

Outlook

Naval Medical Research and Development Command



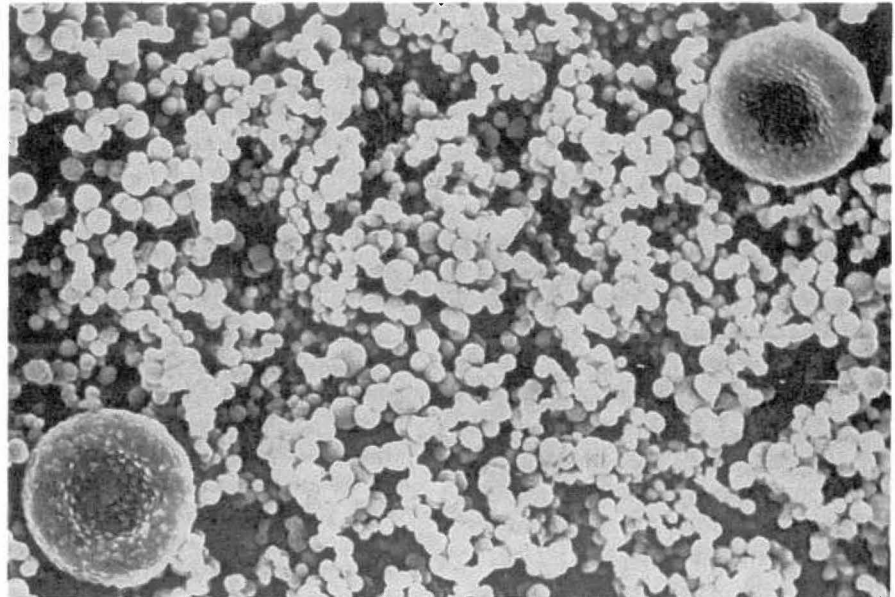
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Our mission is to provide timely solutions to Navy and Marine Corps medical and operational problems through biomedical research, development, test, and evaluation

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Scanning electronmicrograph (3000X) of liposome encapsulated hemoglobin (LEH) units and two human red blood cells.

NMRDC Review of the Navy's Blood Substitute Program

Liposome encapsulated hemoglobin (LEH), a promising blood substitute that closely mimics red blood cells, is being developed by a consortium of Navy, academic, and industrial scientists. LEH is an oxygen carrying resuscitation fluid made up of genetically engineered hemoglobin (oxygen carrying protein) encased in microscopic lipid droplets with walls similar to cell membranes. LEH can be prepared as a liquid or lyophilized (freeze-dried) product (see photo on page 3).

During September 1994 a panel of expert military and civilian scientists, clinicians and research administrators gathered at the Uniformed Services University of the Health Sciences to participate in a program review of the Navy's LEH research accomplishments. The panel was tasked to evaluate the current status of the program and to define what future course should be taken with regard to the Navy's goal of developing LEH. The panel

members considered LEH development in the context of supplementing or replacing blood in the field, for far forward casualties, during the golden hours of trauma and following bleeding injury. In particular, the Navy was interested in defining the remaining technical issues, the time-course for possible LEH product development, and the likelihood of achieving established goals and milestones.

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According to CAPT Sheila R. Weinberg, MSC, USN, from NMRDC, "The Navy has had long-standing requirements that document the need for blood products (red blood cells and platelets) and blood substitutes aboard ships and in the forward echelons of medical care for combat casualties. At this time, there is no satisfactory substitute for the oxygen-carrying red blood cells when treating severe hemorrhage. Fresh donated blood loses its usefulness rapidly unless refrigerated, requires crossmatching to minimize the ever present risk of transfusion reactions, and can transmit diseases such as hepatitis, malaria, and AIDS. LEH can be produced in virtually unlimited quantity, free from contamination by all disease causing organisms, has a longer shelf-life than fresh donated blood, and requires no crossmatching prior to administration."

Current research efforts focus on demonstrations of LEH efficacy (oxygen delivery), safety (immune response and vasoactivity), and the ability to manufacture the product on a large scale.

Alan S. Rudolph, Ph.D., the LEH Project Manager, pointed out in his opening remarks the specific goals of the program. "First is to define

the biological responses following the administration of LEH to a combat casualty; then to develop large scale manufacturing methods and finally, to conduct preclinical studies to collect data in support of a future Investigational New Drug (IND) filing with the FDA." He also pointed out the future needs to transition the technology and facilitate the clinical trials with a corporate partner by the turn of the century.

Operationally, the successful development of an artificial oxygen carrying resuscitative fluid would reduce the need for donated blood and reduce complications associated with blood banking (no histocompatibility antigens and elimination of transmitted infectious disease) and ease logistical burdens associated with blood delivery in the field.

Dr. Rudolph said, "LEH will not completely replace red blood cells. It is a temporary application of oxygen carrying fluid intended to stabilize victims with loss of blood that will be supplemented with already existing blood products. Blood substitutes, would provide a temporary delivery of oxygen for combat casualties during the golden hour following a bleeding injury. This would allow the transport of combat casualty victims back to

pre-positioned blood sources. The additives used to freeze-dry LEH allow for rapid reconstitution of the freeze-dried LEH and infusion of oxygen carrying fluids into hypovolemic casualties."

Recently researchers have developed a lyophilized form of liposome encapsulated hemoglobin (LyoLEH). LyoLEH has the additional advantages of an extended shelf-life and allows for large volume prepositioning at far forward echelons of medical care.

The panel report, delivered in October 1994, was very positive and supportive of the Navy's LEH program. The panel evaluated four major areas: manufacturing, safety, efficacy, and applicability of the program to the Navy's needs. In the report, it was noted that tremendous progress has been made over the past six years in developing a stable LEH formulation.

The report also noted that enough research data exists to clearly allow the Navy to move to the next phase of LEH research development. This would include working with a corporate partner to refine the LEH manufacturing technique and initiating pre-IND consultation with the FDA.

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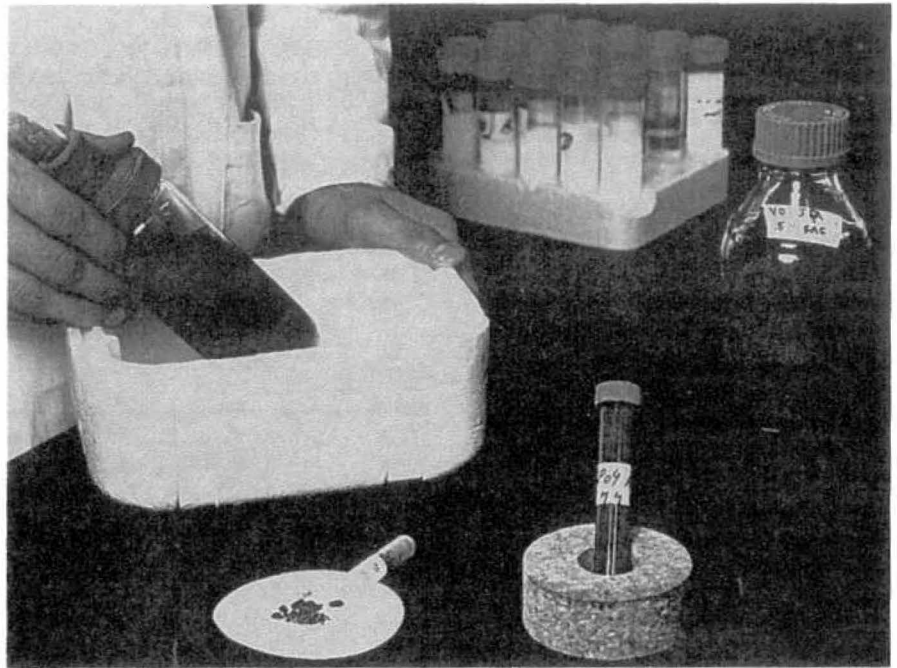
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The suggestions provided in the panel report will assist the Navy toward deployment of LEH for combat casualty care. NMRDC is in the process of coordinating a round table discussion with key managers of the program to implement the suggestions presented in the report.

NMRDC coordinated the program review with the assistance of Jack E. McKenzie, Ph.D., Associate Professor of Physiology, at the Uniformed Services University of the Health Sciences.

The panel members were Jack McKenzie, Ph.D., (Chairman); Thomas M.S. Chang, M.D., Ph.D., Director, Artificial Cells and Organ Research Centre, McGill University; Joseph Fratantoni, M.D., Director, Division of Hematology, Food and Drug Administration, Center for Biologics Evaluation and Research; Jack Goldstein, Ph.D. Cell Biochemistry Laboratory, New York Blood Center; George Nemo, Ph.D., Chief, Transfusion Medicine Branch, Division of Blood, Diseases and Resources, National Heart, Lung and Blood Institute, NIH; CAPT Bruce D. Rutherford, MSC, USN, Head, Navy Blood Program, Navy Bureau of Medicine and Surgery; and Pang Shek, Ph.D., Defense and Civil Institute of Environmental Medicine, University of Toronto, Ontario Canada.

Eight principal investigators presented their specific research component of the LEH program to the panel. Presenters were Alan Rudolph, Ph.D., Naval Research Laboratory; Reuven Rabinovici M.D., Thomas Jefferson University; William Phillips M.D., University of Texas; Janos Szebeni Ph.D., Walter Reed Army Institute of Research; Victor MacDonald Ph.D., Walter Reed Army Institute for Research; Florence Rollwagen Ph.D., Naval Medical Research Institute; Giora Feuerstein, Ph. D., SmithKline Beecham Pharmaceuticals; Crispin Eley, Ph.D., Vestar, Inc.



Working clockwise around the photo beginning with the hands holding the bottle in the styrofoam container - Technician freezing LEH in liquid nitrogen; liquid empty liposomes in test tubes; bottle of lyophilized LEH (Lyo-LEH); tube containing rehydrated LEH; and on the filter paper, Lyo-LEH powder.

NAVY UPWARD BOUND CADETS AND MATH/SCIENCE STUDENTS INTERN AT NHRC

by CAPT T. J. Contreras, MSC, USN, NHRC Executive Officer

For the third year, the Naval Health Research Center (NHRC) has participated in the Navy Upward Bound Program. Sponsored by the U.S. Department of Education, the Navy Upward Bound Program sponsors academically gifted high school students. The purpose of the program is to help students develop the skills and motivation necessary for success in college. Several NHRC investigators volunteered as mentors.

Tabian Cole mentored with Ms. Marcie Beckett, research physiologist on a project titled, "Validity of Navy Body Fat Estimation Among Racial Groups". Two students, Heriberto Oliver and Marcos Sisenando interned with Mr. Eddie Shaw and Mr. Jerry Pange, computer analysts, on the "Evaluation of the Performance of Transcutaneous Analyte Measurement Methods (TAMM)" project. LT

Luis Ramierz, research physiologist, mentored Naomi Woods studying the "Effects of Anti-Exposure Suits on Performance During Simulated Shipboard Damage Control Operations". Jerry Moreno was tutored by CDR Greg Gray, preventive medicine, with the assistance of ENS Debby Brummitt (TAD from MCSD), analyzing data for the study, "Unexplained Illness of Gulf War Veterans". LCDR Rick Shaffer, environmental health officer, with ENS John Lisky, worked with Jose Serrano in obtaining and analyzing data for the "Overuse Musculoskeletal Injury" Program. Finally, Dr. Robert Pozos, research physiologist, with a former Upward Bound student, Jershonda Hartsfield, deployed two students, Mike McMullen and Sergio Benitez, to obtain head and neck EMG data from male and female Navy pilots.

OCCUPATIONAL SAFETY: LABORATORY-ACQUIRED INFECTIONS

Kip Johnson, NMRDC Staff Asst. for Occupational Safety and Health/Safety Mgr -NMRI

It has been just over 100 years since microorganisms were first implicated as agents that cause disease. In the early days of microbiological research, a number of scientists who were pioneering studies in this new arena fell ill to the very diseases they were investigating. The first case of Q-fever in the U.S. was reported from a laboratory worker. Since the 1890's, more than 5000 cases of laboratory infections have been reported and at least 200 of these caused the death of the worker.

Although laboratory-acquired infections cases have decreased in recent years, many reports continue to surface from infections caused primarily from well-known and frequently handled microorganisms. Many others were reported from 'new' organisms that were not expected to cause disease (e.g. E. coli). It is expected that many more infections had occurred than were reported. All microbiological laboratory workers are exposed to various infections each day they report to work in the lab.

To those who say it can't happen to us, just this past summer an R&D laboratory worker was infected with malaria. Reports further show that senior 'highly-trained' laboratory personnel are twice as likely to become infected as their "novice" co-workers.

Laboratory workers learned early that a firm conviction to good laboratory practice is the key to laboratory safety. By utilizing safe practices with safe equipment, infections can be avoided. Tables 1, 2 and 3 are various surveys of laboratory-acquired infections (world-wide figures) where we can learn which agents cause most infections, how they are caused and what types of accidents preceded their infections.

Prevent Aerosols

Infectious airborne particles are released during many bacteriological procedures. Opening rubber stoppers, streaking culture plates, blending, homogenizing, vortexing, shaking and using ultrasonic cleaners on cultures will create aerosols. Besides being an obvious inhalation hazard, the particles will eventually settle out of the air and contaminate the working surfaces of the lab where workers

will come in contact with the agent. Consider limiting all operations that generate aerosols to the inside of biosafety cabinets.

Although rare, centrifuge accidents can infect a large number of people. Tubes or containers can break while rotating and their con-

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Centrifuges

Table 1
Laboratory-acquired infections (through 1989)
World-wide figures

Infection	No. of Infections	No. of Deaths
Brucellosis	428	5
Q-fever	280	1
Hepatitis *	271	3
Typhoid fever	258	20
Tularemia	225	2
Shigellosis	212	5
Tuberculosis **	194	4
Dermatomycosis	162	0
Venezuelan equine encephalitis	146	1
Psittacosis	116	10
Coccidioidomycosis	93	2

* most common laboratory infection in the U.S.
** has seen a great increase in the past 5 years

Table 2
Sources of Laboratory-acquired Infections
World-wide figures

	No.	%
Accident	703	18
Animal or ectoparasite	659	17
Clinical specimen	287	7
Discarded glassware	46	1
Human autopsy	75	2
Intentional infection	10	.5
Aerosol (known)	522	13
Working with agent	827	21
Others, unknown	783	20

NMRI SCIENTISTS DISCLOSE PROMISING MALARIA VACCINE RESULTS

Scientists from the Naval Medical Research Institute (NMRI), Bethesda, MD and a private biopharmaceutical firm disclosed the results of research that may lead to a new vaccine to combat malaria.

The vaccine belongs to a new class of naked DNA vaccines that consist of highly purified strands of genetic material (DNA) that instruct cells to make antigenic proteins. The immunity generated by this approach can eliminate cells infected with the pathogen, in addition to destroying the pathogen itself. Naked DNA vaccines previously have been shown effective in animal models of influenza, herpes and rabies virus infections. This report is the first demonstration of the effective use of naked DNA immunization in a parasitic disease

(*Proc. Natl. Acad. Sci. USA* Vol. 91, pp. 9866-9870, October 1994, Immunology).

The researchers reported that mice injected with the naked DNA vaccine encoding a protein from the malaria parasite induced high levels of specific antibodies and cytotoxic T lymphocytes. This immune response protected over 80 percent of the mice from subsequent challenge with a highly infectious dose of parasites.

"Immunization with naked DNA induces protective cellular immune

responses superior to those induced by all other synthetic and recombinant anti-malaria vaccine we have tested," said CAPT Stephen L. Hoffman, MC, USN, director of NMRI's Malaria Program. "This new technology may allow us to construct the multivalent, highly immunogenic vaccines that we believe will be required for optimal protection against malaria. These data constitute an important first step, although we have much work ahead of us before testing this approach in man."

LABORATORY-ACQUIRED INFECTIONS Cont from page 4

tents will be dispersed throughout the laboratory. We can prevent these aerosols by using sealed rotors or sealed buckets (safety caps).

Pipettes

If mishandled, pipettes may pierce the skin of the operator. Don't "blow" the last drop out the tip of the pipette as this will create thousands of droplets that will likely be inhaled. Some researchers may still be tempted to mouth pipette when in a hurry. The cotton plug will not keep out the liquid. Place contaminated pipettes in proper sized decontamination baths, don't overcrowd. Consider using plastic vs. glass pipettes.

Contaminated Containers

Every time we transfer samples to a different container, we risk the possibility of contaminating the outside of the new and old container. Collection, packaging, transport and unpacking of infectious agents must be strictly regulated by properly trained laboratory personnel. Care must be given to transport infectious items in strong, spill-proof containers.

Personal Protective Equipment

The primary mode of transmission of hepatitis to the laboratory worker is via hand contact from infected/contaminated material. Often, these infections were through inapparent cuts and

abrasions in the skin. Simply using latex gloves and frequent hand washing with bacteriocidal soap would prevent over half of these infections. Goggles, face shields and gowns must be used if splashing is expected.

Needlesticks

Over 25% of all infections can be traced to skin punctures from infected needles. Most needlesticks occur in the act of recapping. If we must recap, use the one hand "scoop" method or use tongs to hold the cap. Use vacutainers vs. syringes for venipuncture. If you can use a needleless system (especially for IV piggybacks) use it. If you do get stuck, clean the wound with soap and water.

Experience has demonstrated the credence of biosafety practices, procedures and facilities in the prevention of laboratory-acquired infections. Strict adherence to these recommendations will contribute to a healthier and safe work environment for laboratory workers, their commands and the surrounding community. More specific guidelines can be found in the HHS publication No. (COC)93-8395. Biosafety in Microbiological and Biomedical Laboratories May 1993, and the third edition of Laboratory - acquired infections, by C. H. Collins, 1993.

Table 3
Types of Mishaps Preceding Infections
world-wide figures

Mishap	No.	%
Spills/splashes	188	27
Needle and Syringe	177	25
Sharp objects, broken glass	112	16
Bite or scratch from animal	95	13.5
Aspiration through pipette	92	13
Other/unknown	39	5.5

NMRDC's DEFENSE WOMEN'S HEALTH RESEARCH PROGRAM

The changing demographic character of the military with the increasing proportion of women in non-traditional ratings and assignment to combat roles raises questions concerning the impact of such jobs on women's health, the mechanisms employed by women to cope with new occupational demands, and the requirements for Navy medicine to provide care to women engaged in the full spectrum of occupational sites and situations. NMRDC is actively involved in research concerning database development, health surveillance, epidemiologic studies, and studies of specific health issues related to military service (background information OUTLOOK August 94, pg. 5).

Women Aboard Navy Ships: A Comprehensive Health And Readiness Project

Principal Investigator: Frank C. Garland, Ph.D.
Naval Health Research Center, San Diego, CA

This is the cornerstone project of the Navy's efforts to assess the needs and availability of health care for military women. This study is a comprehensive, integrated health assessment of women aboard ship focusing on (1) shipboard occurrence of illnesses and injuries, (2) subject-reported conditions, diseases, injuries, and exposure to occupational hazards, (3) health care utilization, (4) health promotion services and lifestyle factors, (5) risk factors for reproductive health problems (6) interviews with shipboard health care providers, and (7) the development of an integrated, relational database. All research questions and questionnaires will be developed in coordination with appropriate personnel at BUMED and BUPERS, CINCLANTFLT and CINCPACFLT Fleet Surgeons and Force Medical Officers. Initially, 1,000 women aboard ship and matched comparison groups of 1,000 women ashore and 1,000 men aboard ship will be selected for detailed study. The techniques and instruments developed from the initial study will be expanded to cover all women assigned to ships and other deployed women. The data collected will assist BUMED and fleet decision-makers in several ways. The data will help define the personnel, resources, and training required to meet the medical needs of women aboard Navy ships. The results of this study will help to advance the operational objective of maintaining maximal readiness of the entire crew.

The Health Status of Women in the Military: An Epidemiological Study of Active Duty Navy and Marine Corps Personnel

Principal Investigator Rebecca Calderon, Ph.D., M.P.H.
Naval Health Research Center, San Diego, CA

The purpose of this study is to conduct a large-scale military self-report health questionnaire that includes cardiovascular (blood pressure, heart rate) and physical measurements (height, weight, skinfolds) of Navy and Marine Corps active duty women. The results of this study (designed for tri-service utilization) will transition to the operational forces and provide information on women's health problems, risk factors and health care needs and practices in the following general areas: reproductive, medical/nutritional, psychosocial, lifestyle, occupational/environmental, and health services. Results will also be used to identify appropriate populations for subsequent studies needed to address specific health issues.

Hospitalization Rates for Military Women: Feasibility and Design of a Tri-Service Relational Database Architecture Allowing Service-Specific and Tri-Service Reporting

Principal Investigator: Frank C. Garland, Ph.D.
Naval Health Research Center, San Diego, CA

This project will determine the feasibility of and specifications

for a common Navy, Marine Corps, Air Force, and Army relational database architecture and interface to allow service-specific and tri-service reporting of hospitalization rates of disease and injury in women serving in the military. Hospitalization rates will be determined according to occupation, paygrade, duty station assignment, and other military-relevant variables and it will allow comparative studies by gender, branch of service, and national hospitalization rates. The tri-service relational database architecture will build on the data architecture developed and currently in use by the Navy. This architecture will be designed to support sharing of data in a timely manner, while maintaining service-specific, geographically separated databases, controlled by each service.

The Epidemiology of Illness, Injury and Attrition Among Select U.S. Military Training Female Populations

Principal Investigator: LCDR Richard A. Shaffer, MSC, USN
Naval Health Research Center, San Diego, CA

The goal of this study is to collect real-time data regarding illness and injury in military women during training. Researchers will use a computer-based tracking system to establish rates and risk factors in subject training populations. The software features a user-friendly menu-driven format, electronic mail, and specific ICD-9 codes for illnesses and injuries. Data will be collected at three training sites (Naval Training Center, Great Lakes, IL; MCRD Parris Island, SC; Officer Candidate School, Quantico, VA) focusing on female enlisted Marine recruits and officer candidates and all female Navy enlisted recruits. The information will quantify the impact of women's health issues on attrition, training costs, and operational readiness. Research results will target areas for preventive interventions and provide a mechanism to test the effectiveness of the interventions.

Gender Differences in Emergency Shipboard Damage Control Task Performance: Human Factors Solutions

Principal Investigator: CDR Edward J. Marciniak, MSC, USN
Naval Medical Research Institute, Bethesda, MD

All personnel assigned aboard U.S. Navy ships must be fully capable of performing sustained emergency damage-control tasks. The approach of this study is to modify the demands of the tasks by either redesigning the equipment, modifying procedures, or using mechanical aids. Researchers will observe 100 active duty men and women performing a set of representative emergency shipboard damage-control tasks, analyze and modify the tasks to reduce the physical demands, measure physical and damage-control task performance, and compare performance before and after the ergonomic intervention. Products resulting from this research will optimize shipboard operational readiness, safety, and worker productivity.

Performance-based Occupational Strength Testing for Candidate Navy Pilots/Naval Flight Officers

Principal Investigator: LCDR T. L. Pokorski, MSC, USN
Naval Aerospace Medical Research Laboratory, Pensacola, FL

Successful operation of an aircraft is critical to completing mission requirements as well as to the safety of aircrew and equipment. In this study researchers will identify appropriate strength requirements needed to safely perform duties in all naval aircraft (by type and mission) that will be in the inventory beyond the year 2000. Performance requirements will incorporate instantaneous strength; sustained strength; and endurance for routine, emergency and survival situations (i.e., high G maneuvers, manual landing gear extension, ejection seat actuation, manual opening and closing of hatches and canopies). Once requirements are identified, occupational performance tests and strength test batteries will be developed, validated and established as strength performance standards. When this study is completed, a screening device and physical training program will be delivered to the Commanding Officer, Naval Aviation Schools Command, and an Occupational Standards Strength Test Battery will be delivered to Chief, Naval Education and Training.

Countermeasures to Heat Stress in Females

Principal Investigator: Robert S. Pozos, Ph.D.
Naval Health Research Center, San Diego, CA.

High-heat environments impair work performance and can compromise combat mission success. To decrease the incidence of heat stress and increase performance capability, microcooling countermeasures have been developed for personnel working in encapsulated garments (i.e. chemical, biological, radiological ensembles and firefighting ensembles). This study will generate a new database regarding gender differences pertaining to these countermeasures by determining the effectiveness of existing microclimate cooling systems (MCS) (a whole-body water-cooled system, a vest air-cooled system, and a vest phase-change material system). This data will serve as a basis for development or modification of a MCS to be used in a mixed-gender population. Results of this project will be reported to Office of Naval Research, Bureau of Medicine and Surgery, and to DoD Warfare platforms.

The Impact of Health Care Perception on Women's Health

Principal Investigator: Lex L. Merrill, Ph.D.
Naval Health Research Center, San Diego, CA

Women's health care perceptions and the perceptions of their health care providers may affect women's health. To determine the impact of perceptions on women's health, variables related to their health, health care facilities, interactions with health care provider (physicians, physician's assistants, and independent duty corpsmen), and patient satisfaction during visits to health care facilities aboard ships will be evaluated. Women's subjective perceptions will be combined with their medical histories and the health care provider's perceptions and assessments to create recommendations for enhanced health care delivery.

Assessment and Intervention for the Reduction of Adverse Gynecologic and Obstetric Clinical Events in Women Aboard Ship

Principal Investigator: CAPT Stephanie K. Brodine, MC, USN
Naval Health Research Center, San Diego, CA

Reproductive health problems, sexually transmitted diseases (STD), or unplanned pregnancies among active duty women aboard ship adversely impact combat readiness. Women who are identified as pregnant while on a prolonged deployment such as a Western Pacific deployment, must be evacuated to CONUS. This results in personnel loss, reassignment and costly evacuations. Using a multidisciplinary approach, researchers will define the demographic, biopsychosocial, behavioral, health and situational concerns leading to reproductive health problems, STD, or unplanned pregnancies. Surveys will be conducted with focus groups in the target population, with key medical personnel, and with ship-based line personnel. The data from this study will establish the groundwork for the development of effective prevention strategies such as slide presentations, interactive educational games, group discussions and videos.

Neck and Back Strain Profiles of Rotary-Wing Female Pilots

Principal Investigator: Robert S. Pozos Ph.D.
Naval Health Research Center, San Diego, CA

The number of women entering naval aviation is at an all-time high and a majority will be assigned to helicopter squadrons. With the increasing number of female pilots participating in rotary-wing operations there is a need to study how female pilots respond to the stressful helicopter environment. Researchers will develop a database of normal neck and back fatigue profiles of women focusing on the effects of cockpit ergonomics, helmet design, peripherals on the helmet, vibration and fatigue leading to soft tissue injury. The database will assist in the formulation of methodologies to minimize neck and back strain that may lead to long-term soft tissue injuries in female rotary-wing pilots.

Use of Noninvasive Bone Structural Measurements to Evaluate Stress Fractures Among Female Recruits in USMC Basic Training

Principal Investigator: LCDR, Richard A. Shaffer, MSC, USN
Naval Health Research Center, San Diego, CA

Military personnel subject to physical fitness standards are prone to suffer musculoskeletal overuse injuries. These problems are amplified in recruit and training populations when strenuous activity is dramatically increased. These injuries often result in lost training time, failure to complete training, increased training costs, and decreased operational readiness. This study will develop predictive models of stress fractures and other overuse injuries seen in female military trainees at MCRD Parris Island, SC by using noninvasive measurements of bone structure using a commercial bone mineral scanning system. Scanning data are to be coordinated with epidemiological data to plan preventative strategies for overuse injuries among Navy and Marine Corps personnel. This will allow military training staffs to develop training regimens that attain the desired operational readiness with a minimum impact from these problems.

ANIMAL BYTES

by LTC Jack Bley, U.S. Army Veterinary Corps, Special Assistant for Veterinary Medicine, Naval Medical Research and Development Command

The view from the eleventh floor of the Navy Bethesda tower is spectacular. As I try to overcome first-time-writer's-block and put something worthwhile and coherent on the screen, my eyes and mind are wandering off through a north-facing window to the woods below and to the horizon in and around Rock Creek Park. Lady Fall has taken out her paintbrush and drops of paint can be seen in the red and yellow splashes of the earlier-changing maples and poplars. It can only get better.

I wish I could say the same for the business of using animals in biomedical research; things just seem to be getting worse for all of us who have relied upon animal models to study the human condition. Seems like every month there is another major attack against animal-related research, and those of us who do that research. Instead of doing bench work, we must take valuable time to answer our critics.

I recently sent out a packet to every one of the Navy labs care of your local veterinarian. The packet included several items that (of course) require your immediate attention. Most important is the **FY 1994 data call for the Annual DoD Report of Animal Use to Congress**. The House Armed Services Committee was "disappointed" with last year's effort, so this year we have changed the format slightly. In addition you will see that you must provide a synopsis in the NIH CRISP-type format of each of your protocols so that these can be made available over the so-called "information super-highway" to any "concerned constituents".

The final version of the **DoD IG's Phase 2 "Review of the Use of Animals in Department of Defense Research Facilities"** has also been sent to each lab. Take a few minutes and read the recommendations of this program evalua-

tion. This is a good report; the authors have done a superior job of capturing the vast amount of data and the many sources of that data into a readable and fair appraisal of our laboratories. If you have not seen the Phase 1 review, ask your vet for a copy. In my cover letter accompanying this quarter's information/action packet I have summarized all of the recommendations that the IG has made.

These IG recommendations will be incorporated into the latest version of **DoD Directive 3216.1 "The Use of Animals in DoD Programs"**, a draft of which has also been distributed. You will be seeing this again soon when it becomes the implementing SEC-NAVINST.

All DoD-conducted or DoD-sponsored animal research will now use a **standard DoD protocol format**. That too has been sent to your labs. Much work and discussion has gone into creating this protocol format, and on behalf of the Joint Technical Working Group that developed the format, I must thank everyone who sent suggestions for consideration. This is it folks; everyone will now be singing off of the same sheet of music. I am available for answering any questions or concerns regarding the format, but don't call to complain; it's a done deal.

Now a word about your **Institutional Animal Care and Use Committees** (IACUC's). According to the Animal Welfare Act (AWA) each IACUC, as the agent of the Director of the research facility, has the final word on the animal research conducted at its facility. A requirement for additional oversight or centralized review is not in the AWA. We have been doing that in the DoD as an additional safeguard because we are very sensitive to public perception and pressure, for good or bad. As long as I am in this office, I will expect that all studies in which nonhuman primates, dogs, cats,

and marine mammals, or any potentially controversial studies (i.e. unrelieved pain in any species) will be sent here for a final review. This does not remove the responsibilities from the IACUC's, nor does it imply that the IACUC's are not trusted. This is primarily an "administrative" review to assure that the protocol format has been properly used.

For this **minimal oversight** to be a success your IACUC's must be just as good as I have maintained that they are. To assure that is the case, Principal Investigators must demand that the IACUC's ask the tough questions, have the highest expectations of every investigator in the lab, and follow through on all incidents and concerns. I strongly believe that we can continue to self-regulate and that we are already doing an outstanding job of "minding our own business", but remember that there are folks out there who would love to see us fail at this. There are those who will not be satisfied until there are more bloodhounds on our heels, or watchdogs such as the "ombudsman" and the "11-member panel of biomedical experts and animal experts to investigate the animal use and care programs of the DoD" as called for in the recently proposed legislation (HR 4971) by Representative Robert Toricelli of New Jersey. More on this later.

Further guidance will be forthcoming on the proper function and constitution of your IACUC's. Refer to the AWA or the OPRR Guide for help if you are not sure. In the meantime you have enough to keep you busy and to keep ahead of those hounds. I am proud to be running with you; I'm proud of our product and of the great folks who are producing. Thanks for letting this Army vet be a member of the Navy biomedical research team.

UPDATE FROM THE NAVAL MEDICAL RESEARCH UNIT NO. 3

Change of Command at the Naval Medical Research Unit No. 3

CAPT Alfred J. Mateczun, Jr. relieved CAPT Richard G. Hibbs, Jr. as Commanding Officer of Naval Medical Research Unit No. 3, Cairo Egypt on 15 September 1994. The guest speaker was Navy Surgeon General VADM Donald F. Hagen. Other distinguished speakers included the Honorable Edward Walker, American Ambassador to Egypt, Dr. Ali Abdel Fattah, Egypt's Minister of Health and, CAPT Thomas N. Jones, Commanding Officer of NMRDC.

CAPT Mateczun reported aboard from Naval Aerospace Medical Research Laboratory, Pensacola where he served as Commanding Officer. CAPT Hibbs has been assigned as Executive Officer, NMRDC where he will continue his involvement with Navy medical research and development.

"Sailor of the Quarter" 3rd Quarter 1994

HM1 Mary E. Fisetle was selected as NAMRU-3 Sailor of the Quarter for the 3rd Quarter 1994. HM1 Fisetle reported on board January of 1993. As an Advanced Laboratory Technician she was assigned to Research Sciences. Among her duties she has been the supervisor of the Clinical Laboratory and has participated in field studies.

Due to personnel shortages HM1 Fisetle is currently the Head of the Military Personnel Branch and has done much in the way of customer service. Her many contributions in this area ensured that this summer's major turnover of more than 20 military personnel and their dependents was managed with optimum efficiency. HM1 Fisetle is

also involved in various command and community activities and volunteered to take charge of the Color Guard for the recent Change of Command.

BRAVO ZULU to HM1 Fisetle!

NAMRU-3 Supports Military Operations

NAMRU-3 was asked by U.S. Naval Central Command to provide vector serology surveillance in support of a Medical/Dental Civic Action Project (MED/DEN CAP) conducted in the Duqm region of Oman as part of the exercise Sea Soldier IX.

LT Steven Presley and LT Eric Hall, responded and deployed to U.S. NAVCENTCOM, Bahrain.

Working with Amphibious Squadron Three and the Marine Expeditionary Unit, MSSG-15 of the First FSSG, LT Presley and LT Hall conducted surveillance and screening of vector borne infectious diseases including chloroquine resistant malaria, leishmaniasis, tick-borne arboviruses and indigenous mammalian infectious disease reservoirs.

Serum samples were collected from the indigenous population and over 200 ticks from central coastal and southern coastal Oman were collected for further analysis.

NAMRU-3 also responded to the Commander Amphibious Task Force Surgeon in providing antivenom for indigenous venomous snakes in the area of operations.

THE NAVAL MEDICAL RESEARCH INSTITUTE DETACHMENT BROOKS AIR FORCE BASE

**The Naval Medical Research Institute Detachment
(NMRIDet Brooks) Brooks Air Force Base officially stood up
1 October 1994.**

CAPT Robert G. Walter, DC, USN, Commanding Officer of the Naval Medical Research Institute took command of the detachment at a commissioning ceremony 28 October 1994 at Brooks Air Force Base. On hand for the activities were CAPT Thomas N. Jones, MSC, USN, Commanding Officer of NMRDC; Brig. Gen. Robert Belihar, Commander of Human Systems Center; and Col. Boyd Campbell, Commander, Army Medical Microwave Bioeffects Branch.

Established with existing assets from the Naval Aerospace Medical Research Laboratory in Pensacola, FL, NMRIDet Brooks is the culmination of efforts begun in 1991 as a result of the DoD Base Closure and Realignment Report (Project Reliance). This effort supports the collocation of the Army Medical Microwave Bioeffects Program, the Navy Electromagnetic Radiation Program and the Army and Navy Laser Bioeffects Programs.

The new detachment's primary mission is to conduct research, development, testing and evaluation on the biomedical effects of electromagnetic radiation to enhance the health, safety and readiness of Navy and Marine Corps personnel. Under the triservice program the detachment will share information with the other services. With the collocated laboratories, the DoD can downsize and yet maintain a "critical mass" of researchers to collaborate on the collection of scientific and technical data.

Areas of research to be addressed by the detachment include providing service members and workers with a safe work environment, the performance and survival of armed forces in hostile environments, and the commitment of environmental responsibility to communities that house military installations.

NOTES FROM COUNSEL

By A. David Spevack, NMRDC Intellectual Property Counsel

Limited Cooperative Research and Development Agreed for Transferring Biological Materials

After many promises and several years of stop-gap measures, the Chief of Naval Research has approved a limited purpose cooperative research and development agreement referred to as an MTA for the transfer of biological materials. MTAs are used to transfer biological materials from the Navy to a non-Federal party and from a non-Federal party to the NAVY. Researchers must use MTAs. Any material, including biological materials, created by Government employees or contractors, with the use of Government funds, belongs to the Government and is considered Government property. Biological materials created by non-Federal parties are the property of that party. There are laws having severe penalties for giving away Government property without permission. There are also laws controlling accepting "gifts" on behalf of the Government.

The MTAs are the only approved means of making an exchange of a biological material with a non-Federal party. The text of the MTAs cannot be changed without prior approval of the Chief of Naval Research.

NMRDC will issue an instruction delegating signature authority to the Commanding Officers of NMRI, NDRI, NAMRU-2 and NAMRU-3, because these commands are the principle users and developers of biological materials. Principal Investigators do not have authority to sign an MTA on their own.

A model Memorandum of Understanding (MOU) for exchange of biological materials between Federal laboratories will also be included with the instruction. This special MOU is used to transfer biological material from one Federal party to another Federal party (CRADAs are used only between a Federal party and a non-

Federal party). The MOU can be modified at the laboratory level, if conditions require, with prior approval from the NMRDC Office of Counsel.

Use of the MTA is simple

When a researcher wants a biological material from a non-Federal party: (1) the researcher fills out the MTA stating what is wanted and what purpose it will be used for, (2) the MTA is signed by CO of the Command if authorized by direction, or, if not, the MTA is referred to the NMRDC Office of Counsel, (3) the researcher sends a letter of request and the original MTA to the "owner" of the biologi-

cal material. If there are questions or problems call the NMRDC Office of Counsel.

If a researcher receives a request from a non-Federal party for transferring a biological material, the researcher should determine if the Navy wants to provide the material; if yes, refer the requestor to NMRDC Counsel for information on an MTA; after receiving a signed MTA from the non-Federal party, the NMRDC researcher can send the biological materials.

The MOU is used in a similar manner between Federal agencies. In all cases, send Office of Counsel a copy or the original of the signed agreement.

LEGAL TOOLS FOR WORK

FAR, CRADA, MOU, MOA, Cooperative Agreements, Grants, a veritable alphabet soup of confusing legal tools. Some can be used to assist research and some can't. Lets look at what the alphabet soup stands for and how we use them.

An **MOU/MOA** is a Memorandum of Understanding or Agreement. This has no statutory basis and is as enforceable as a hand shake. It should be used **ONLY** between Federal government agencies to define and clarify work. It is illegal to transfer materials, money or anything else to a non-Federal party by an MOU/MOA.

There are only four legal means of interacting with non-Federal parties. These are (1) FAR contracts, (2) Grants, (3) Cooperative Agreements, and (4) Cooperative Research and Development Agreements (CRADA).

FAR contract means a contract for goods or services, including research, written under the Federal Acquisition Regulations. A FAR contract must be signed by a Contracting Officer who has a warrant to bind the United States Government up to a certain amount of money. This is the only means the Government has for acquiring goods and services. Equipment can be loaned to a contractor if provision is made in the contract. There is not supposed to be any supervisory responsibility to the Government except for approval of the goods or services meeting the work statement or performance specifications.

A **Grant** is a formal agreement under which a certain amount of money is given to a performer to do certain work and publish. The Government gets nothing

except satisfaction of assisting in increasing the body of knowledge and has only a small amount of control (mostly fiscal) over the conduct of the research.

A **Cooperative Agreement** is a new instrument having some of the aspects of a Grant and some aspects possible only under a CRADA. It is an instrument by which the Government provides funds to a non-Federal party with plans for cooperation and collaboration between a non-Federal performer and a Federal performer to accomplish the work.

A **Cooperative Research and Development Agreement** is a special type of agreement provided by Congress to advance technology transfer. A CRADA is not bound by FAR and can truly be negotiated. The CRADAs must be approved (or pre-approved under certain conditions) by the Chief of Naval Research. Under a CRADA a Federal Laboratory can, "accept, retain, and use funds, personnel, services, and property from collaborating parties and provide personnel, services, and property to collaborating parties". The CRADA statute is one of the few means of accepting money for a particular project. The CRADA statute also provides language that allows the protection of trade secrets and exchange of intellectual property.

This is a highly useful research tool. If you have any question about which legal tool to be used in your situation, CALL COUNSEL.

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HIGHLIGHTS OF NMRDC RESEARCH

RESEARCHERS STUDY THE BIOMECHANICAL FACTORS OF OVERUSE INJURY DURING NAVAL SPECIAL WARFARE (NAVSPECWAR) TRAINING

NAVSPECWAR personnel are subject to physically demanding tasks during military training, exercises and operations which result in a high incidence of overuse injuries. These cause unnecessary morbidity, protracted recovery periods and decreased readiness. Researchers at the Naval Health Research Center, San Diego, CA are currently studying the biomechanical factors (i.e. ground reaction force patterns, quantification of shock wave transmission, foot pressure distribution, and bilateral motion analysis) related to the development of overuse injuries. Study results will be used to develop a model to predict specific overuse injuries. Also, the information will be used to develop screening programs, and prevention and rehabilitation strategies that will be implemented by medical care providers, the Military Entrance Processing Command and the training commands. The study was requested by the offices of the Commander, Naval Special Warfare Command; the Chief, Bureau of Personnel; and the Chief, Bureau of Medicine and Surgery.

ENTOMOLOGICAL AND RIFT VALLEY FEVER SURVEILLANCE SUPPORT TO OPERATION BRIGHT STAR 94

Operation BRIGHT STAR is a biennial joint military exercise in Egypt involving U.S. and Egyptian forces. Troops perform maneuvers and cross-training exercises at remote sites under field and simulated combat conditions. As a result, troops are at increased risk of exposure to biting arthropods and arthropod-borne diseases (i.e. Rift Valley fever, West Nile fever, malaria, leishmaniasis and filariasis), as well as encounters with snakes, scorpions and spiders. The U.S. Naval Medical Research Unit No. 3 (NAMRU-3) in Cairo, Egypt historically assists in disease and vector surveillance support and as a reference resource to BRIGHT STAR operations. During the 1994 exercise NAMRU-3 field teams collected nearly 1,000 mosquitoes during 126 trap-nights. *Culex pipiens* was the most prevalent species collected, accounting for more than 87%, while *Culex perexiguus* and *Aedes caspius*, accounted for 3.6% and 7.9% respectively. Two potential malaria vectors, *Anopheles pharoensis* and *Anopheles multicolor*, accounted for 0.3% and 0.7%, respectively. Additionally, 490 U.S. troops were enrolled in an oral diagnostic protocol to assess their exposure to Rift Valley fever. Neither the virological screening of collected mosquitoes, nor salivary screening efforts resulted in detection of Rift Valley fever virus. Professional and technical support provided by NAMRU-3 during BRIGHT STAR 94 is yet another indicator of how extremely valuable military overseas research laboratories are in supporting deployed troops.

MEDTAG MOVES FORWARD IN DEVELOPMENT

Field corpsmen must document patient status and treatment at forward echelons of care to maintain continuity of care during combat and to facilitate follow-on care when the patient is evacuated. Field testing of MEDTAG, a prototype electronic battlefield medical data collection device, demonstrated its operational effectiveness during exercises at Fleet Marine Force Training, Field Medical Services School, Camp Pendleton, CA. Now, MEDTAG is being enhanced to interface with the Multi-Technology Automated Reader Card (MARC) being evaluated by OSDA(HA) for the Theater Medical Information System (TMIS). Using recent advances in electronic data storage technology, researchers at the Naval Health Research Center, San Diego, CA are evaluating and planning for several additional enhancements. These include the feasibility of providing expert decision support for personnel at the first and second echelons of care, automating the capture of physiologic information using voice-activated data entry, increasing the efficiency of the machine-user interface, and assessing equipment reliability.

DEVELOPMENT OF HEPATITIS E VIRUS VACCINES (Epidemiology and Immunology of Hepatitis E)

Hepatitis E Virus (HEV) has been identified as a major military disease threat. Although the epidemiology of HEV has yet to be fully described, HEV infections apparently mirror Hepatitis A Virus (HAV) infection relative to transmission determinants. Fecal/oral transmission via contaminated water sources seems the most likely mode of spread. Evidence from outbreaks in countries like Indonesia, where hundreds of people have been afflicted at the same time, highlights the importance of HEV as an infectious disease that has the potential to impact a large number of people (such as deployed military units) at a single time and from a single source. While a vaccine to prevent HAV infection is now available, there is currently no vaccine or specific treatment for HEV. Researchers from the Naval Medical Research Unit No. 2 (NAMRU-2), Jakarta have recently completed a comprehensive two year follow-up investigation of an HEV outbreak in West Kalimantan, Indonesia. The research findings included: household clustering of anti-HEV positives; a significant increase in cross-sectional prevalence of anti-HEV positivity with increasing age; and a positive association with the use of river water for drinking/cooking, bathing, or human waste disposal and serological evidence of infection. The results of the Kalimantan investigation suggest HEV endemicity with possible reservoir maintenance in human and/or animal populations. The area investigated may prove ideal in describing the natural history of HEV and as a future site for candidate vaccine trials.