Traumatic Wounds

12. SCIENTIFIC AND TECHNOLOGICAL AREAS: 012900 Physiology; 002400 Bioengineering; 002600 Biology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY		16. PERFORMANCE METHOD
69 01	CONT	DA		C. IN-HOUSE

17. CONTRACT/GRANT
a. DATES/EFFECTIVE: EXPIRATION:
b. NUMBER:
c. TYPE: d. AMOUNT:
e. KIND OF AWARD: f. CUM. AMT.

18. RESOURCES ESTIMATE		a. PROFESSIONAL MAN YRS	b. FUNDS (In Thousands)
FISCAL YEAR	PREVIOUS		
	83	1.5	110
	CURRENT		
	84	1.5	122

19. RESPONSIBLE DOD ORGANIZATION
NAME: U.S. Army Institute of Dental Research
ADDRESS: Washington, DC 20307

RESPONSIBLE INDIVIDUAL
NAME: SWEENEY, T.P.
TELEPHONE: (202) 576-3484

20. PERFORMING ORGANIZATION
NAME: U.S. Army Institute of Dental Research
ADDRESS: Washington, DC 20307

PRINCIPAL INVESTIGATOR (Provide last name, first name, middle initial)
NAME: HOLLINGER, J.O.
TELEPHONE: (202) 576-3764
SOCIAL SECURITY ACCOUNT NUMBER: POC:DA

ASSOCIATE INVESTIGATORS
NAME: WOODYARD, S.
NAME: O'NEAL, R.

21. GENERAL USE
Foreign Intelligence Considered

22. KEYWORDS (Provide Each with Security Classification Code): (U) Tricalcium Phosphate; (U) Ceramic Block; (U) Segmental Mandibular Defects; (U) Granular Tricalcium Phosphate; (U) Laboratory Animals

23. (U) Current methodologies for managing combat maxillofacial wounds and preventing/treating dental emergencies in the field will be extremely difficult to apply under the condition anticipated in future war. New methods are required which will permit more rapid definitive care, reduce morbidity and decrease logistic load. Thus the objective of this work unit is to develop simple, rapid methods for soft tissue or bone grafting utilizable by the dental specialist in the field.

24. (U) The fate, metabolism, osteogenic potential and tissue compatibility of ceramic and copolymer materials will be studied alone and in combination. The application of these and other materials to avulsive type wounds in both animals and humans will be pursued.

25. (U) Due to loss of principal investigator and difficulties in the production of biodegradable, unidirectional porousity Tricalcium Phosphate (TCP), no significant progress has been made. A third generation TCP is in production and will be evaluated in experimental animals as soon as it becomes available. Implants of 50:50 Polylactic-Polyglycolic Acid (PLA/PGA) have been surgically inserted in five dogs. Two dogs have been sacrificed. The remaining surgery will be completed by Dec 1983. The remaining animals will be sacrificed by DEc 1983. Histologic preparation of the specimens and evaluation of results should be completed by June 1984.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

				DA OK 6020		83 10 01		
82 10 01	D CHANGE	U	U			NL		
	62775A	3S162277SA825		AA		008		
		STOG 82/83-6.2/4						

(U) Biogradable Materials for the Treatment of Fractures and Soft Tissue Wounds in cha Military Situation

012900 Physiology - 010300 Miscellaneous Materials

68 01	CONT	DA		C IN-HOUSE	
				83	0.7	75
				84	0.7	83

USA Institute of Dental Research
Washington, DC 20307

SWEENEY, T.P.
202 576-3484

Foreign Intelligence Considered

USA Institute of Dental Research
Washington, DC 20307

Hollinger, J.
202 576-3764
POC:DA

(U) Biodegradable Copolymer; (U) Tracheal Grafts (U) Diphosphoinositide-Lysozyme; (U) Laboratory Animals

23. (U) To develop rapid and improved methods of treating combat injuries of the head and neck in the field using biodegradable materials. To develop premedicated biodegradable tissue fixation devices.

24. (U) Biodegradable polylactic acid, polyglycolic acid and various combinations of these polymers as well as other polymers being developed will be applied in the development of surgical procedures for a variety of hard tissue, soft tissue and hollow organ injuries in animals and extended to man where appropriate.

25. (U) Implant blocks have been inserted and evaluated in 8 dogs. By 7 months, implant-treated defects were completely healed. Implants for an additional 25 dogs were synthesized. Preparatory surgery has been performed on 3 animals. Biochemical and histochemical assays demonstrated suitable host reponse to the implant.

PROJECT: 3S]622775A825

WORK UNIT TITLE: (U) Biodegradable Materials for the Treatment of Fractures and Soft Tissue Wounds in the Military Situation

PRINCIPAL INVESTIGATOR: LTC Jaffrey O. Hollinger, DC

A Study to Evaluate Copolymer of PLA:PGA and Diphosphoinositide-Lysozyme for Bridging a Surgically Prepared Bone Discontinuity Defect in Dogs

PROBLEM: Materials such as bone grafts and implants, collagen gels, ceramics, bone derivatives, and biopolymers are some of the many agents which have been employed for initiating osseous repair or for replacing bone. Failure rates ranging from 13% to greater than 30% have lead to a renewed interest in the development of more predictable compounds. A material was formulated, therefore, that consisted of the biopolymers PLA&PGA combined with a proteolipid (mucopeptide-N-acetylmuramolyhydrolase:phosphatidyl inositol 4,5-diphosphate).

APPROACH: Two series of experiments were performed on a group of eight and a group of 25 adult mongrel dogs (mixed sexes, weighing 45-55 lbs). Selective, surgical extraction of teeth in ipsilateral arches was accomplished, and this preceded preparation of the host bed for receiving the implant. The implant was made by dissolving 50:50 PLA:PGA into methylene chloride and reprecipitating with anhydrous methanol. The proteolipid was added to this mixture which was placed into a Teflon mold. The mold was inserted into a vacuum oven at 50°C, 5 millitorr for 48 hours, followed by ethylene oxide sterilization. Host sites in the dogs' mandibles were prepared in the following manner: 1. Following 8 weeks of post-extraction healing, a 20mm segment was ablated, producing a complete discontinuity. This procedure was done on both sides of the mandibular arch. 2. A block of the implant of identical geometry to the defect was fabricated and was inserted into one defect. Stabilization and fixation were accomplished using ligature wire, a stainless steel plate, and stainless steel screws. 3. The contralateral defect was left untreated to serve as a control. All dogs were evaluated clinically at periodic intervals and lateral mandibular radiographs were taken.

RESULTS: The discontinuity defects in the mandibles of the group of 8 dogs that had been treated with the PLA:PGA-proteolipid implant developed an osseous union after six months. Bilateral palpation and manipulation of the mandible following removal of the internal fixation revealed complete stability. Radiographically, host-implant sites appeared within normal limits. The group of 25 dogs displayed results parallel to the group of 8 animals. Presently, histomorphometric and microdensitometric analyses of bone enzymes are underway. In both groups, complete tissue tolerance to the implant was demonstrated. Initial indications suggest that the PLA:PGA proteolipid may be useful for stimulating bony repair at intramembranous wound sites.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

DA301488	01 OCT 83	REPORT CONTROL SYMBOL Z01708				
20 JUN 83	A. NEW	U	U		NL	A. WORK UNIT
10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER		
a. PRIMARY	62775A	3S162775A825	AA	016		
b. CONTRIBUTING						
c. CONTRIBUTING	MISS. OBJ. STOG : 82/83-0.2/5 :					

11. TITLE: (U) TUMORIGENICITY STUDY OF ISOBUTYL 2-CYANOACRYLATE

12. SCIENTIFIC AND TECHNOLOGICAL AREAS: 012900 PHYSIOLOGY 016200 STRESS PHYS

13. START DATE: JUN 83 | 14. ESTIMATED COMPLETION DATE: SEP 88 | 15. FUNDING AGENCY: DA | 16. PERFORMANCE METHOD: C. IN-HOUSE

17. CONTRACT/GRANT: F. CUM/TOT: $ 0

18. RESOURCES ESTIMATE:

FISCAL YEAR		PROFESSIONAL MAN YRS	FUNDS (In thousands)
PRECEDING	1983	0.1	$ 3
CURRENT	1984	0.5	$ 75

19. RESPONSIBLE DOD ORGANIZATION: 038870 11

NAME: HSRDC INSTITUTE OF DENTAL RSCH USAIDR

ADDRESS: WASHINGTON DC 20307

RESPONSIBLE INDIVIDUAL

NAME: SWEENEY, T P MD 20

TELEPHONE: 202-576-3484

21. GENERAL USE: F.I.C.A.

20. PERFORMING ORGANIZATION: 038870 H1

NAME: HSRDC INSTITUTE OF DENTAL RSCH USAIDR

ADDRESS: WASHINGTON DC 20307

PRINCIPAL INVESTIGATOR

NAME: CARPENTER, W M DA

TELEPHONE: 202-576-3258

ASSOCIATE INVESTIGATORS

NAME: KOPPELMAN, E

22. KEYWORDS: (U) ISOBUTYL 2-CYANOACRYLATE;(U) TUMORIGENICITY STUDY (U) LAB ANIMALS ;(U) TISSUE ADHESIVE ;(U) LIVER SURGERY ;(U) RATS ;(U) RAM IV;

OBJECTIVE:(U) ISOBUTYL 2-CYANOACRYLATE (IBC) HAS BEEN DEMONSTRATED TO BE AN EFFECTIVE TISSUE ADHESIVE FOR USE IN SUTURLESS WOUND CLOSURE. THE USE OF THIS MODALITY COULD PROVIDE A TIME SAVING AND SOMETIMES LIFE-SAVING DIMENSION TO THE MANAGEMENT OF COMBAT WOUNDS. THE PURPOSE OF THE PRESENT STUDY IS TO DETERMINE OF ANY TUMORIGENIC EFFECTS ARE PRODUCED BY THE LONG-TERM IMPLANTATION OF IBC.

APPROACH: (U) THREE HUNDRED AND SIXTY ALBINO RATS WILL BE EQUALLY DIVIDED INTO A CONTROL AND EXPERIMENTAL GROUP; EACH GROUP CONTAINING EQUAL NUMBERS ACCORDING TO SEX. EACH ANIMAL WILL BE OPENED, THE LIVER EXPOSED AND EITHER TREATED WITH A THIN FILM OF IBC IN THE CASE OF THE EXPERIMENTALS OR SALINE IN THE CASE OF THE CONTROLS. THE INCISION WILL BE CLOSED AND ALL ANIMALS WILL BE MAINTAINED UNDER CAREFULLY CONTROLLED CONDITIONS. THE DURATION OF THE STUDY WILL BE TWO YEARS WITH HALF OF THE ANIMALS BEING SACRIFICED AT THE 384TH DAY. NECROPSIES WILL BE PERFORMED ON ALL ANIMALS AND HISTOLOGIC EXAMINATION UNDERTAKEN OF ALL ESSENTIAL TISSUES.

PROGRESS: (U) NONE.

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY | DA302718 | 21 OCT 83 | REPORT CONTROL SYMBOL 201708

A. NEW | U | U | NL | A. WORK UNIT

10. NO./CODES: PROGRAM ELEMENT 62775A | PROJECT NUMBER 3S162775A825 | TASK AREA NUMBER AA | WORK UNIT NUMBER 001

FORMER

MCSS. OBJ. STOG : 82/83-6.2/5 :

(U) THE EFFECTIVENESS OF THE DENTAL RECORD IN THE IDENTIFICATION OF COMBAT CASUALTIES

000400 ADMIN - MGT 008700 MATH STAT 011700 OPER RES

OCT 83 | MAY 85 | DA | C. IN-HOUSE

F. CUM/TOT: $ 0

	1983	0	0
	1984	0.	$ 65

038670 11 | 038670 11

MDRDC INSTITUTE OF DENTAL RSCH USAIDR

WASHINGTON DC 20307

SWEENY, T P MD 20

202-576-3484

F.I.C.A.

MILITARY

MDRDC INSTITUTE OF DENTAL RSCH USAIDR

WASHINGTON DC 20307

SHULMAN, J D DA

202-576-3520

BURNETT, P

LEWIS, D

(U) OPERATIONS RESEARCH ;(U) DENTAL IDENTIFICATION ;(U) HEALTH SERVICES RESEARCH;(U) LOGISTIC MODELS ;(U) RAM IV

OBJECTIVE:(U) TO DETERMINE THE RELIABILITY OF THE MILITARY DENTAL RECORD IN POSTMORTEM IDENTIFICATION OF A COMBAT CASUALTY.

APPROACH: (U) DENTAL IDENTIFICATION OF COMBAT CASUALTIES WILL BE SIMULATED USING AT LEAST 200 ACTIVE DUTY ARMY PATIENTS PRESENTING FOR ROUTINE EXAMINATIONS AT WALTER REED DENTAL CLINIC. SIMULATED ANTEMORTEM RECORDS (DENTAL RECORD AND RADIOGRAPHS) WILL BE DUPLICATED AND ASSIGNED A UNIQUE NUMBER. A SIMULATED POSTMORTEUM RECORD WILL BE PREPARED SUBSEQUENT TO THE EXAMINATION. IT WILL CONSIST OF A ROUTINE DENTAL CHARTING AND DUPLICATES OF ANY RADIOGRAPHS ORDERED BY THE EXAMINING OFFICER. THE RECORD WILL ALSO BE ASSIGNED A UNIQUE NUMBER. A PANEL OF DENTAL OFFICERS WILL ATTEMPT TO MATCH THE SIMULATED ANTEMORTEM AND POSTMORTEM RECORDS. A LOGISTIC MODEL WILL BE CONSTRUCTED TO PREDICT THE PROBABILITY OF A CORRECT IDENTIFICATION AS A FUNCTION OF THE QUANTITY AND QUALITY OF THE INFORMATION IN THE SIMULATED ANTEMORTEM RECORD.

PROGRESS: (U) NONE.

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

				0A302899	01 OCT 83		REPORT CONTROL SYMBOL ZO1700
	A. NEW	U	U		NL		A. WORK UNIT
10. NO./CODES: a	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER	WORK UNIT NUMBER		
	62770A	3S162770A82B		0A	011		

(U) STORAGE STABILITY OF MEDICAL AND DENTAL MATERIALS

012700 PHYS CHEM	008200 INORG CHEM	003500 CLIN MED	
OCT 83	CONT	DA	C. IN-HOUSE

	PRIOR		
FISCAL YEAR	1983	0.0	$ 0
CURRENT YEAR	1984	1.0	$ 60
P. CUM/TOT:			$ 0

038870	11	038870 M1

MDRDC INSTITUTE OF DENTAL RSCH USAIDR

WASHINGTON DC 20307

SWEENEY, T P MD 20

202-576-3484

F.I.C.A.

MILITARY

MDRDC INSTITUTE OF DENTAL RSCH USAIDR

WASHINGTON DC 20307

WOOLSEY, G D DA

415-561-5740

MOFFA, J

(U) STORAGE STABILITY ;(U) SHELF-LIFE ;(U) MEDICAL MATERIEL ;(U) DENTAL MATERIALS ;(U) RAM IV;

OBJECTIVE:(U) MEDICAL AND DENTAL MATERIEL FOUND IN THE MILITARY LOGISTIC SYSTEM IS STORED IN SIX MAJOR DEPOTS WORLDWIDE. THE EXTREMES OF TEMPERATURE AND HUMIDITY CAN POTENTIALLY RENDER SOME OF THESE SUPPLIES INEFFECTIVE. ACCURATE SHELF-LIFE DATA ON POTENTIALLY PERISHABLE MEDICAL AND DENTAL MATERIEL IS VITAL TO INSURE THE VIABILITY OF SUPPLIES AFTER PERIODS OF STORAGE AND TRANSPORTATION.

APPROACH: (U) BACKGROUND INFORMATION ON THE MILITARY LOGISTICS SYSTEM WILL BE STUDIED TO IDENTIFY POTENTIALLY PERISHABLE SUPPLIES, DETERMINE METHODS CURRENTLY USED FOR STORAGE AND IDENTIFY SPECIFICS OF ENVIRONMENTAL FACTORS TO WHICH MEDICAL AND DENTAL SUPPLIES ARE EXPOSED. THE SECOND PHASE OF THIS WORK WILL BE THE PHYSICAL TESTING OF IDENTIFIED MATERIEL AND THE DETERMINATION OF ACCURATE SHELF-LIFE DATA AFTER EXPOSURE TO AN ENVIRONMENTAL TESTING CHAMBER. THIS PROJECT WAS S[illegible]RTED AS DA0G8033.

PROGRESS: (U) NONE.

DD [illegible]

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				DA302800	01 OCT 83		REPORT CONTROL SYMBOL Z01708
	A. NEW	U	U		NL		A. WORK UNIT
10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER	
PRIMARY	62775A	3S162775A825		AA		014	
CONTRIBUTING							
MISS. OBJ. STOG : 82/83-0.2/8 ;							

(U) STATISTICALLY BASED METHOD FOR PREDICTING DENTAL EMERGENCIES

007500 HUMAN FAC EN; 003500 CLIN MEDICINE

START DATE	ESTIMATED COMPLETION DATE	FUNDING AGENCY	PERFORMANCE METHOD
OCT 83	CONT	DA	C. IN-HOUSE

F. CUM/TOT: $ 0

FISCAL YEAR		PROFESSIONAL MAN YRS	FUNDS (In Thousands)
PRECEDING	1983	0.0	$ 0
CURRENT	1984	0.4	$ 50

RESPONSIBLE DOD ORGANIZATION: 038870 11

NAME: HSRDC INSTITUTE OF DENTAL RSCH USAIDR

ADDRESS: WASHINGTON DC 20307

RESPONSIBLE INDIVIDUAL

NAME: SWEENEY, T P MD 20

TELEPHONE: 202-576-3484

GENERAL USE: F.I.C.A.

MILITARY/CIVILIAN APPLICATION: MILITARY

PERFORMING ORGANIZATION: 038870 11

NAME: HSRDC INSTITUTE OF DENTAL RSCH USAIDR

ADDRESS: WASHINGTON DC 20307

PRINCIPAL INVESTIGATOR

NAME: GROVER, P DA

TELEPHONE: 415-561-3162

ASSOCIATE INVESTIGATORS

KEYWORDS: (U) RAM IV;(U) DENTAL EMERGENCIES;(U) PREDICTIVE METHODS (U) INTERCEPTIVE METHODS ;

OBJECTIVE:(U) EMERGENCY VISTIS TO THE DENTAL CLINIC DEPLETE THE FIGHTING STRENGTH OF A COMBAT UNIT. CAUSES AND TREATMENT OPTIONS FOR THE EMERGENCY PATIENTS OF REPRESENTATIVE TROOP UNITS WILL BE EXAMINED AND TABULATED. THE OBJECTIVE IS TO WEIGH CASUAL FACTORS AND DEVELOP PREDICTIVE AND/OR INTERCEPTIVE METHODS TO DECREASE UNPLANNED DENTAL VISITS AND THUS TO INCREASE THE TIME THE SOLDIER CAN BE PRESENT FOR DUTY.

APPROACH: (U) RECORDS OF EMERGENCY AND ROUTINE VISITS TO THE TROOP DENTAL CLINICS AT THREE DIFFERENT MILITARY POSTS WILL BE ANALYZED. STATISTICAL TECHNIQUES WILL BE USED TO ESTABLISH THE FACTORS IN THE DENTAL STATUS THAT CONTRIBUTE TO THE EMERGENCY VISITS. IF POSSIBLE AN INDEX WILL BE CONSTRUCTED THAT WILL ALLOW THE PREDICTION OF FUTURE DENTAL EMERGENCY VISITS FROM PATIENT HISTORY AND PRESENT DENTAL HEALTH. THIS PROJECT WAS STARTED UNDER DA0E6022.

PROGRESS: (U) NONE.

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY | DA302801 | 01 OCT 83 | REPORT CONTROL SYMBOL CSO1708

A. NEW | U | U | NL | A. WORK UNIT

16. NO./CODES: PROGRAM ELEMENT | PROJECT NUMBER | TASK AREA NUMBER | WORK UNIT NUMBER

62770A | 3S162770A828 | AB | 013

(U) DESIGN AND EVALUATION OF A COMBAT FIELD X-RAY UNIT USING A RADIOGRAPHIC SOURCE

006800 ISOTOPES 006800 MED MDSP EQ

OCT 83 | CONT | DA | C. IN-HOUSE

	PRIOR	CURRENT	YEAR
PROFESSIONAL MAN YRS	1983	1984	0.0 / 0.5
FUNDS (In Thousands)			$ 0 / $ 70

F. CUM/TOT: $ 0

PERFORMING ORGANIZATION: 038870 | 11

NORDC INSTITUTE OF DENTAL RSCH USAIDR

WASHINGTON DC 20307

SWEENEY, T P MD 20

202-576-3484

F.I.C.A.

MILITARY

PERFORMING ORGANIZATION: 038870 | N1

NORDC INSTITUTE OF DENTAL RSCH USAIDR

WASHINGTON DC 20307

VANDRE, R H DA

415-561-3182

(U) RADIOISOTOPE;(U) X-RAY PORTABLE ;(U) DENTAL RADIOLOGY ;(U) RAM IV;

OBJECTIVE:(U) THE PRESENT DENTAL X-RAY UNIT IS A CUMBERSOME, RELATIVELY DELICATE INSTRUMENT. IT IS NOTHING MORE THAN AN OFFICE X-RAY UNIT THAT FITS INTO A CARRYING CASE. IT REQUIRES TWO MEN TO TRANSPO'T IT AND NEEDS 110 VOLTS OF AC TO POWER IT. THIS UNIT ALSO REQUIRES A DARKROOM AND PROCESSING EQUIPMENT WHICH ALSO TEND TO REDUCE THE PORTABILITY OF THE SYSTEM.

APPROACH: (U) IN CONCERT WITH THE DENTAL RADIOLOGY DEPARTMENT OF THE UNIVERSITY OF CALIFORNIA AT SAN FRANCISCO, AN EXTREMELY PORTABLE DENTAL X-RAY UNIT IS BEING DEVELOPED WHICH WILL USE A RADIOACTIVE SOURCE TO GENERATE X-RAYS. THE USE OF POLAROID FILM WITH IMAGE INTENSIFYING SCREENS IS BEING EXPLORED TO REMOVE THE NEED FOR A DARKROOM AND DEVELOPER. THIS PROJECT WAS STARTED UNDER DA0G8870.

PROGRESS: (U) NONE.

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				DA302902	01 OCT 83	REPORT CONTROL SYMBOL Z01708
	A. NEW	U	U		NL	A. WORK UNIT
10. NO./CODES:*	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER	WORK UNIT NUMBER	
	62775A	3S162775A825		AA	018	
FORMER					[redacted]	
KYSS. OBJ. STOQ : 82/83-8.2/8 ;					[redacted]	

(U) HISTOLOGIC EVALUATION OF BONY DEFECTS FILLED WITH TRICALCIUM PHOSPHATE AND COVERED WITH POLYLACTIC ACID AND POLYGLYCOLIC ACID

002300 BIOCHEMISTRY 012900 PHYSIOLOGY 002600 BIOLOGY

OCT 83	CONT	DA	C. IN-HOUSE

FISCAL YEAR	1983	0.0	$ 0
	1984	0.2	$ 25

F. CUM/TOT: $ 0

038870 11

NAME: NMRDC INSTITUTE OF DENTAL RSCH USAIDR

ADDRESS: WASHINGTON DC 20307

NAME: SWEENEY, T P MD 20

TELEPHONE: 202-576-3484

F.I.C.A.

MILITARY

038870 H1

NAME: NMRDC INSTITUTE OF DENTAL RSCH USAIDR

ADDRESS: WASHINGTON DC 20307

NAME: ONEIL, R B DA

TELEPHONE: 202-576-3383

NAME: HOGAN, D W

(U) BIODEGRADABLE ;(U) CERAMIC ;(U) OSSEOUS ;(U) IMPLANT ;(U) PLA/PGA COVERING ;(U) RAM IV;

OBJECTIVE:(U) THE TECHNICAL OBJECTIVE OF THIS STUDY WAS TWOFOLD: (1) TO DETERMINE CLINICALLY, IF A 50:50 MIXTURE OF PLA AND PGA CAN BE USED TO CONTAIN TCP IN OSSEOUS DEFECTS. (2) TO DETERMINE HISTOLOGICALLY IF THIS PLA/PGA COVERING WILL ACT AS A BARRIER TO EPITHELIAL MIGRATION IN SURGICALLY CREATED LESIONS ADJACENT TO TEETH.

APPROACH: (U) SEVEN DOGS WERE USED. THE ANATOMY OF THE MANDIBLE OF EACH DOG ALLOWED FOR THE CREATION OF FOUR EXPERIMENTAL AND TWO CONTROL SITES PER QUADRANT. DEFECTS WERE MADE 2MM WIDE AND 4MM DEEP ADJACENT TO A TOOTH. TWO DEFECTS WERE FILLED WITH TCP AND TWO DEFECTS WERE FILLED WITH TCP AND COVERED WITH THE MIXTURE OF PLA/PGA. ANIMALS WERE SACRIFICED TO OBTAIN SPECIMENS AT 1, 2, 4, 6, 8, 12, AND 16 WEEKS. THE SPECIMENS WILL BE PREPARED FOR HISTOLOGIC EVALUATION. THIS PROJECT WAS STARTED UNDER DA0H8037.

PROGRESS: (U) NONE.

DD FORM 1 MAY 66 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY	DA3C2903	01 OCT 83	REPORT CONTROL SYMBOL XO170
A. NEW	U	U	ML	A. WORK UNIT
PROGRAM ELEMENT: 62775A	PROJECT NUMBER: 3S162775A82D	TASK AREA NUMBER: AB	WORK UNIT NUMBER: 020
FORMER			
TECS, ONL STOG : 82/83-9.2/F ;			

(U) A METHOD OF FIXATION FOR THE REDUCTION OF MAXILLOMANDIBULAR FRACTURES

00??00 CLIN MEDICINE 003800 MED HOSP EQ 002400 BIOENGIN

START DATE	ESTIMATED COMPLETION DATE	FUNDING AGENCY	PERFORMANCE METHOD
MAY 83	JUN 84	DA	C. IN-HOUSE

	FISCAL YEAR	PROF. WORK YEARS	FUNDS (In thousands)
PRECEDING	1983	0.4	$ 29
CURRENT	1984	0.4	$ 55

F. CUM/TOT: $ 0

038670 11

RESPONSIBLE DOD ORGANIZATION
NAME: HORDC INSTITUTE OF DENTAL RSCH USAIDR
ADDRESS: WASHINGTON DC 20307
RESPONSIBLE INDIVIDUAL
NAME: SWEENEY, T P MD 20
TELEPHONE: 202-576-3484
F.I.C.A.
MILITARY

PERFORMING ORGANIZATION 038670 11
NAME: HORDC INSTITUTE OF DENTAL RSCH USAIDR
ADDRESS: WASHINGTON DC 20307
PRINCIPAL INVESTIGATOR
NAME: KOPPELMAN, E S DA
TELEPHONE: 415-561-2206
ASSOCIATE INVESTIGATORS
NAME:
NAME:

KEYWORDS: (U) INTERMAXILLARY FIXATION ;(U) BONDING AGENTS ;(U) ANCILLARY PERSONNEL ;(U) LAM IV

OBJECTIVE:(U) DEVELOP AN INTERMAXILLARY FIXATION TECHNIQUE THAT WILL SIMPLIFY AND EXPEDITE THE TREATMENT OF CASUALTIES WHO HAVE SUSTAINED MAXILLOFACIAL INJURIES. IN THIS MANNER, THE PROCEDURE WILL LESSEN THE CLINICAL BURDEN OF THE ORAL AND MAXILLOFACIAL SURGEON OR QUALIFIED DENTAL OFFICER SO THAT HE MIGHT BE AVAILABLE TO TREAT INJURIES OF FAR GREATER CONSEQUENCES.

APPROACH: (U) DESIGN OF A LUG-BRACKET PROTOTYPE WHICH WILL BE BONDED TO APPROPRIATE TEETH FOR THE PURPOSE OF FIXATING THE MAXILLA TO THE MANDIBLE. ESTABLISH WHICH BONDING AGENT, CYANOACRYLATES, ACRYLICS OR GLASS IONOMERS, WILL BE SUITABLE TO MEET THE CRITERIA AS ESTABLISHED IN THE PROTOCOL.

PROGRESS: (U) IN THE TIME PERIOD TO 8305 TO 8311, A LUG-BRACKET HAS BEEN DESIGNED ON A MACRO AND CLINICAL SCALE TO MEET NECESSARY PRACTICAL REQUIREMENTS. VARIOUS BONDING AGENTS, SUCH AS CYANOACRYLICS, ACRYLICS AND GLASS IONOMERS, HAVE BEEN TESTED IN AN IN VITRO ENVIRONMENT FOR THEIR RESPECTIVE BONDING STRENGTHS. AT THE PRESENT TIME, THE CYANOACRYLATES DEMONSTRATE TO BE THE BEST AGENT AVAILABLE. FURTHER IN VITRO INVESTIGATION WILL BE CARRIED OUT ON THE NEWLY DEVELOPED CYANOACRYLATES.

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				DA302804		01 OCT 83	REPORT CONTROL NUMBER Z01708
	A NEW	U	U		CX		A. WORK UNIT
16. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER	WORK UNIT NUMBER		
	62770A	3S162770A825		AB	023		
FORMER							
NEXT, OBJ, STOA	82/83-84/85						

(U) CLINICAL, RADIOGRAPHIC, AND HISTOLOGIC EVALUATION OF SERRATED CERAMIC TOOTH IMPLANTS

0801 BIOCHEMISTRY 0805 CLIN MEDICINE 0816 PHYSIOLO

OCT 83	CONT	DA	C. IN-HOUSE

	PRIOR YEARS	PROFESSIONAL MAN YEARS	PLANNED TOTAL
	1983	0.0	$ 0
	1984	0.2	$ 40

F. CUM/TOT: $ 0

035870	11	035870	11

MDRDC INSTITUTE OF DENTAL RSCH USAIDR

WASHINGTON DC 20307

SWEENEY, T P MD 20

202-576-3484

F.I.C.A.

MILITARY

MDRDC INSTITUTE OF DENTAL RSCH USAIDR

WASHINGTON DC 20307

ONEAL, R B DA

202-576-3383

GALAN, N J

(U) SERRATED ;(U) CERAMIC ;(U) TOOTH ;(U) IMPLANTS ;(U) RAM IV;(U) LAB ANIMALS ;(U) DOGS ;(U) MONKEYS

OBJECTIVE:(U) THE PURPOSE OF THIS RESEARCH PROPOSAL IS FOURFOLD. FIRST, IT IS TO EXAMINE THE EARLY HEALING AT THE TISSUE-IMPLANT INTERFACE THROUGH HISTOLOGIC EVALUATION. SECOND, TO DETERMINE IF EARLY HEALING CAN BE ENHANCED WITH PLACEMENT OF TRICALCIUM PHOSPHATE IN ANY VOIDS BETWEEN THE OSSEOUS SOCKET AND THE IMPLANT. THIRD, TO DETERMINE THE USEFULNESS OF A PLA:PGA BANDAGE OVER THE IMPLANT WAS ALSO EVALUATED. FINALLY, TO DETERMINE, USING HISTOLOGIC DATA, THE EARLIEST TIME THE SERRATED TOOTH ROOT CAN BE PLACED INTO FUNCTION.

APPROACH: (U) FOUR ALUMINA CERAMIC TOOTH IMPLANTS WERE PLACED IN EACH OF FOUR MACACA MULATTA MONKEYS IN FRESH EXTRACTION SOCKETS. THE FOUR IMPLANTS IN EACH MONKEY WERE PLACED IN A SIMILAR MANNER BUT EACH IMPLANT WAS TREATED IN THE FOLLOWING MANNER: (A) A PLAIN ROOT IMPLANT, (B) A ROOT IMPLANT WITH TCP FILLING ALL SERRATIONS AND VOIDS, (C) A ROOT IMPLANT WITH PLA:PGA BANDAGE, AND (D) A ROOT IMPLANT WITH TCP PLUS A PLA:PGA BANDAGE. IMPLANTS WERE PLACED SO THAT EACH ANIMAL WOULD REPRESENT A 30, 45, 60, AND 85 SPECIMEN. THIS PROJECT WAS STARTED UNDER DA0G8874.

PROGRESS: (U) NONE.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

DA302808 | 01 OCT 83 | REPORT CONTROL SYMBOL 201706

A. WORK UNIT

A. NEW | U | U | NL

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
PRIMARY	62775A	3S162775A825	AB	024

FORMER

MASS. OBJ. STDG : 12/83-0 2/8 :

(U) SURFACE PHENOMENON OF OPAQUE PORCELAIN SUSPENSIONS ON OXIDIZED METAL

008300 INORG CHEM | 003700 CHEM ENGR | 012700 PHYS CHE

OCT 83 | CONT | DA | C. IN-HOUSE

		PROFESSIONAL MAN YRS	FUNDS (In Thousands)
FISCAL YEAR	1983	0.0	$ 0
	1984	1.0	$ 20

F. CUM/TOT: $ 0

038870 | 11

038870 | 11

NAME: NDRDC INSTITUTE OF DENTAL RSCH USAIDR

ADDRESS: WASHINGTON DC 20307

RESPONSIBLE INDIVIDUAL

NAME: SWEENEY, T P

TELEPHONE: 202-576-3484

NO 20

NAME: NDRDC INSTITUTE OF DENTAL RSCH USAIDR

ADDRESS: WASHINGTON DC 20307

PRINCIPAL INVESTIGATOR

NAME: WOOLSEY, G D

TELEPHONE: 415-561-5740

DA

ASSOCIATE INVESTIGATORS

NAME: LORTON, L

F.I.C.A.

MILITARY

(U) MATERIELS ;(U) DENTAL MATERIALS ;(U) DENTAL PORCELAIN ;(U) OPAQUE PORCELAIN ;(U) RAM IV;

OBJECTIVE:(U) THE EASE OF MANIPULATION OF PORCELAIN AND METAL SYSTEMS IS OF PARAMOUNT IMPORTANCE IN THE MODERN MILITARY DENTAL LABORATORY. KNOWLEDGE OF THE HANDLING CHARACTERISTICS OF PORCELAIN OPAQUE SUSPENSIONS ON OXIDIZED METAL SURFACES CAN HASTEN THE FABRICATION TIME OF RESTORATIONS AND BENEFIT THE MILITARY DENTAL LABORATORY IN TRAINING AND UTILIZATION OF CONSTANTLY ROTATING PERSONNEL.

APPROACH: (U) FIVE PORCELAIN OPAQUE LIQUIDS WERE EVALUATED PHOTOGRAPHICALLY BE SESSILE DROP CONTACT ANGLE MEASUREMENTS ON FIVE BRANDS OF METAL. CONTACT ANGLE MEASUREMENTS WERE MADE ON BOTH SMOOTH AND SAND BLASTED METAL SURFACES AFTER AN EQUILIBRIUM PERIOD OF ONE MINUTE. THIS PROJECT WAS STARTED UNDER DA0G8033.

PROGRESS: (U) NONE.

DD FORM 1498M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY

1. AGENCY ACCESSION: DA OG 0717	2. DATE OF SUMMARY: 83 10 01	REPORT CONTROL SYMBOL: DD-DRAE(AR)636					
3. DATE PREV SUMMARY: 82 10 01	4. KIND OF SUMMARY: D. CHANGE	5. SUMMARY SCTY: U	6. WORK SECURITY: U	7. REGRADING:	8. HANDLING: NL	8a. SPECIFIC DATA - CONTRACTOR ACCESS: ☒ YES ☐ NO	9. LEVEL OF SUM: A. WORK UNIT

10. NO./CODES:	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER
a. PRIMARY	62734A	3M162734A875	AD	002
b. CONTRIBUTING				
c. CONTRIBUTING	///////////	STOC 82/83-6 2/4		

11. TITLE (Include with Security Classification Code): (U) Study of Saliva as a Diagnostic Tool for Presence of Lethal Agents

12. SCIENTIFIC AND TECHNOLOGICAL AREAS: 002300 Biochemistry 012600 Pharmacology - 012900 Physiology

13. START DATE	14. ESTIMATED COMPLETION DATE	15. FUNDING AGENCY	16. PERFORMANCE METHOD
79 10	CONT	DA	C. IN-HOUSE

17. CONTRACT/GRANT

a. DATE/EFFECTIVE:	EXPIRATION:
b. NUMBER:	
c. TYPE:	d. AMOUNT:
e. KIND OF AWARD:	f. CUM. AMT.

18. ESTIMATED RESOURCES

		a. PROFESSIONAL MAN YRS	b. FUNDS (In Thousands)
FISCAL YEAR	PRECEDING 83	1.2	113
	CURRENT 84	1.0	122

19a. RESPONSIBLE DOD ORGANIZATION

NAME: USA Institute of Dental Research

ADDRESS: Washington, DC 20307

RESPONSIBLE INDIVIDUAL

NAME: Sweeney, T.P.

TELEPHONE: 202 576-3484

21. GENERAL USE

20. PERFORMING ORGANIZATION

NAME: USA Institute of Dental Research

ADDRESS: Washington, DC 20307

PRINCIPAL INVESTIGATOR (Provide SSAN if U.S. Academic Institution)

NAME: Miller, R.A.

TELEPHONE: 202-923-4915

SOCIAL SECURITY ACCOUNT NUMBER: POC:DA

ASSOCIATE INVESTIGATOR

NAME: Setterstrom, J.A.

NAME:

22. KEYWORDS (Provide KEY-WORD Security Classification Code): (U) Salivary Amylase; (U) Nerve Agent; (U) Salivary Physiology; (U) Salivary Enzyme; (U) Laboratory Animal (Rhesus Monkey)

23. TECHNICAL OBJECTIVE. 24. APPROACH. 25. PROGRESS (Provide brief technical paragraphs identified by number. Precede each with security classification code.)

23. (U) To determine if saliva can be used as a diagnostic tool in evaluating the exposure of combat troops to chemical agents. To determine if constituents in saliva can be used to monitor the progress of therapy for chemical agent exposure. Develop a rapid, simplified field technique for diagnosis of chemical agent exposure in the combat soldier.

24. (U) Changes in saliva produced by chemical agents and prophylactic antidotes will be evaluated. The particular areas of study will be enzyme, nucleotide, and protein components. Possible methodology developed will be evaluated in the field and at the hospital level.

25. (U) (8210-8310) Previous work had suggested that variations in salivary amylase/total protein ratios may serve as the basis for the diagnosis of chemical agent exposure in the field. A new micro technique for the analysis of salivary cholinesterase has been developed. Salivary cholinesterase levels were determined for baseline and experimental salivary collections following exposure to the chemical agents and one of the prophylactic pretreatments. Work to date suggests that salivary cholinesterase may be useful for the diagnosis of nerve gas poisoning because organophosphates may be differentiated from the prophylactic levels of carbamates. Future work will examine enzyme levels of other agents and other carbamates as well as various combinations of each.

DD FORM 1498 PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE

PROJECT: 3S162775A825

WORK UNIT TITLE: A Study of Saliva as a Diagnostic Tool for Presence of Lethal Agents

PRINCIPAL INVESTIGATOR: Robert A. Miller

Study of Saliva as a Diagnostic Tool

for Presence of Lethal Agents

PROBLEM: One of the major concerns of the U. S. Army Medical Department is the survival of combat soldiers who have ben exposed to chemical agents. In order to provide proper medical therapy, rapid diagnosis of nerve agents must be made. Presently, clinical signs are the basis of diagnosis of chemical agents in the field. The objective of this study was to determine if a biological parameter could be identified in saliva which could serve as the basis of a non-invasive method for the diagnosis of nerve gas poisoning in the combat soldier.

APPROACH: Biological parameters will be identified by monitoring changes in salivary composition produced by the organophosphate DFP (diisopropyl-fluorphosphate) and the prophylactic carbamates pyridostigmine, physostigmine and Mobam. Rhesus monkeys will be exposed to the anticholinesterases because of the biochemical similarity of its saliva to that of man. The particular parameters of study will be salivary flow rate, protein and the enzymes: cholinesterase, kallikrein, lysozyme, and amylase.

RESULTS: Work to date indicates that variations in salivary cholinesterase may serve as the basis for the diagnosis of chemical agent exposure. A radio-metric technique has been developed for the analysis of salivary cholinesterase. Salivary cholinesterase levels were determined for baseline and experimental collections following exposure to DFP and physostigmine. The results indicate that cholinesterase levels in saliva reflect blood cholinesterase levels following exposure to the organophosphate DFP. On the other hand, salivary cholinesterase levels were increased rather than inhibited like the blood cholinesterase levels following exposure to the carbamate physostigmine. Both physostigmine and DFP decreased salivary levels. They also increased the salivary levels of total protein, amylase, and lysozyme, but not significantly. The cholinergic drug physostigmine increased salivary flow rate. The organophosphate (DFP) caused a decrease in the rate of salivation which is in disagreement with previously reported signs of organophosphate poisoning.

Implications for Medical Defense Against Chemical Agents.

One of the characteristic clinical signs of nerve gas poisoning is increased salivation; however, this was not evident following exposure to 3/5 LD_{50} dose of DFP. In fact, a decrease in flow rate was observed. This direct disagreement with previously reported characteristic signs of

organophosphate intoxication indirectly questions other reported signs of CW agent poisoning. Blood cholinesterase is the current clinical diagnostic procedure for organophosphate exposure. Findings to date suggest that using salivary cholinesterase for diagnosis of CW agent exposure is superior to the existng procedure because it can be used to differentiate organophosphate agents from the prophylactic carbamate pretreatment. In addition, a non-invasive technique can possibly be developed into a test strip for the soldier in the field.

USAIDR PUBLICATIONS

ABSTRACTS PRESENTED AT 1983 IADR MEETING

PUBLISHED IN THE JOURNAL OF DENTAL RESEARCH SPECIAL ISSUE A, 1983

G. L. Henley, J.C. Baumgartner*, annd J.R. Wynkoop: Cytochemical Localization of Acetylcholine Esterase and Catecholamines In Injured Pulps.

M.L. Bryant*, J.O. Hollinger, and W.M. Carpenter: Computer Assisted Cytologic Assessment.

J.R. Wynkoop, R.A. Miller, N.F. Dalessandro*, A. Yancey, C. Mason, and J. VonBredow: Kallikrein and Flow-Rate Differences in Rhesus Saliva During Anesthesia.

M.A. Derevjanik*, J.A. Setterstrom, and L.N. Booker: Evaluation of Sporicidin and Cidex Following Clinical In-Use Conditions.

J.O. Hollinger, S.L. Finley*, and S.A. Gee: A Histomorphometric Assessment of PGE_2 Effect on Bone In Vitro.

P.S. Grover*, and J.O. Hollinger: Quantitiative Assessment Comparing Scalpel and CO_2 laser Treatment of Soft Tissue Wounds.

J.R. Wynkoop, J.R. Heath*, R.A. Miller, N. Dalessandro, A. Yancey, and D. Mahon: Levels of Cyclic AMP in Rhesus Saliva After Anesthetic Injection.

G.L. Henley*, J.R. Wynkoop, and J.C. Baumgartner: Cytochemical Localization of Histamine and Dopamine in Injured Dental Pulps.

J.O. Hollinger: Histomorphometric Evaluation of Bone Healing at Endochondral and Intramembranous Sites.

J.R. Wynkoop, L. Kazyak*, R.A. Miller, and J.S. Harrington: Determination of Circulating Lidocaine Levels in Rabbits by GC/MS/DS.

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