CLINICAL INVESTIGATION

ANNUAL PROGRESS REPORT

30 JUNE 1968

MADIGAN GENERAL HOSPITAL

TACOMA, WASHINGTON 98431

AD _____

RCS MEDDH - 288 (R1)

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT REPORT ANNUAL REPORT FY 68

RESEARCH AND DEVELOPMENT
MADIGAN GENERAL HOSPITAL
TACOMA, WASHINGTON 98431

JULY 1968

In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care". as promulgated by the Committee on the Guide for Laboratory Animal Resources, National Academy of Sciences - National Research Council.

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REPORTS CONTROL SYMBOL MEDDH-288 (R1)

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT REPORT

ANNUAL REPORT FY 68

RESEARCH AND DEVELOPMENT
MADIGAN GENERAL HOSPITAL
TACOMA, WASHINGTON 98431

July 1968

Project No. 3A025601A826 00 Clinical Investigations

Project No. 3A025601A825 00 Oral and Maxillofacial Sciences

FOREWORD

The FY 1968 research program at Madigan General Hospital increased in scope and size during this past fiscal year.

The construction projects "Canine Husbandry and Holding Facility" and "Isolation, Primate and Small Animal Facility" were approved by The Surgeon General and completed during FY 68. These projects will provide isolation facilities for dogs and subhuman primates to support the growth and expansion of the Medical Research and Development Program at Madigan General Hospital.

Appreciation is expressed to the many military, clinical and administrative personnel whose contribution is vital to the successful implementation of clinical research projects.

Robert W Lipscomb

ROBERT W. LIPSCOMB
Captain, VC
Acting Director, Research Program

ANNUAL PROGRESS REPORT - FY 1968

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1 07 68	D. Change (17 10 67)	U U	NA	QR	A. Work Unit

5. GOVT ACCESSION: | 6. AGENCY ACCESSION: DA ØC 6834 | REPORT CONTROL SYMBOL: CSCRD 103

10a. CURRENT NUMBER/CODE: 62156011 3A025601A825 00 313

10b. PRIOR NUMBER/CODE: None

11. TITLE: (U) Oral Cryosurgery

12. SCIENTIFIC OR TECH. AREA: 003500 Bio-Medical Sciences

13. START DATE: NA | 14. CRIT. COMPL. DATE: NA | 15. FUNDING AGENCY: Other DA

16. PROCURE. METHOD: C. In-House

17. CONTRACT/GRANT — a. NUMBER — b. TYPE: NA — c. DATE — d. AMOUNT: NA

18. RESOURCES EST. — a. PROFESSIONAL MAN YEARS — b. FUNDS (In thousands)

	a. PROFESSIONAL MAN YEARS	b. FUNDS (In thousands)
PRIOR FY 68		
CURRENT FY 69	2	1

19. GOV'T LAB/INSTALLATION/ACTIVITY
NAME: Headquarters
ADDRESS: U.S. Army Medical Res & Dev Command
Washington, D. C. 20315
RESP. INDIV. Knapp, LTC, M. J.
TEL. 202 - OX 65472

20. PERFORMING ORGANIZATION
NAME: Madigan Gen Hosp
ADDRESS: Tacoma, Washington 98431
INVESTIGATORS PRINCIPAL ASSOCIATE: Bohanan, MAJ, Jack R.
Lilly, LTC, G. E.
TEL 967-6811 TYPE DA

21. TECHNOLOGY UTILIZATION: Bio-Medical Sciences

22. COORDINATION: USA Med Res Unit, Presidio, SF, Calif.

23. KEYWORDS: Oral cryosurgery; tissue response; wound healing; white adult rats

26.

(U) Objective: To evaluate the response of oral tissues to cryotherapy.

(U) Local areas of tissue will be destroyed bilaterally in the buccal mucosa of young adult rats. One area of destruction will be produced with a cryosurgery probe. A contralateral area will be injured in a comparable manner with an electrocautery instrument. At sacrifice the injured areas will be removed by block section and fixed in 10% neutral buffered formalin. Formalin fixed specimens will be mailed to the USAMRU-P for histologic processing and interpretation.

(U) Information on the response of oral mucous membranes to cryosurgery has been experimentally obtained as well as an evaluation to the relative merits of this technique in oral therapeutics. A study on 40 white rats has been completed. Specimens from the right and left cheeks of these experimental animals have been completed and forwarded to LGH for histopathological and radioisotope examination by LTC Lilly.

28.

27. COMMUNICATIONS SECURITY: ☐ a. COMSEC ☒ b. NOT COMSEC RELATED

29. | 30. DOD CODE: BR | 30. BUDGET CODE: 1

31. MISSION OBJECTIVE: Medical Research

32. PARTICIPATION

33. REQUESTING AGENCY

34. SPECIAL EQUIPMENT

35. EST. FUNDS (In thousands) CPFF:

36.

DD FORM 1 AUG 64 1498A (Items 1 to 26 identical to NASA Form 1121)

ORAL CRYOSURGERY

MAJ Jack R. Bohanan, DC, et al

Information on the response of oral mucous membranes to cryosurgery has been experimentally obtained as well as an evaluation to the relative merits of this technique in oral therapeutics. A study on 40 white rats has been completed. Specimens from the right and left cheeks of these experimental animals have been completed and forwarded to Letterman General Hospital for histopathological and radioisotope examination by LTC Lilly. To date, communication with LTC Lilly revealed experimental techniques of the above submitted specimens were very satisfactory. Compiled data from all H & E stained sections are submitted. Conclusions or trends from this data have not been established yet. Microautoradiography sections have been prepared from the tritiated thymidine injected specimens, (specific activity of 0.50 curie per millimole).

This portion of the study is a rather lengthy time consuming technique and as yet is not completed. Consequently no real conclusions can be made until this portion of the study is finished.

CRYOSURGERY

2 HOURS POST-OP

Subepithelial vesicles. Sparse lymphocyte and PMN infiltrate in lamina propria. Slight hypereamia. Vesicle has ruptured in 4170 and there is more severe tissue damage. Connective tissue is basophilic and contains numerous basophilic granules (mast cells ?). Injury extends through cheek in 4170.

4 HOURS POST-OP

Intracellular epithelium edema with loss of cellular detail and nuclei. Small intraepithelial vesicles. Subepithelial vesicles are observed. Epithelium is present in every case. The lamina propria is edematous. Vascular congestion is prominent and numerous intravascular PMNs exhibiting marginization are observed. An occasional mast cell and a diffuse but sparse neutrophilic infiltrate is present.

6 HOURS POST-OP

Intraepithelial edema with nuclear degeneration. Subepithelial vesicles and subepithelial separation. No ulceration. Lamina propria is edematour and contains a diffuse mild neutrophilic infiltrate. Vascular congestion is apparent in some instances as is neutrophilic marginization. Occasional mast cells are observed.

8 HOURS POST-OP

Subepithelial vesicles in all specimens. Overylying epithelium stains poorly and many nuclei are lost, (evidence of cellular degeneration). Minimal to moderate edema throughout cheek. Mild diffuseinflammatory infiltrate is primarily neutrophilic with some lymphocytes. A variable number of mast cells are present.

ONE DAY POST-OPERATIVE

3 of 4 specimens are ulcerated. Fragments of anuclear epithelium are present. In some areas subepithelial vesicles and microabcesses are noted. Edema is moderate to severe. Inflammatory infiltrate is moderate in degree and diffuse in extent. It is primarily neutrophilic. Dense focal infiltrates are observed in some areas. Surface bacterial growth is observed in some cases. There is however, no evidence of invasion of tissue. Mast cells are numerous.

TWO DAYS POST-OPERATIVE

3 of 4 specimens definitely ulcerated. Edema severe and fibrin formation evident. Epithelial, fibroblastic and endothelial proliferation evident. Moderate and diffuse inflammatory infiltrate which is primarily neutrophilic in areas of ulceration and lymphocytic in deeper areas. Dense focal neutrophilic infiltrate is present in some areas. Mast cells present, but not as prominent as previously. Some superficial bacteria, but no invasion.

4 DAYS POST-OPERATIVE

All specimen are ulcerated. Edema mild to moderate. Fibrin clot is prominent in all specimens. Inflammatory infiltrate is moderate and primarily neutrophilic. Surface bacterial colonies are present, and there is evidence of superficial invasion. Endothelial and fibroblastic proliferation is marked. Mast cells are present in variable numbers at the margins of the reaction.

8 DAYS POST-OPERATIVE

2 of 4 specimen are ulcerated. Non-ulcerated specimens exhibit mild hyperkeratosis at site of injury. No evidence of edema. Inflammatory infiltrate is circumscribed and mild-to-moderate in intensity. Infiltrate is mixed in nature. A focal neutrophilic infiltrate is observed in some areas. Surface bacterial colonies, although present in some cases, do not show invasion. In ulcerated specimen epithelial proliferation is marked. Progressive collagenization is evident. Mast cells, although present, are not very prominent and appear reduced in number.

12 DAYS POST-OPERATIVE

All wounds are epithelized. Very mild inflammatory infiltrate, primarily lymphocytes. In specimen 4231 infiltrate is moderate with foci of neutrophils and greater fibroblastic proliferation. Mast cells are not prominent.

14 DAYS POST-OPERATIVE

All wounds are epithelized. Inflammatory infiltrate is mild and primarily lymphocytes. Foreign body giant cells and histiocytes are evident in areas of hair follicle and sebacceous gland degeneration. Fibrosis is evident with increased collagen formation. Mast cells are present in some cases. Epithelium is acanthotic in some areas.

ELECTROCAUTERY

2 HOURS POST-OP

Subepithelial vesicles are apparent, these vesicles are very small, and contain pale fluid. Vascular congestion appears more prominent and infiltrate more neutrophilic. Basophilic coagulum is observed in some areas.

4 HOURS POST-OP

Intracellular epithelial edema observed in two specimens with loss of cellular detail and nuclei. Subepithelial vesicles observed in two specimens. Little evidence of edema in lamina propria. There are more mast cells and these are occasionally ruptured. In one specimen (4177) epithelium is detached and all nuclei are missing. Vascular congestion prominent, but little inflammatory infiltrate, even though epithelium is frequently missing.

6 HOURS POST-OP

Large subepithelial vesicles are present in all specimens. Intraepithelial degeneration and edema are noted in a few areas. Connective tissue edema is not marked. Basophilic C. T. degeneration is present, but does not appear as marked as in previous specimen. Inflammatory, infiltrate is mixed lymphocyte and neutrophil. Mast cells are more numerous than in cryosurgery specimens. Some have ruptured.

8 HOURS POST-OP

Epithelium is missing in all specimens. Moderate to severe edema in loose fibrous C. T. Eosinophilic staining of edema in area of injury. (Suggests coagulation). Inflammatory infiltrate is diffuse and mild-to-moderate in intensity. Evidence of surface bacterial colonies which in some cases have invaded "viable" tissue. Inflammatory infiltrate is primarily neutrophils,

but some lymphocytes are observed. Mast cells do not appear to be as abundant and there is evidence of their degranulation.

ONE DAY POST-OPERATIVE

All specimens have areas of missing epithelium. Two are definitely ulcerated, two suggest epithelial loss was post mortem. Fragments of detached anuclear epithelium are observed. Subepithelial microabcesses are noted. C. T. edema is severe with local eosinophilic coagulum. Inflammatory infiltrate is moderate in degree and diffuse in nature with focal dense concentrations. It is primarily neutrophilic. Surface bacteria are present and there is some evidence of invasion. Mast cells are present, but are less numerous than in cryosurgery. Epidermal surface damage is evident.

2 DAYS POST-OPERATIVE

All specimens are ulcerated and inflammatory infiltrate is more severe than cryosurgery. Edema slightly less and much less fibrin clot. Little evidence of coagulation. Dense diffuse neutrophilic infiltrate. Proliferation is not as evident. Bacterial invasion present. Mast cells more prominent.

4 DAYS POST-OPERATIVE

All specimens are ulcerated on both mucosal and epidermal surface. Edema is more severe than cryosurgery. Fibrin clot, although present, is more diffuse and does appear as prominent. Surface and deep bacterial colonies are present. Inflammatory infiltrate is more severe and is primarily neutrophilic. Numerous dense focal infiltrates are observed. Some of these are microabscesses. Tissue necrosis is evident. Cellular proliferation, although present, is not as evident as in cryosurgery. Peripherally located mast cells are observed in approximately the same number.

8 DAYS POST-OPERATIVE

All specimens are ulcerated on both mucosal and epidermal surfaces. Inflammatory infiltrate is severe and is primarily neutrophilic. It is not circumscribed. Necrosis is extensive. Bacterial invasion is marked. Mast cells are prominent.

12 DAYS POST-OPERATIVE

Mucosal surfaces are ulcerated in all cases. Epidermal surface is ulcerated in one case (4230). Inflammatory infiltrate is moderate and diffuse. It is primarily lymphocytic, but comtains neutrophils. Endothelial and fibroblastic proliferation is marked. There is evidence of hair follicle and sebaceous gland degeneration. Superficial bacterial colonies are observed in some cases without evidence of invasion. Mast cells are prominent at the margins of the reaction.

Epithelial hyperplasia at margins of the wound.

14 DAYS POST-OPERATIVE

Mucosal ulceration in 3 of 4 cases. Epidermal ulceration in one case (4234). 4240 showsno evidence of previous injury. Moderate inflammatory infiltrate mixed in nature, but primarily lymphocytes. Hair follicle and sebaceous bland degeneration and occasional foreign body giant cells are associated with these areas. Histiocytes are present and mast cells are seen throughout. Increased collagen formation is evident. Superficial bacterial colonies are observed in some areas, but no evidence of invasion.

RESEARCH AND TECHNOLOGY RESUME

1.	2. GOVT ACCESSION	3. AGENCY ACCESSION	REPORT CONTROL SYMBOL
		DA ØD 6830	CSCRD 103

4. DATE OF RESUME	5. KIND OF RESUME	6. SECURITY (APT / WRK)	7. REGRADING	8. RELEASE LIMITATION	9. LEVEL OF RESUME
01 07 68	D. Change (05 10 67)	U / U	NA	QR	A. Work Unit

10a. CURRENT NUMBER/CODE
62156011 3A025601A826 00 314

10b. PRIOR NUMBER/CODE
None

11. TITLE:
(U) Coagulation Abnormalities in Meningococcal Sepsis

12. SCIENTIFIC OR TECH. AREA	13. START DATE	14. CRIT. COMPL. DATE	15. FUNDING AGENCY
003500 Clinical Medicine	10 67	NA	Other / DA

16. PROCURE. METHOD	17. CONTRACT/GRANT a. NUMBER b. TYPE	c. DATE d. AMOUNT	18. RESOURCES EST.	a. PROFESSIONAL MAN-YEARS	b. FUNDS (In thousands)
C. In-House	NA	NA	PRIOR FY 68	1	2
			CURRENT FY 69	1	3

19. GOVT LAB/INSTALLATION/ACTIVITY
NAME: Headquarters
ADDRESS: U.S. Army Medical Res & Dev Command
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TEL. 202 - OX 65472

20. PERFORMING ORGANIZATION
NAME: Madigan General Hosp
ADDRESS: Tacoma, Washington 98431
INVESTIGATORS PRINCIPAL: Lobell, CPT, Michael
ASSOCIATE: Evans, MAJ , Roger W.
TEL 967 - 6846 TYPE DA

21. TECHNOLOGY UTILIZATION
Medicine

22. COORDINATION
NA

23. KEYWORDS
Meningococcal sepsis; coagulation abnormalities

24.
(U) To study all patients with meningococcal sepsis for evidence of disseminated intravascular coagulation (DIC) and to evaluate treatment with Heparin.

25.
(U) All services will be informed that one of the investigators is to be notified upon suspicion of a case of meningococcemia. Working with the attending physician, the following studies will be obtained immediately: (1) Direct platelet count (phase method); (2) Fibrinogen quantitative assay; (3) One stage quick prothrombin time (PT); (4) Partial thromboplastin time (PTT); and (5) Thromboplastin screening test (TST). The diagnosis of DIC will be provisionally made on the basis of thrombocytopenia, hypofibrinogenemia and abnormal TST, PT and PTT (the latter two tests with a normal source of fibrinogen). The diagnosis will be confirmed as soon as feasible with a thromboplastin generation test (TGT) and quantitative assay for factors V, VIII, IX, and X. A Fi test and a serial thrombin time with and without epsilon-amino caproic acid (EACA) will be done if the fibrinogen level is reduced.

26.
Summary and/or Conclusions:

(U) To date, 5 patients with meningococcemia and a 6th with presumed meningococcemia have been studied for coagulation abnormalities. Of these, 2 demonstrated thrombocytopenia and incoagulable prothrombin times, partial thromboplastin tests, and hypofibrinogenemia. Both of these patients progressed to die, with extensive purpura, shock, and cardiac arrhythmias despite the early use of heparin. Both showed the classical fibrin thrombi in arterioles, capillaries, and veins at autopsy.

27. COMMUNICATIONS SECURITY	28.	29. DOD CODE	30. BUDGET CODE
☐ a. COMSEC OR COMSEC RELATED ☒ b. NOT RELATED		BR	1

31. MISSION OBJECTIVE	32. PARTICIPATION
Medicine	NA

33. REQUESTING AGENCY	34. SPECIAL EQUIPMENT

35. EST. FUNDS (In thousands) CPFF	36.

DD FORM 1 AUG 64 1498A (Items 1 to 36 identical to NASA Form 1132)

COAGULATION ABNORMALITIES IN MENINGOCOCCAL SEPSIS

CPT Michael Lobell, MC
MAJ Roger Evans, MC
BG Richard I. Crone, MC

Coagulation abnormalities and in particular, intravascular consumption coagulopathy are being increasingly recognized in meningococcal disease. We proposed to perform selected coagulation tests in all patients with a presumptive diagnosis of meningococcal sepsis or meningitis. To date 16 such patients have been evaluated.

Immediately upon suspicion and presumptive diagnosis of meningococcal sepsis, a platelet smear, prothrombin time and partial thromboplastin time were performed in these patients. If any abnormalities were discovered, a fi test for fibrinogen split-products was performed on the serum and a qualitative fibrinogen assay and serial thrombin time for fibrinolysins were performed. On initial evaluation two-thirds of our patients had detectable coagulation abnormalities while one-third were normal. In those patients who had coagulation abnormalities repeat studies were performed within several hours or upon change in clinical course and, particularly, development of hypotension or increasing purpura.

Of the ten patients who had coagulation abnormalities, four had incoagulable blood, hypofibrinogenemia and thrombocytopenia on initial evaluation. These patients all progressed to die in shock and either cardiac arrest or ventricular fibrillation despite massive supportive care. The other patients with initial coagulation abnormalities improved clinically and by coagulation tests, including one patient who was treated with heparin. It should be noted that the patients who died with IVCC all received heparin, fibrinogen, fresh plasma for clotting factor replacement, and all had demonstrable fibrin thrombi at autopsy. At the present time we are continuing to evaluate the use of heparin in IVCC and feel that any patient who has demonstrable coagulation abnormalities by clotting tests, and in particular those who are not clinically improving should be treated with heparin, clotting factor replacement and platelets as soon as possible. For those patients who are not having active bleeding at the time IVCC is diagnosed, heparin alone may suffice. However, clotting factor replacement, i.e., fresh plasma, fibrinogen is certainly warranted should bleeding be present. Our results and report of five patients who have demonstrated these coagulation phenomena are currently being submitted for publication.

RESEARCH AND TECHNOLOGY RESUME

1.	2. GOVT ACCESSION	3. AGENCY ACCESSION	REPORT CONTROL SYMBOL
		ØD 6832	CSCRD 103

4. DATE OF RESUME	5. KIND OF RESUME	6. SECURITY	7. REGRADING	8. RELEASE LIMITATION	9. LEVEL OF RESUME
01 07 68	A. New	U (DEF) U (OTH)	NA	QR	A. Work Unit

10a. CURRENT NUMBER/CODE: 62156011 3A025601A826 00 316

10b. PRIOR NUMBER/CODE: None

11. TITLE: (U) Mechanisms Producing Anemia and Granulocytopenia in Plasmodium Vivax Malaria

12. SCIENTIFIC OR TECH AREA	13. START DATE	14. CRIT. COMPL. DATE	15. FUNDING AGENCY
003500 Clinical Medicine	05 68	05 69	Other DA

16. PROCURE. METHOD	17. CONTRACT/GRANT	a. DATE	18. RESOURCES EST	a. PROFESSIONAL MAN-YEARS	b. FUNDS (In thousands)
C. In-House	b. NUMBER NA	NA	PRIOR FY 68	1	
	c. TYPE	d. AMOUNT	CURRENT FY 69	1	2

19. GOV'T LAB/INSTALLATION/ACTIVITY
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TEL.: 202 - OX 65472

20. PERFORMING ORGANIZATION
NAME: Madigan Gen Hosp
ADDRESS: Tacoma, Washington 98431
INVESTIGATORS PRINCIPAL: Pierce, CPT, Irving H.
ASSOCIATE: Lobell, CPT, Michael
TEL: 967-6911 TYPE: DA

21. TECHNOLOGY UTILIZATION: Medicine

22. COORDINATION: NA

23. KEYWORDS: Mechanisms; anemia; granulocytopenia; plasmodium vivax malaria.

24.

(U) a. To determine the incidence and degree of severity of granulocytopenia (absolute granulocytes less than 1500/mm^3) and anemia in documented cases of P. vivax malaria.

b. To attempt to determine the underlying mechanisms producing granulocytopenia and anemia. It is assumed here that the anemia of P. vivax malaria is due to intravascular hemolysis. However, because of low absolute parasite counts with P. vivax infestations, it would seem unlikely that this is the sole cause of anemia. Whether erythrocyte enzyme deficiency, abnormalities of iron kinetics or other unknown factors are operative has not previously been systematically studied. The mechanism of leukopenia is uncertain.

(U) All patients admitted to the Pulmonary and Infectious Disease Service, with a diagnosis of P. vivax malaria (confirmed by procedures outlined in formal study) are to be included in the study. It is intended that 10 malarial patients with anemia and/or leukopenia be evaluated. Patient consent will be obtained prior to study. Studies (as outlined in protocol) should be completed within 48 hours. If, however, an anemia and/or leukopenia does not become apparent initially, steps 1, 2, 5 and 6 will be repeated at periodic intervals throughout the first three weeks of hospitalization, and if then abnormal, further investigation as previously outlined will be performed.

Summary and conclusions: Deferred

27. COMMUNICATIONS SECURITY	28.	29. OSD CODE	30. BUDGET CODE
☐ a. COMSEC OR COMSEC RELATED ☒ b. NOT RELATED		BR	1

31. MISSION OBJECTIVE	32. PARTICIPATION

33. REQUESTING AGENCY	34. SPECIAL EQUIPMENT

35. EST. FUNDS (In thousands)	36.
CFY+1	

DD FORM 1 AUG 64 1498A (Items 1 to 26 identical to NASA Form 1122)

MECHANISMS PRODUCING ANEMIA AND GRANULOCYTOPENIA IN PLASMODIUM VIVAX MALARIA

CPT H. Irving Pierce, MC, et al

The purpose of this study is to determine the incidence and degree of severity of granulocytopenia (absolute granulocytes less than 1500/mm^3) and anemia in documented cases of P. vivax malaria. Also, to attempt to determine the underlying mechanisms producing granulocytopenia and anemia. It is assumed here that the anemia of P. vivax malaria is due to intravascular hemolysis. However, because of low absolute parasite counts with P. vivax infestations, it would seem unlikely that this is the sole cause of anemia. Whether erythrocyte enzyme deficiency, abnormalities of iron kinetics or other unknown factors are operative has not previosuly been systematically studied. The mechanism of leukopenia is uncertain. Three possible explanations exist: (1) Decreased production of leukocytes in bone marrow due to suppression of maturation or interference with release of mature granulocytes. (2) A physiologic intravascular shift of granulocytes with resultant increase in marginal granulocyte pool (MGP). (3) Increased granulocyte turnover rate occurring singly or in association with the first two mechanisms.

All patients admitted to the Pulmonary and Infectious Disease Service with a diagnosis of P. vivax malaria (confirmed by the following procedures) are to be included in the study. It is intended that 10 malarial patients with anemia and/or leukopenia be evaluated. Patient consent will be obtained prior to study.

Definitive diagnosis of P. vivax malaria by:

1. Malaria smears
2. Fluorescent antibody titers on acute and convalescent sera, the latter drawn 14 days later.

Hematologic evaluation performed prior to institution of antimalarial therapy is to be performed on each patient so diagnosed. Those not demonstrating either an anemia or leukopenia will serve as control patients. If hematologic abnormalities are not noted during the initial phase of the disease, and if such patient's illness is of such severity to preclude a delay in treatment, they will so be treated by conventional means (i.e., Chloroquine and Primaquine). If anemia and/or leukopenia then develops after initiation of therapy, they will be evaluated in the same manner. Routine hemolytic, ferrokinetic and granulocyte kinetic studies to be performed upon admission include:

1. Hematocrit, hemoglobin, WBC (every 3 days for 2 weeks)
2. Reticulocyte count; direct Coombs test
3. Serum iron and TIBC
4. Bone marrow aspiration (sternal) - calculate M:E ratio
5. Urine urobilinogen
6. Serum bilirubin (total and direct), weekly
7. Fecal urobilinogen

Mechanisms Producing Anemia and Granulocytopenia in Plasmodium Vivax Malaria - Pierce

8. G6PD screen test
9. Osmotic fragility
10. Autohemolysin test
11. Serum B_{12} and folic acid determinations
12. Plasma radio-iron disappearance
13. Parasite: RBC index
14. Intravenous infusion of epinephrine (0.3cc 1:1000 in 500 cc D-5-W given)
15. Intravenous infusion of endotoxin (Priomen^{R})

The preceding studies should be completed within 48 hours. If, however, an anemia and/or leukopenia does not become apparent initially, steps 1,2,5 and 6 will be repeated at periodic intervals throughout the first three weeks of hospitalization, and if then abnormal, further investigation as previously outlined will be performed.

Summary and/or conclusions: Deferred

RESEARCH AND TECHNOLOGY RESUME

2. GOVT ACCESSION	3. AGENCY ACCESSION	REPORT CONTROL SYMBOL
	DA 6831	CSCRD 103

4. DATE OF RESUME	5. KIND OF RESUME	6. SECURITY	7. REGRADING	8. RELEASE LIMITATION	9. LEVEL OF RESUME
01 07 68	D. Change (26 07 67)	U	NA	OR	A. Work Unit

10a. CURRENT NUMBER/CODE: 62156011 3A025601A826 00 305

10b. PRIOR NUMBER/CODE: 62156011 3A025601A826 01 305

11. TITLE:
(U) Early Intravenous Feeding of the Premature.

12. SCIENTIFIC OR TECH. AREA	13. START DATE	14. CRIT. COMPL. DATE	15. FUNDING AGENCY
003500 Clinical Medicine	NA	NA	Other 1 DA

16. PROCURE. METHOD	17. CONTRACT/GRANT a. NUMBER / b. TYPE / c. DATE / d. AMOUNT	18. RESOURCES EST	a. PROFESSIONAL MAN-YEARS	b. FUNDS (In thousands)
C. In-House	NA / NA	PRIOR FY 68		
		CURRENT FY 69	1	2

19. GOV'T LAB/INSTALLATION/ACTIVITY
NAME: Headquarters
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TEL: 202 - OX 65472

20. PERFORMING ORGANIZATION
NAME: Madigan Gen Hosp
ADDRESS: Tacoma, Washington 98431
INVESTIGATORS PRINCIPAL ASSOCIATE: Schers, LTC. Robert G.
TEL: 967-6743 TYPE: DA

21. TECHNOLOGY UTILIZATION: Medicine

22. COORDINATION: NA

23. KEYWORDS: Effect: early intravenous feedings; premature infants; correlation: neonatal findings.

24. (U) The purpose of this study is to evaluate the effect of early intravenous feedings to premature infants.

(U) In 100 low birth weight neonates, the effect of early intravenous feeding on several biochemical and clinical parameters was evaluated by comparing this regimen to one with oral feedings after a 24 hour fast.

(U) Further studies are required to establish with clarity which circumstances warrant the early provision of fluids in the care of the low birth weight neonate. A follow-up study will be implemented within the next 12 months to attempt to determine if there is any statistical difference in developmental landmarks or neurologic disease between LBW infants fed initially intravenously versus late oral feeding.

25.

27. COMMUNICATIONS SECURITY	29.	29. OSD CODE	30. BUDGET CODE
a. COMSEC OR COMSEC RELATED ☐ b. NOT RELATED ☑		BR	1

31. MISSION OBJECTIVE	32. PARTICIPATION
medicine	

33. REQUESTING	34. SPECIAL EQUIPMENT

35. EST. FUNDS (In thousands)	36.
CPY++	

DD FORM 1 AUG 64 1498A (Items 1 to 26 identical to NASA Form 1122)

EARLY INTRAVENOUS FEEDING OF THE PREMATURE

Peter Mamunes, MD *

ABSTRACT

In 100 low birth weight neonates, the effect of early intravenous feeding on several biochemical and clinical parameters was evaluated by comparing this regimen to one with oral feedings after a 24 hour fast.

Blood glucose determinations obtained on eleven occasions during their first five days of life revealed a statistically significant higher mean value for the IV group through the first 60 hours of life. An unexpectedly high percentage (21%) of infants from both groups had glucose values below 30 mg% within 1-2 hours after birth.

Fasted infants under 1500 grams had significantly lower glucose levels than the entire fasted group through most of the first 3 1/2 days of life. Only fasted infants (10%) developed consecutive glucose values below 30 mg%, all were males, and 4/5 were below the 20th weight percentile for their gestational age.

Sudden cessation of the intravenous infusion was at times associated with a precipitous drop in the blood glucose, especially in the infants under 1500 gms. Rate of weight loss or subsequent gain, mean maximum bilirubin levels, incidence of respiratory distress syndrome, and mortality were not altered by the intravenous fluid, but a slight hemodilution did occur.

Key Words: Hypoglycemia; blood sugar; bilirubin; premature infant, infant nutrition.

SUMMARY

In a comparative study of 100 consecutively born low birth weight infants, the effect of early intravenous administration of 10% glucose on several biochemical and clinical parameters was evaluated during the first five days of life. In comparison to infants orally fed after a 24 hour fast, those receiving intravenous fluid for 3 days had statistically significant higher mean glucose values through age 60 hours. Whereas 10% of the fasted group had 2 or more consecutive glucose values below 30 mg%, there were no such occurrences in the IV group. A large number of the single values under 30 mg% in the IV group was associated with a sudden cessation of IV administration, and this possible danger is emphasized. Gestational

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* Formerly Resident, Pediatric Service, Madigan General Hospital
Presently Dept of Pediatrics, New Jersey College of Medicine,
Newark, New Jersey

age and weight percentile status had no significant effect on the neonatal glucose curve, but a birth weight below 2000 gms was associated with lower values during the first 36 hours. An unexpectedly high percentage (21%) of glucose values at 0-1 hour of age were below 30 mg% but the explanation for this finding was not apparent from the available data.

Intravenous fluid and dextrose administration had no demonstrable effect on mortality, incidence of respiratory distress syndrome or bilirubin levels. It was associated with less weight loss in infants greater than 2000 gms but there was no effect on the rate of either regaining the birth weight or attaining of a weight of 5 lbs. A slight hemodilution was observed with early intravenous feeding.

Further studies are required to establish with clarity which circumstances warrant the early provision of fluids in the care of the LBW neonate.

A follow-up study will be implemented within the next 12 months to attempt to determine if there is any statistical difference in developmental landmarks or neurologic disease between LBW infants fed initially intravenously vs late oral feeding.

RESEARCH AND TECHNOLOGY RESUME

1.	2. GOVT ACCESSION	3. AGENCY ACCESSION	REPORT CONTROL SYMBOL
		DA ØC 6833	CSCRD 103

4. DATE OF RESUME	5. KIND OF RESUME	6. SECURITY	7. REGRADING	8. RELEASE LIMITATION	9. LEVEL OF RESUME
1 07 68	D. Change (12 01 67)	U U	NA	OR	A. Work Unit

10a. CURRENT NUMBER/CODE: 62156011 3A025601A826 00 312

10b PRIOR NUMBER/CODE: 6.11.25.01.1 3A0125o1808

11. TITLE:
(U) Chromosome Analyses of Children with Multiple Congenital Malformations

12. SCIENTIFIC OR TECH. AREA	13 START DATE	14 CRIT. COMPL. DATE	15. FUNDING AGENCY
003500 Clinical Medicine	NA	NA	Other DA

16. PROCURE. METHOD	17. CONTRACT/GRANT a. DATE / b. NUMBER / c. TYPE	18 RESOURCES EST	a PROFESSIONAL MAN-YEARS	b. FUNDS (In thousands)
C. In-House	NA / d. AMOUNT NA	PRIOR FY 68		
		CURRENT FY 69	2	2

19. GOV'T LAB/INSTALLATION/ACTIVITY
NAME Headquarters
ADDRESS U.S. Army Med Res & Dev Command
Washington, D. C. 20315
RESP. INDIV. Project Monitor
TEL 202 - OX 65472

20. PERFORMING ORGANIZATION
NAME Madigan Gen Hosp
ADDRESS Tacoma, Washington 98431
INVESTIGATORS PRINCIPAL ASSOCIATE Scherz, LTC, Robert G.
TEL 967-6743 TYPE DA

21. TECHNOLOGY UTILIZATION
Clinical Medicine

22. COORDINATION
NA

23. KEYWORDS
Chromosome; children; congenital malformations

24.
(U) The purpose of this study is to evaluate infants and children with multiple congenital abnormalities and to correlate phenotypic expression with gross chromosome abnormalities.

(U) Chromosome preparations were made from peripheral blood cultures of lymphocytes. Karyograms were prepared by laboratory technicians and cytogenetic analyses performed by the investigator.

(U) During the year the R&D laboratory developed the ability to process photographic material necessary to produce karyograms. Thirty-seven patients were evaluated for a variety of disorders. A new familial syndrome was evaluated. Chromosome studies thus far have been indistinguishable from normal.

25.

27. COMMUNICATIONS SECURITY	28.	29. OSD CODE	30. BUDGET CODE
☐ a. COMSEC OR COMSEC RELATED ☒ b. NOT RELATED		BR	1

31. MISSION OBJECTIVE	32. PARTICIPATION

33. REQUESTING AGENCY	34. SPECIAL EQUIPMENT

35. EST. FUNDS (In thousands)	36.
CPY++	

DD FORM 1 AUG 64 1498A (Items 1 to 26 identical to NASA Form 1122)

CHROMOSOME ANALYSES OF CHILDREN WITH MULTIPLE CONGENITAL MALFORMATIONS

LTC Robert G. Scherz, MC

The purpose of this study is to evaluate infants and children with multiple congenital abnormalities and to correlate phenotypic expression with gross chromosome abnormalities.

Chromosome preparations were made from peripheral blood cultures of lymphocytes. Karyograms were prepared by laboratory technicians and cytogenetic analyses performed by the author.

During the year, the R & D Laboratory developed the ability to process photographic material necessary to produce karyograms. Thirty-seven patients were evaluated for a variety of disorders. A new familial syndrome with an apparent autosomal dominance characterized by:

mental retardation
microcephaly
dwarfism
abnormal dermatoglyphics
including

1. simian line
2. displaced palmar triradial axis
3. clinodactyly
4. single flexion crease - 5th finger -

was evaluated. So far three affected family members have been evaluated. Chromosome studies thus far have been indistinguishable from normal. It is anticipated that future support of this project can be best obtained by individual pilot projects since all necessary equipment is available for the production of karyograms in the R & D Laboratory.

RESEARCH AND TECHNOLOGY RESUME

1.	2. GOVT ACCESSION	3. AGENCY ACCESSION	REPORT CONTROL SYMBOL
		NA	CSCRD 103

4. DATE OF RESUME	5. KIND OF RESUME	6. SECURITY	7. REGRADING	8. RELEASE LIMITATION	9. LEVEL OF RESUME
1 07 68	A. New	U U	NA	QR	A. Work Unit

10a. CURRENT NUMBER/CODE: NA

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11. TITLE: See Below

12. SCIENTIFIC OR TECH. AREA	13. START DATE	14. CRIT. COMPL. DATE	15. FUNDING AGENCY
003500 Clinical Medicine	NA	NA	Other DA

16. PROCURE. METHOD	17. CONTRACT/GRANT			18. RESOURCES EST.	a. PROFESSIONAL MAN-YEARS	b. FUNDS (In thousands)
	a. TYPE	b. NUMBER	c. DATE / d. AMOUNT			
C. In-House	NA		NA	PRIOR FY 68		Less than
				CURRENT FY 69	NA	$500 each

19. GOVT LAB/INSTALLATION/ACTIVITY
NAME: Headquarters
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20. PERFORMING ORGANIZATION
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TEL 967-6511 TYPE DA

21. TECHNOLOGY UTILIZATION: NA

22 COORDINATION: NA

23. KEYWORDS: Antacid therapy; oral glucose; balloon implants; rubella; lenticular subcapsular epithelium; immunization; meningococcal disease; acrylic teeth; triatiated digoxin; routine physical; betadine; intrauterine; instrumentation; sterility, primary hemostasis; persistent hypochloremia; placental membrane; burn therapy.

24.
1. Effect of Intensive Antacid Therapy on Aspirin Injury and Absorption - CPT Simon,etal.
2. Effect of Varying Strengths of Oral Glucose on Blood Sugar in the Low Weight for Gestational Age Neonate and Premature Infant - CPT Landes & LTC Scherz.
3. Balloon Implants for Retinal Detachment Surgery - LTC Galas.
4. Incidence of Rubella in a Basic Combat Training Company - LTC Ionno & CPT Bybee.
5. Inhibition of Lenticular Subcapsular Epithelium - CPT Roy.
6. Meningococcal Disease and its Association with Acute Respiratory Disease - LTCs Cooper and Hall.
7. Implantation of Acrylic Teeth in Comparison with Intentional Replantation in Primates - LTC Loke.
8. Uptake of Triatiated Digoxin in the Myocardium of Infarcted vs Control Hearts - CPT Kearbey.
9. Routine Periodic Physical Examination - CPT Politte, LTCs Moyer & Cooper.
10. The Effect of Betadine Preparation on Maternal and Cord PBI - CPT Alden, et al.
11. Intrauterine Growth Retardation in Rabbits - CPT Bowes.
12. Instrumentation Development for Anterior Capsulectomy - CPT Roy.
13. Effect of the IUCD on the Sterility of the Endometrium - MAJ Perry.
14. A Five-Year Evaluation of D&C's on Women over Forty - MAJ Bobitt.
15. The Effect of Aspirin Therapy on Primary Hemostasis - CPT Lutcher.
16. The Relationship of Persistent Hypochloremia to the Blood and Urine Nitrate Levels during Topical Silver Nitrate Therapy for Extensive Burns - CPT McGroarty.
17. Use of Placental Membranes in Burn Therapy - CPT Latham, et al

27. COMMUNICATIONS SECURITY	28.	29. OSD CODE	30. BUDGET CODE
a. COMSEC OR COMSEC RELATED ☐ b. NOT RELATED ☒		BR	1

31. MISSION OBJECTIVE	32. PARTICIPATION

33. REQUESTING AGENCY	34. SPECIAL EQUIPMENT

35. EST. FUNDS (In thousands)	36.
CFY 61	

DD FORM 1 AUG 64 1498A (Items 1 to 36 identical to NASA Form 1122)

THE EFFECT OF INTENSIVE ANTACID THERAPY ON THE ABSORPTION AND TOXICITY OF ASPIRIN

CPT Francis R. Simon, MC, et al

In this study we are attempting to answer two questions: (1) Can we decrease the gastrointestinal bleeding induced by aspirin, and (2) Does antacid therapy influence the absorption of aspirin? These studies were stimulated by the work of Schanker and Hogben who demonstrated that aspirin requires an acid medium to be absorbed at an optimal rate and that as the gastric PH rises from PH 1 to 8 there is a progressive decrease in absorption. Davenport and others have extended these studies to dogs and man demonstrating that in an acid media aspirin causes a breakdown in the gastric mucosal barrier and can lead to bleeding. Although the studies are conflicting, it appears that the presence of an excess of antacid, in the region of 20m-eq per tablet, does reduce the extent of gastrointestinal bleeding.

We have used the patient as his own control in this study in which aspirin is given in 6 day blocks and .3gm calcium carbonate per hour is alternated with no antacid therapy simultaneously with the aspirin therapy which is given as 900 mg before meals and at bed time. We are measuring gastrointestinal blood loss by the Cr^{51} labeled blood cell technique utilizing four stool collections; an initial control collection, a collection during first administration of aspirin, a second control period after 9 days of no aspirin, and a final estimate of blood loss after the second administration of aspirin. Gastrointestinal absorption is measured by blood salicylate levels and two 24 hour urine salicylate excretions. In this study we have used normal, young, healthy male volunteers.

At the present time only two persons have completed the study in its entirety and therefore no conclusions can be reached. However, in these two volunteers the effect of antacids did not change gastrointestinal blood loss nor the serum salicylate levels. There is a suggestion that absorption of aspirin was decreased because the urine salicylate excretion was consistently reduced following administration of antacids.

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EFFECT OF VARYING STRENGTHS OF ORAL GLUCOSE ON BLOOD SUGAR IN THE LOW WEIGHT FOR GESTATIONAL AGE NEONATE AND PREMATURE INFANT

CPT Richard D. Landes, MC
LTC Robert G. Scherz, MC

Recent studies have revealed that the blood sugar in newborn infants drops to low levels during the first few hours following birth. This drop is marked in premature and low birth weight infants, often falling to dangerously low values. This study has been designed to evaluate the effect of early feeding using 10 and 20% dextrose in water, while the body temperature is maintained in normothermic levels.

Three groups of infants are being studied.

I. Full term infants of normal birth weight.

II. Premature infants whose gestational age is less than 37.0 weeks and birth weight less than 5.5 lbs.

III. Low birth weight infants meaning those whose birth weight is below the 25th percentile for gestational age.

To date the following number of infants have been studied.

I. Full term infants - 14
II. Premature infants - 5
III. Low birth weight infants - 7

Attached are the results obtained on those infants studied.

PLAN: The intention of the investigators is to study an additional number in each group as follows.

I. Full term infants - 6
II. Premature infants - 7
III. Low birth weight infants - 5

NORMOTHERMIC FULL-TERM INFANTS

Range of gestational age (wks from LMP)	38 - 46 wks
71 percent between	40 - 43 wks
Weight range	2820 - 3730 gms
86 percent between	2900 - 3500 gms

NORMOTHERMIC FULL-TERM INFANTS

Relationship between Blood Sugar and Age

Age (hours)	No. of Determinations	Mean	
		10 percent feeding	20 percent feeding
Cord	28	89.64	126.0
1	28	46.93	47.61
2	26	43.66	44.64
4	28	45.10	42.71
6	28	46.35	45.82
12	28	50.64	59.42
18	26	52.33	49.21
24	26	59.50	55.57
48	27	52.50	57.92

NORMOTHERMIC PREMATURE INFANTS

Range of gestational age (wks from LMP)	32 - 36 wks
86 percent between	34 - 36 wks
Weight range	1587 - 2381 gms
60 percent between	1900 - 2100 gms

NORMOTHERMIC PREMATURE INFANTS

Relationship between Blood Sugar and Age

Age (hours)	No. of Determinations	Mean	
		10 percent feeding	20 percent feeding
Cord	10	70.00	104.25
1	10	25.00	29.50
2	10	25.66	26.50
4	10	41.50	32.75
6	10	40.00	39.75
12	10	56.00	78.25
18	10	51.66	43.25
24	9	39.00	45.75
48	10	54.66	42.25

NORMOTHERMIC TERM-UNDERWEIGHT INFANTS

Range of gestational age (wks from LMP)	38 - 43 wks.
60 percent between	39 - 40 wks.
Weight range	1899 - 2835 gms.
60 percent between	2200 - 2700 gms.

NORMOTHERMIC TERM-UNDERWEIGHT INFANTS

Relationship between Blood Sugar and Age

Age (hours)	No. of Determinations	Mean	
		10 percent feeding	20 percent feeding
Cord	14	71.73	99.87
1	14	27.00	46.12
2	14	30.86	30.75
4	14	33.66	41.25
6	14	37.00	44.87
12	14	51.00	55.12
18	13	42.83	46.37
24	14	43.83	53.25
48	11	51.75	52.87

BALLOON IMPLANTS FOR RETINAL DETACHMENT SURGERY

LTC Stanley M. Galas, MC

Implants of silicone rubber-solid are invaluable in the surgical treatment of retinal detachments. The surgical procedure requires frequent adjustments in size and position of the silicone band and implants presently utilized.

This study is an attempt to use a balloon implant to replace the present implants. The size of the implant can be controlled simply by increasing the size of the balloon in a scleral pocket.

Personal background consists of 18 months fellowship in retinal detachment surgery with implant studies as a research project.

The study will consist of implantation of balloon implants into dog eyes noting feasibility and effect of implant. Different types of scleral resections will be utilized, as well as scleral pockets, in the study of the effects of surgical procedure on the buckles produced by a balloon. The balloon will be inflated with air or saline solution of chloramphenicol sufficient to produce an intraocular buckle.

Three dogs will be required for each of the following subgroups.

1. Fifteen minutes prior to surgery each dog will receive 10 ml/dog of glycerin by mouth.
2. IV diamox.
3. Paracentesis of the anterior chamber.

Items 2 and 3 will be utilized as necessary to relieve intraocular pressure sufficiently to allow production of a buckle without occluding the central retinal artery.

A. Scleral Resection
1. Air inflation
2. Saline solution of chloramphenicol

B. Scleral Pocket
1. Air inflation
2. Saline solution of chloramphenicol

After surgery each of the subgroups will be evaluated daily up to one week by the following parameters.

1. Intraocular buckle
2. Extraocular buckle
3. Duration of buckle
4. Complications
   a. early
   b. late

Silicone implants will have to be fabricated prior to instituting any work on this procedure.

Summary and/or conclusions: Deferred.

INCIDENCE OF RUBELLA IN A BASIC COMBAT TRAINING COMPANY

CPT Joseph D. Bybee, MC
LTC Joseph A. Ionno, MC

The purpose of this study is to determine the sero-conversion and "clinical" incidence of Rubella rate in a basic combat training company during basic training.

Serum specimens have been obtained at periodic intervals during the basic training course of a single company and are being held for determination of rubella hemagglutination inhibition titers.

We are currently awaiting the resolution of technical problems in performance of the serologic test.

INHIBITION OF LENTICULAR SUBCAPSULAR EPITHELIUM

CPT F.H. Roy, MC

The purpose of this study was to use X-rays and drugs in the first week after surgery to inhibit the subcapsular epithelium and avoid pupillary obstruction at a later time.

Approach: Part I. Animal: Adult Cat. A variation of the linear extraction operation was performed on both eyes under Nembutal and local anesthesia. Various doses of radiation was given during the first week following surgery. Thirteen cats were operated and followed clinically and sacrificed at five months. Pathological sections were stained with hemotoxylin and eosin and studied.

Part II. Vinblastine 0.1 mg/Kg to 0.5 mg/Kg; Vincristine 0.01 mg/Kg to 0.1 mg/Kg was given intravenously at the time of surgery. The same surgical procedures and laboratory studies were performed as in Part I and the animals sacrificed at five months.

Progress: Part I. Eleven animals had bilateral lens surgery and varying dosages of X-ray as indicated in study. All animals are doing quite well. They will be sacrificed approximately five months post-surgery. Four control eyes were operated. One of these has been enucleated due to post-operative infection.

Part II. Twenty-five animals or 50 eyes have been operated. Five animals had intravenous Vincristine at the time of surgery. Five animals had intravenous Vinblastine at the time of surgery. Two animals who had the largest dose (0.4 and 0.5 mg/Kg) expired and two other animals had surgery and the same dosage of Vinblastine. These two animals also expired 3-5 days after surgery.

Vincristine and Vinblastine have been shown to have a direct inhibitory effect on cell mitosis. In addition to inhibiting the lenticular subcapsular epithelium, it inhibits healing of the corneal wound. Thus, these systemic drugs would never be of value in human use. All animals who had these drugs were sacrificed. The eyes were removed and studied histologically.

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MENINGOCOCCAL DISEASE AND ITS ASSOCIATION WITH ACUTE RESPIRATORY DISEASE

LTC Everett B. Cooper, MC
LTC William H. Hall, MC

The purpose of this study is to determine whether basic trainees hospitalized with acute respiratory disease have concomitant inapparent meningococcal infection.

A group of basic trainees admitted to Madigan General Hospital were evaluated for evidence of viral infection by culture of throat washings for viruses and by serologic investigation to detect antibody rises to common respiratory viruses. These same patients were studied for evidence of meningococcal infection by nasopharyngeal and blood culture for meningococci and acute and convalescent serum to detect rise in antibodies against the meningococci.

The same studies were performed on a group of basic trainees without overt evidence of respiratory disease.

By comparing the incidence of evidence for meningococcal infection between patients with acute respiratory disease and well controls, some insight can be gained into whether inapparent meningococcal infection occurs associated with the acute respiratory disease syndrome.

Approximately 100 patients with acute respiratory disease and 75 well controls have been evaluated. The clinical evaluation of patients has been completed. Conclusion will be made upon receipt of laboratory analysis of submitted specimens.

IMPLANTATION OF ACRYLIC TEETH IN COMPARISON WITH INTENTIONAL REPLANTATION IN PRIMATES

LTC M. W. Loke, DC

Our knowledge of tissue implantation and intentional replantation are only in the initial stage of development. From the survey of literature reviewed there seems to be a wide range of differences in success and failure.

The purpose of this study is to investigate more thoroughly the implantation of acrylic teeth in comparison with intentional replantation in primates. The success of replacing teeth using heat cured methylmethacrylate implant will give us a "third dentition". It will also overcome problems associated with hemogenous, hetergenous and autogenous implanting of teeth.

A total of six primates will be utilized in the study. Four teeth will be used on each primate, thus giving a total of 24 teeth to be evaluated in the experiment. Four central incisors, two maxillary central incisors and two mandibular central incisors will be used in each primate. Procedures on the four teeth involved in the experiments will be rotated in a clock-wise manner as follows.

Primate 1	Implantation of Acrylic Tooth	Root Canal Replantation
	Control	Implantation of Natural Tooth
Primate 2	Control	Implantation of Acrylic Tooth
	Implantation of Natural Tooth	Root Canal Replantation
Primate 3	Implantation of Natural Tooth	Control
	Root Canal Replantation	Implantation of Acrylic Tooth
Primate 4	Root Canal Replantation	Implantation of Natural Tooth
	Implantation of Acrylic Tooth	Control

Implantation of Acrylic Teeth - Loke

Primate 5	Implantation of Acrylic Tooth	Root Canal Replantation
	Control	Implantation of Natural Tooth
Primate 6	Root Canal Replantation	Implantation of Acrylic Tooth
	Control	Implantation of Natural Tooth

Six primates of the species Macaca nemestrina (pigtail) were purchased in March 1968. We received five females and one male weighing an average of 6.0 Kg each.

Study models of stone were made from alginate impressions of the maxillary and mandibular dental arches. The primates were premedicated with 0.1 mg Atropine subcutaneously prior to Sernylan (phencyclidine hydrochloride) at 1 mg per pound by intermuscular injection. Radiographs were then obtained. Periapical films of the anterior incisors of the maxilla and the mandible were taken plus panorex films of each mouth.

On 24 April 1968 work was started on primate #6. Preanesthetic: Atropine sulfate 0.1 mg subcutaneous and demerol 1 mg per lb intermuscular were administered followed 25 minutes later with the anesthetic - sodium pentobarbital given intravenously; dosage 10 mg per lb given to effect. This maintained a satisfactory plane of anesthesia for approximately one and one-half hours. Gold cast cap-splints were made from the study stone casts. They fitted the four anterior incisors of the maxillary and mandibular arches. Using suitable forceps #151 and #150, the right and left maxillary centrals and the left mandibular central were carefully extracted. The left maxillary central was reduplicated in acrylic - (Hue-lon caulk) heat cured for 45 minutes at 120 C (212°F). The right maxillary central was soaked in a pan of normal saline and a root canal procedure was accomplished. Lateral condensed gutta percha points were used and retrograde amalgam was placed in the apex of the root and the cingulum of the crown.

Both the maxillary centrals were inserted into the refreshened sockets. The gold cast cap-splints were cemented in place with ZnP04 cement to stabilize the implanted teeth. The left mandibular central was extracted and immediately reimplanted into the socket. The mandibular gold cast splints were cemented in place. The primate was then placed in the primate restraining chair designed to prevent it from tampering with the oral cavity and the cemented gold crowns. The lower crown splints came off on the 25th of April - and was not replaced. The primate was chaired for 12 days and was granted limited access to mouth with her hands after five days. At the end of 12 days the primate had adapted to the crowns being in her mouth and was returned to the cage. Daily checks were made and it was found that she ate with her premolars and molars carefully avoiding the use of her incisors. All implanted teeth are still in place. Progress thus far is satisfactory. Work on primate #2 will begin soon.

UPTAKE OF TRITIATED DIGOXIN IN THE MYOCARDIUM OF INFARCTED VS CONTROL HEARTS

CPT Dale E. Kearbey, MC

It has been a clinical observation that postmyocardial infarction patients in congestive heart failure are more sensitive to digitalis toxicity than are patients in congestive failure who have not had a prior myocardial infarction. From this observation, the following hypothesis was formed. As the heart selectively concentrates the digitalis glycosides, and as the concentration of digitalis in the myocardium parallels the serum concentration, it was hypothesized that the infarcted area of myocardium did not take up digitalis, thus leaving more unbound serum digitalis, and thus a parallel of digitalis in the remaining viable myocardium, causing toxicity.

The anterior descending branch of the left coronary artery will be ligated in a two-stage procedure, then 0.09 mg/Kg tritiated digoxin (Sp. Activity 1264 C/Ml) will be injected 1/2 hour after ligation. Serum samples will be taken at one and two hours after injection. After two hours the animals will be sacrificed and specimens of myocardium taken from the infarcted zone, and from the remaining viable myocardium. Control animals will be done in identical fashion and corresponding samples will be taken. The samples will be digested in a NCS ™ solution, diluted, and counted in a liquid scintillation counter. Renal function will be evaluated with BUN prior to surgery. Thirty dogs will be utilized to give an adequate series for evaluation.

To date eight animals have been completed. The artery was tied off in four of these animals; a sham operation was performed on three (the artery was not ligated; one animal had the artery ligated but did not receive digoxin. This animal was observed for three hours using an electrocardiograph machine.

The animals that have had the ligation of the anterior descending branch of the left coronary artery have demonstrated marked evidence of toxicity to the digoxin, whereas the other two groups failed to demonstrate any electrocardiographic evidences of toxicity or to an intrinsic propensity towards arrhythmia when the artery was ligated without digoxin.

The other laboratory studies such as renal function tests and uptake of the tritiated digoxin will be performed this summer.

ROUTINE PERIODIC PHYSICAL EXAMINATIONS

CPT Lenard L. Politte, MC, et al

The purpose and objective of this study is to establish the incidence, approximate cost, and significance of new findings detected by routine periodic physical examinations as presently done at Madigan General Hospital. The findings of these examinations will then be correlated with parameters such as reason for the examination, (personal interest or administrative), age, race, sex, cigarette smoking habits, blood pressure, and routine laboratory findings. By analyzing these data, we hope to better evaluate what we are accomplishing by these examinations and in what ways might be made more productive.

The data from approximately 750 consecutive routine physical examinations are recorded on IBM cards. These examinations are done by the physicians in the Adult Clinic. The basic data are put on the cards by administrative assistants and the diagnoses, significance of findings and a review of the already punched cards are made by the investigators of this study. All of the work generated by the examination in order to establish or confirm the diagnoses are recorded so that overall cost of each finding can be established. The cards thus generated are then analyzed with the help of the University of Washington Computer Facilities.

Approximately 750 patients have been incorporated in the study. Of these about 450 have been completed. Of the completed cases, about 300 have been preliminarily analyzed by computer to evaluate the card format and accuracy of the punching process. Both of these factors were found to be quite satisfactory and the rest of the cases are now being completed for final analysis. After this initial evaluation a decision will be made whether the basic questions raised in the initiation of the study have been answered and whether further evaluation will be needed.

THE EFFECT OF BETADINE PREPARATION ON MATERNAL AND CORD PBI

CPT Errol R. Alden, MC, et al

This study is designed to help differentiate and clarify the effect of an iodine containing compound topical povidone iodine (Betadine) on both maternal and cord PBI's.

Under ordinary circumstances the determination of the protein blood iodine is the best and most reliable index of thyroid activity [1]. The most common cause for a falsely elevated PBI is the administration of drugs containing iodine. Among others incriminated have been topical povidone iodine (Betadine) which is used in many delivery rooms for perineal prep prior to delivery.

Quagliana [2] has reported that the PBI was significantly elevated in surgical patients after receiving preparation with Betadine as compared to Phisohex. The greatest increase was 3.4 mcg/100 ml in the skin prepped with Betadine group while the greatest rise was 6.8 mcg/100 ml in the group with vaginal douches.

While most values remained within the normal range, five abnormally low PIB's were elevated to normal and two normals were elevated beyond the range of normal. There is no report, however, on the effect of Betadine perineal preping on the cord blood PBI. This variable becomes quite important when trying to ascertain thyroid disorders. Cretinism and neonatal Grave's disease being two prominent examples.

Cord blood is the simplest and most readily obtainable sample of fetal blood. Ante and postpartum samples from the mother and a cord blood sample and maternal blood PBI at the time of delivery will be obtained. T_3 will be obtained in conjunction as a test not related to or affected by iodine containing drugs for control purposes.

To date 30 patients have been included in the study. Ten were prepped with Phisohex, 10 were prepped with Betadine on the perineum only, and 10 received Betadine for all sterile procedures. Analysis of variance performed by the University of Washington's statistician indicated no difference in the PBI of the three groups. However, he suggested for more meaningful data, the Phisohex and Betadine group should be extended to 30 patients each. It is, therefore, planned to proceed with more patients as soon as possible.

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INTRAUTERINE GROWTH RETARDATION IN RABBITS

CPT Watson A. Bowes, MC

The syndrome of intrauterine growth retardation in humans has been described, and an increased perinatal morbidity and mortality has been noted in these infants. It is suspected that "placental insufficiency" plays a role in the growth retardation of some fetuses. However, the causes of intrauterine growth retardation in the otherwise normal fetus have not been well defined, nor has the condition been well investigated in suitable experimental conditions.

The purpose of this study is to produce growth retardation in a controlled reproducible manner in an experimental animal by restricting the increase in uterine blood flow that occurs in normal pregnancy.

Approach: Female, Dutch rabbits are being used. In the nonpregnant state a radio-opaque, sterile teflon band (diameter 0.09 to 0.13 cm) is placed around the uterine artery of one horn of the uterus. The vaginal and ovarian collateral circulation to this horn is ligated. The blood supply to the other uterine horn is not altered. The teflon band does not restrict blood flow through the uterine artery in the nonpregnant state but is of such a diameter that enlargement of the artery which accompanies normal pregnancy should be prevented. Two to four weeks after the surgical procedure the animals are bred and given 25 IU of human chorionic gonadotropin to enhance ovulation. At 29 to 30 days gestation (normal gestational duration - 31 days) abdominal delivery will be carried out and fetuses in the operated uterine horn will be compared with those in the uterine horn with intact uterine circulation. Comparisons will be made with the number of fetuses, weight of fetuses, placentas, as well as fetal tissues including brain, lungs, liver and spleen.

Progress: To date eight female rabbits have been successfully operated and subsequently bred to a single buck. None of the rabbits have yet been delivered, consequently results are pending. If significant intrauterine growth retardation can be demonstrated in the animals operated so far, additional rabbits will be similarly treated to define such things as time in gestation when growth retardation begins, histological changes associated with growth retardation, affect on postnatal growth and so forth.

INSTRUMENTATION DEVELOPMENT FOR ANTERIOR CAPSULECTOMY

CPT F. H. Roy, MC

The purpose of this study was to develop instrumentation to remove a larger piece of anterior lens capsule and thus diminish the after-cataract.

Approach: Two instruments are being made according to specifications.

1. Forceps - curved to fit the surface of the lens on Dewecker handles.

2. Nitrogen powered rotary blade in a double chambered cylinderical housing to remove as much anterior capsule as possible.

These two instruments will be evaluated first on pig eyes from the packing house and then about 20 cats will be operated using the instruments and then sacrificed at 5 months.

Progress: Phase I of one instrument was made and evaluated. Phase II of the same instrument is being constructed currently by the Mechanical Engineering Instrument Development Section of the University of Washington.

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EFFECT OF THE IUCD ON THE STERILITY OF THE ENDOMETRIUM

MAJ Roger W. Perry, MC

Previous attempts to culture the endometrium transcervically has generally shown that about 50% [1,2,3] of cultures will be positive for bacteria (pathogenic or non-pathogenic). Cultures of the endometriums with IUCD in place by Willson et al [4] showed similar findings and it was concluded that the IUCD did not alter the relative sterility of the endometrium. In 1967, Dr. Ansbacher et al [5] found that when culturing the endometrium directly at time of hysterectomy only 6.4% (5 of 78) demonstrated bacterial growth.

Over a period of five months all women to have abdominal or vaginal hysterectomies will receive identical preoperative vaginal preparation for surgery. All women will have endocervical cultures taken two to six weeks preoperatively. Approximately one-half will have an IUCD (safety coil) inserted following culture. The cervix will be recultured in all women after the final preoperative vaginal preparation. The endometrium will be cultured directly through a fundal incision at time of surgery. All cultures will be aerobic and anaerobic. We anticipate a total of eighty patients - 40 controls and 40 with IUCD in place. Results will be evaluated by the method of sequential trial to determine the validity of results and indication for further study. Preoperative preparation will consist of a Betadyne douche on the night prior to surgery followed by the insertion of a Furacin vaginal suppository. At the time of surgery the vagina will be scrubbed with Betadine solution (duplicates Ansbacher Study[5]). Cultures will be taken with swabs and transported in Difcos transport media. Cultures will be plated as follows: 1. Aerobic: Blood agar and MacConkey Plates. 2. Anaerobic: Blood agar under nitrogen and chocolate agar in 10% CO_2.

Summary and conclusions: deferred.

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A FIVE-YEAR EVALUATION OF D&C's ON WOMEN OVER FORTY

MAJ John R. Bobitt, MC

A large number of uterine dilatation and curettages are performed by the OB GYN Service of Madigan General Hospital.

The purpose of this study is to determine the types of pathologic diagnosis and etiology in patients over 40 with abnormal bleeding. It also is the purpose of the study to determine how many of these women are on hormonal treatment and whether there is a relationship between the type of hormonal treatment and abnormal bleeding.

All hospital records for the past five years will be reviewed on those women 40 and over who were admitted to the OB GYN Service for diagnostic D&C because of abnormal uterine bleeding.

Summary and conclusions deferred.

THE EFFECT OF ASPIRIN THERAPY ON PRIMARY HEMOSTASIS

CPT Charles L. Lutcher, MC

The purpose of this study is to evaluate primary hemostasis in patients receiving salicylate therapy.

Mechanisms of platelet interaction have recently been the subject of intense investigation in a number of research laboratories (1-4). The spectrum of disease states influenced by platelet dysfunction is wide and includes a variety of bleeding diatheses, syndromes of intravascular clotting, and thromboembolic phenomena in general.

Primary hemostasis is principally a function of the platelet thrombus that forms at the site of vessel injury. It is now well established that adenosine diphosphate (ADP), in the presence of divalent cation and one or more plasma factors, plays the major role in forming the hemostatis thrombus. ADP is liberated from platelets and erythrocytes upon the exposure of collagen at the site of vessel injury. Until recently the bleeding time (a gross test at best) has been the only method for evaluating primary hemostasis. Significant advances in this area include methods for evaluating (1) platelet aggregation in response to ADP (5,6) or collagen and (2) platelet adhesiveness (7,8).

Quick (9) has recently proposed an aspirin tolerance test as a means of diagnosing occult pseudohemophilia (Von Willebrand's disease). More important to this study is his observation that acetyl salicylic acid also significantly prolongs the bleeding time in greater than 50% of normal controls. This observation, if confirmed, is highly pertinent to the study of aspirin induced gastrointestinal toxicity (emphasis on bleeding) currently being conducted in our hospital.

The evaluation of parameters influencing primary hemostasis before, during, and after the administration of aspirin to patients admitted to the study. Methods include the following:

1. Bleeding time (Duke, Ivy, and Borchgrevink methods).
2. Platelet aggregation in response to ADP (modification of the method of Thomas, et al, NEJM 276:1344, 1967).
3. Platelet adhesiveness (Method of Hellum, Scand J Clin Lab Invest 12:suppl 51, 1960; method of Salzman J Lab Clin Med 62:724, 1963).

In addition direct intravascular observations of the effects of aspirin addition to normal blood perfusing an actively metabolizing tissue: The Living Extracorporeal Eye (Seaman, et al, Arch Int Med 119:600, 1967 and Lutcher, et al, Clin Res 14:162, 1966) will be made.

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5, 6, 7, and 8. See preceeding page.

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THE RELATIONSHIP OF PERSISTENT HYPOCHLOREMIA TO THE BLOOD AND URINE NITRATE LEVELS DURING TOPICAL SILVER NITRATE THERAPY FOR EXTENSIVE BURNS

CPT Raymond J. McGroarty, MC

Patients treated with topical 0.5% Silver Nitrate sometimes develop severe and refractory hypochloremia, hyponatremia and at times hypokalemia. These abnormalities have been at times amazingly refractory to correction. According to Moyer, the abnormalities are produced by excessive loss of electrolytes at the burn site due to the hypotonicity of the silver nitrate solution (29.5 mEq/liter). This is probably one factor responsible for the observed abnormalities. However, there is another additional factor which has not been previously explored.

The nitrate anion is freely permeable to many biological membranes. It is absorbed at the burn site in animals when exposed to a bath containing nitrate in place of chloride. Nitrate is a known chloride diuretic and share a resorbtion mechanism with chloride in the kidney. Diuresis with nitrate also obligates a certain amount of sodium and potassium loss in the urine so that animals given an infusion of soidum nitrate will develop a hypochloremic alkalosis.

In view of the described potential of nitrate to produce a similar electrolyte disturbance to that described in the Silver Nitrate treated burn patients, we feel that investigation of blood and urine nitrate levels and electrolyte excretion is warranted. Preliminary work by principal investigator seems to validate the above.

Approach: 1. On patients being treated with Silver Nitrate - Blood and Urine - nitrate levels will be determined by a zinc reduction -- diazotization procedure or by the method of Walser.

2. Matched blood and 24 urine electrolytes will be determined for Na, K, Cl, CO_2 (PH and osmolarity if available).

3. An attempt will be made to correlate the degree of hypochloremia with the elevation in blood and urine nitrate levels.

Progress: Deferred.

USE OF PLACENTAL MEMBRANES IN BURN THERAPY

CPT George H. Latham, MC, et al

When a partial or full thickness burn occurs that area is vulnerable to many local complications in addition to causing system abnormalities.

There has been a constant search for a means of protecting the burn site in order to insure its preparedness for grafting and to prevent the conversion of a partial thickness to a full thickness burn. Recently silver nitrate solution and sulfamylon have been used topically to prevent infection. They have been shown to increase survival in burn patients, but it is felt that they delay grafting and disturb the electrolyte balance. Placental membranes have been suggested as a readily available tissue to cover burns with possible low antigenicity and ability to reduce loss of body fluids and to control infection.

This test is designed to test the efficacy of amnion in preventing fluid and protein loss and preparing the burn for autografting.

Patients for this study will have the following characteristics:

a. Patients of all ages with burns regardless of type or location.
b. Burns of 15% or greater.

Following admission the burn will be cleansed with Phisohex and superficially debrided. The burn will then be closed with a bulky dressing and begun on continuous 0.5% silver nitrate soaks (method of Moyer). If sulfamylon becomes available the silver nitrate will be stopped and that agent will be used.

At the earliest possible date the patient will be taken to the operating room where debridement will be done and autografting carried out on those areas of full thickness which are ready for autografting. If insufficient autograft is available, fresh amnion will be placed on the full and partial thickness areas. This will be allowed to remain until rejection occurs, healing occurs, or the area can be autografted.

Measurement to be made in this study is basically mortality and complications. The overall mortality of the patients will be compared to the expected values for the percent burn.

Summary and/or Conclusions: Deferred

RESEARCH AND TECHNOLOGY RESUME

2. GOVT ACCESSION	3. AGENCY ACCESSION	REPORT CONTROL SYMBOL
	NA	CSCRD-103

4. DATE OF RESUME	5. KIND OF RESUME	6. SECURITY	7. REGRADING	8. RELEASE LIMITATION	9. LEVEL OF RESUME
1 07 68	B. Completed	U	NA	OR	A. Work Unit

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11. TITLE: See Below

12. SCIENTIFIC OR TECH. AREA	13. START DATE	14. CRIT. COMPL. DATE	15. FUNDING AGENCY
003500 Clinical Medicine	NA	NA	Other DA

16. PROCURE. METHOD	17. CONTRACT/GRANT a. NUMBER / b. TYPE / c. DATE / d. AMOUNT	18. RESOURCES EST	a. PROFESSIONAL MAN-YEARS	b. FUNDS (In thousands)
C. In-House	NA / NA	PRIOR FY 68		Less than
		CURRENT FY 69	NA	$500 each

19. GOVT LAB/INSTALLATION ACTIVITY
NAME: Headquarters
ADDRESS: U.S. Army Medical Res & Dev Command
Washington, D. C. 20315
RESP. INDIV: Project Monitor
TEL: 202 - OX 65472

20. PERFORMING ORGANIZATION
NAME: Madigan Gen Hosp
ADDRESS: Tacoma, Washington 98431
INVESTIGATORS PRINCIPAL ASSOCIATE: See Below
TEL: 967-6511 TYPE: DA

21. TECHNOLOGY UTILIZATION: NA

22. COORDINATION: NA

23. KEYWORDS: Mycoplasma pneumoniae pneumonia; background incidence; allergic contact dermatitis; free milk samples; palatal anomalies; respiratory distress syndrome; synovial fluid; vagotomy; pyloroplasty; chromosome changes; live measles virus immunization; lymphadenopathy, children.

1. Universal Intra-Oral Retractor - LTC Schriver.
2. The Effects of Vagotomy and Pyloroplasty Procedures on Gastric Function in Dogs - MAJ James.
3. Chromosome Changes after Diagnostic Radioactive Iodine Tests - LTC Freeman.
4. Delayed Resolution in Mycoplasma Pneumoniae Pneumonia - LTC Ionno, et al.
5. An Investigation of Possible Attenuation of Allergic Contact Dermatitis with Live Virus Vaccination.
6. Hospital Dispensed Free Milk Samples: Their Effect on Influencing Parental Use for Infant Feeding - LTC Scherz, et al.
7. Evaluation of Palatal Anomalies and Apparent Hypohidrosis Inherited as an Autosomal Dominant - CPTs Hodgkin and Rapp.
8. Background Incidence of Mycoplasma Pneumoniae Infections in Basic Combat Trainees - LTC Ionno, et al.
9. Effect of Live Measles Virus Immunization on Circulating Antibodies - LTC Moyer.
10. The Effect of Heparin on Survival Rate of Lambs with Respiratory Distress Syndrome CPT Hodgkin, et al.
11. Concentration of Sodium Methicillin, Ampicillin and Cephalothin in Synovial Fluid Following Systemic Administration - CPT Lipscomb.
12. Blood Glucose Levels in Nonchilled Newborns - LTC Scherz, et al.
13. The Pathogenesis of Lymphadenopathy in Children - CPT Latham.

27. COMMUNICATIONS SECURITY	28.	29. DOD CODE	30. BUDGET CODE
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33. REQUESTING AGENCY	34. SPECIAL EQUIPMENT

35. EST. FUNDS (In thousands) CPY+1	36.

DD FORM 1 AUG 64 1498A (Items 1 to 26 identical to NASA Form 1121)

UNIVERSAL INTRA-ORAL RETRACTOR

LTC William R. Schriver, DC

This study has been completed. A single instrument has been designed, fabricated and clinically evaluated as an adjunct to the surgical removal of the mandibular third molar tooth. This retractor had basic surgical needs incorporated in a manner that maximum clinical needs could be obtained. Resulting from this investigation, it was found that because of the anatomical relationship of the third molar tooth in the human body and the complexity of its surgical removal that a single retractor of this nature is unsuitable.

EFFECTS OF VAGOTOMY AND PYLOROPLASTY PROCEDURES ON GASTRIC FUNCTION IN DOGS

MAJ Edwin C. James, MC

The use of vagotomy and a gastric drainage procedure for the treatment of duodenal ulcer disease has gained increasing popularity in the past decade. The most common method of gastric drainage employed is pyloroplasty. Numerous variations in pyloroplasty technique exist suggesting a diversity of opinion as to the funtional end result. The possible advantages of one pyloroplasty technique over another is not clearly defined either clinically or experimentally. The purpose of this pilot study is to investigate the effect of four types of pyloroplasty on gastroduodenal function in totally vagotomized dogs.

Initial and total gastric emptying times are determined in normal (8-12 Kg) mongrel dogs. After administration of barium sulfate 20 cc/Kg serial radiographs are taken to establish a control initial and total gastric emptying time. A minimum of two trials are run on each dog. Following establishment of normal values, each dog undergoes subdiaphragmatic bilateral vagotomy. At two weeks postoperation initial and total gastric emptying time is again determined. Those dogs which evidence a complete vagotomy are then given one of four different pyloroplastic procedures. All surgical procedures are under aseptic operative technique with 2 1/2% Surital and Metofane the principal anesthetics. Postpyloroplasty barium studies are performed at 2 - 4 weeks post operation.

To date 19 dogs have been submitted to operative procedures. Four dogs died during the early phase of the study. Two deaths were attributed to canine distemper and two were anesthetic complications. Refinement in anesthetic technique and equipment has alleviated this problem. Of the reamining 15 dogs, the study has been completed in all. No significant difference in gastric emptying time has been detected in the operative groups under study. However, the results have not yet been subjected to statistical analysis.

A modification in the initial protocol of this pilot study has been the inclusion of pyloromyotomy for comparison with the four variants of pyloroplasty.

While no definite conclusions are apparent without statistical analysis of the results, it appears that no significant difference in gastric emptying exists in the small groups of dogs studied. Pyloromyotomy would not seem to be as suitable as pyloroplasty because of the possibility of reformation of the pyloric sphincter by scar tissue which occurred in one of three pyloromyotomy dogs.

CHROMOSOME CHANGES AFTER DIAGNOSTIC RADIOACTIVE IODINE TESTS

LTC Mahlon V. R. Freeman, MC
MAJ Edward Christensen, MC

Placental localization utilizing scintillation counter scanning of the lower abdomen following the intravenous administration of radioactive iodine serum albumin (RAISA) has been advocated to evaluate the pregnant patient with third trimester bleeding suspected of having a placenta previa, because of greater reliability of the results and less tissue radiation to the fetus and mother as compared with soft tissue x-ray studies. Due to the low dosage of irradiation involved in diagnostic x-ray studies and radioisotope studies, a very sensitive method must be used to evaluate their relative safety. Chromosomal aberrations have been reported in adults and infants after diagnostic (Bloom, Migeon) and therapeutic x-ray studies (Buckton) as well as after therapeutic treatment with radioactive materials (MacDiarmid, Nofal) and in human leukocyte cultures treated with tritium labeled nucleic acid precursors (Bender). Thus, the frequency of such chromosomal aberrations would be a useful parameter in the evaluation of the radiation effects of RAISA.

If it were shown that there was no increase in the number of chromosomal aberrations in the peripheral blood of patients, both mother and fetus, exposed to RAISA as compared to patients receiving no radioactive materials, this would indicate a decreased incidence of chromosomal aberrations compared to patients exposed to diagnostic x-irradiation and consequently, would indicate diminished, potential or actual, chromosomal damage in the RAISA treated group, at least under the conditions involved in the study.

A pilot study to evaluate the incidence of chromosomal aberrations in the peripheral blood was initiated to estimate the practicality of a larger study utilizing this parameter to try and delineate the relative safety to the mother and the fetus in the use of RAISA in the last trimester of pregnancy.

Method - Ten ml. of peripheral venous blood was obtained from the patient when it was decided by the OB GYN service that the use of RAISA was indicated in the evaluation of the pregnant woman with third trimester vaginal bleeding. The blood was placed in a heparinized bottle and handled according to the instructions in the Difco kit. Metaphase figures were photographed on 35 mm high contrast black and white film utilizing a microscopic magnification on the film of 400 X. An attempt was made to select at least thirty cells per blood sample. Prints were made enlarging the cells to a final magnification of 1200 X. The prints were analyzed for total chromosome count and for structural abnormalities. Only chromosome and chromatid breaks were scored. Gaps were counted but not included in the analysis.

Similar analyses were done on blood samples obtained 48 hours after the RAISA study and again at the time of delivery or shortly thereafter. Cord blood samples were also obtained at delivery, if at all possible, or venous blood samples obtained from other sites on the infant, with parental permission.

Analysis of the photographic prints was done without knowledge of the type of blood sample from which they were obtained. All breaks were confirmed by another observer knowledgeable in the field of chromosome breaks.

Results - Of the 1450 metaphase figures photographed, 102 were not analysed due to poor chromosome separation, leaving 1348 prints which were analysed for chromosome count, chromatid and chromosome (iso-chromatid) breaks. Analysis was done on seven complete sets of blood samples (mother's prior to and 48 hours after exposure to RAISA and at the time of delivery and the infant's at delivery), five near complete sets (one of the four samples not obtained) and five sets prior to and 48 hours after RAISA injection.

Table I

Break rate in sample groups

Group	Number of Patients	Total Cells Analysed	Breaks	Percent Breaks
Prior to RAISA	18	443	4	0.68
48 hours After RAISA	15	410	7	1.71
At Delivery	10	257	3	1.13
Infant at Delivery	11	238	3	1.26
		1348	17	

Table II

a. Break rate in three patients receiving diagnostic x-ray to the pelvis one to six days prior to the RAISA study (one to three standard type diagnostic films per patient)

Group	Cells Analysed	Breaks	Percent Breaks
Prior to RAISA	68	2	2.94
48 hours after RAISA	92	1	1.09
	160	3	1.88

b. Break rate in fifteen patients not receiving pelvic x-ray

Group	Cells Analysed	Breaks	Percent Breaks
Prior to RAISA	375	2	0.56
48 hours after RAISA	318 693	6 8	1.89 1.30

Table III

Break rate in samples from infants born after maternal exposure to RAISA

Interval between Delivery and RAISA	Cells Analysed	Breaks	Percent Breaks
0-1 day	61	2	3.28
5-6 days	90	0	0.00
Over 7 days	87	1	1.15

Table IV

Percent of attempted cultures resulting in useable metaphase figures

Group	Samples	Not Useable	Percent Useable
Prior to RAISA	18	1	94.4
48 hours after RAISA	15	1	93.3
At Delivery	10	1	90.0
Infant at Delivery	11	3	72.7

Discussion - Analysis of the above tables does not reveal any significant differences in any of the groups of figures, however, there appears to be a trend, such as the higher baseline break rate in the group of patients with prior x-ray to the pelvis compared to the break rate in the group without such x-ray (Table II) which might become significant with larger samples. The difficulty encountered in growing newborn blood samples has been encountered before and seems quite variable. The lack of significant numbers of chromosomal aberrations indicates relative, if not definite, safety in the use of

RAISA in the third trimester of pregnancy. The low break rate in the control or baseline samples was unexpected but is quite variable from laboratory to laboratory and must be established for each laboratory. The utilization of the patient as a control seems to be the ideal situation but is not always practical.

Conclusion - If the same break rates would be found in a larger study under the same circumstances as this pilot study, the larger study would have to include at least a seven fold increase in the number of most of the groups to reach the range of statistical significance and would probably need to reach the range of a ten fold increase to be of great value. This would necessitate the study of at least 100 to 120 complete or near complete sets of blood samples (400 to 480 blood samples). Due to incomplete blood sampling, at least 125 patients would have to be studied. With the current incidence of third trimester bleeding, the study would extend over a five year period of time. In excess of 15,000 metaphase figures would have to be analysed, preferably, in the microscope or with photographic prints of the metaphase figures or both and would require at least final reading by an experienced cytogeneticist. The time, expense and effort required to do all of this does not seem indicated from the results of the pilot study.

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DELAYED RESOLUTION OF MYCOPLASMA PNEUMONIAE PNEUMONIA

LTC Joseph A. Ionno, MC
CPT Robert E. Westfall, MC

The purpose of this investigation is to identify those individuals who were admitted to Madigan General Hospital, Pulmonary Disease Service, with pneumonia due to mycoplasma pneumoniae. This patient population was analyzed with particular attention directed to defining the patients who had bronchograms performed in an attempt to determine as to whether or not bronchiectasis is a complication to the delayed resolution. Additional information will be characterization of the clinical course of the pneumonias due to mycoplasma pneumoniae and to accumulate statistics regarding the percentage of pneumonias caused by mycoplasma at our hospital.

An attempt was made to obtain acute and convalescent serum on all patients admitted to the Chest Service with a pneumonia from 1 October 1966 through 31 March 1967. The serum was then tested for mycoplasma pneumoniae complement fixing antibodies. The major technical problems consisted of:

a. Failure to obtain paired serum on some of the patients due to many factors.
b. Problems initially encountered with obtaining adequate supply of antigen.
c. A large volume of work for a single laboratory technician.

SUMMARY: Mycoplasma pneumoniae was found to account for 25% of pneumonias admitted to a hospital providing medical support for an Army training center as well as dependents and retired personnel. Sixty-nine (69%) percent of the cases of mycoplasma pneumoniae pneumonia were in the recruit population. The clinical prodromes as well as clinical course is characterized. Abnormal findings on auscultation of the lungs were present in 80% with wheezing being a prominent finding in 25% of the cases. The latter is felt to be due to bronchiolitis. A delay in resolution of pneumonia occurred in 11 individuals (24%) with four of these eleven having experienced wheezing. In addition, four patients were noted to have abnormalities of the bronchial tree related to their pneumonia.

DEPRESSION OF POISON IVY SKIN TESTS BY THE MEASLES VACCINE

MAJ Ralph Blumhardt
CPT Joseph E. Pappano
LTC Donald G. Moyer

INTRODUCTION

In 1908 von Pirquet[1] observed transient depression of tuberculin skin reactivity, the prototype of delayed hypersensitivity, following naturally occurring measles infection in children. When the measles vaccine became available, Mellman and Wetton[2] demonstrated transient depression of tuberculin skin sensitivity in children given the live attenuated measles virus vaccine. In 1964, Hildreth and Frederic[3] showed depression of tuberculin skin tests following administration of measles vaccine in adults already immune to measles. In the same study, they failed to demonstrate prolongation of skin homograft survival by the vaccine; homograft rejection probably being mediated through delayed hypersensitivity.

Live measles has been the most effective and most frequently studied vaccine causing depression of delayed hypersensitivity. Killed measles virus[4], Sabin oral polio[5], yellow fever[6] and influenza[7] have also been shown to cause mild, transient depression of the tuberculin skin test. The effect of the measles vaccine on most other manifestations of delayed hypersensitivity has not been investigated.

The purpose of the present study was to investigate the effect of the live, attenuated measles virus vaccine on allergic contact dermatitis to poison ivy, another form of delayed hypersensitivity.

METHOD

Ten healthy, adult caucasian male volunteers who had measles in childhood and were sensitive to poison ivy were patch tested with dilutions (1:10, 1:50, 1:100 and 1:500) of an acetone extracted poison ivy antigen* on the volar aspect of the forearm. The acetone dilutions of the poison ivy antigen were stored in air-tight, rubber-stoppered bottles at 4°C throughout the study. The antigens were applied by allowing one drop of each of the four dilutions as delivered through a 27-gauge needle, to fall to the skin from a height of approximately one centimeter with 2.5 cm between each drop. The areas were allowed to air dry and were then covered with Band-Aids for 12 hours. Subjects were instructed not to allow water to come into contact with the skin test sites for 12 hours.

* Poison Ivy Plant Oleoresin for Patch Testing from Hollister-Stier Laboratories, Spokane, Wash., Lot No. L75743012.

Retesting was done on alternate forearms with care being taken not to apply antigen to previously tested sites. The skin tests were read at 48 and 96 hours and again at seven days independently by at least two observers. When the observers varied in the grading of a set of skin tests, a consensus value was agreed upon. The results were recorded in the following manner:

0- - No reaction
1+ - Erythema
2+ - Erythema and Edema
3+ - Erythema, Edema and Microvescicles
4+ - Erythema, Edema and Macrovescicles

During the control period at least two sets of skin tests at 3 week intervals were performed on each subject. In all cases skin reactivity either remained the same or was increasing with subsequent tests. Five subjects then received 1 or 2 cc (1 or 2 doses+), subcutaneously, of the Schwarz strain live measles virus vaccine* and five subjects 1 or 2 cc, subcutaneously, of sterile saline. Two subjects first served as controls and were later given measles vaccine. The test subjects and two of the investigators were not aware of whether an individual received measles vaccine or saline when reading post injection skin tests. Skin tests with poison ivy, as described above, were repeated at approximately one, three, six and nine weeks following the measles vaccine or saline injection.

RESULTS

The results are summarized in Table I. Only the 96 hour readings are shown since this was the time at which the skin tests were found to be most reactive and reproducible. The control values shown, with at least two sets of skin tests at three week intervals being done on each individual, were the final prevaccination skin test reactions obtained.

All subjects given live measles virus vaccine showed suppression of their skin reactivity to poison ivy antigen. The maximum degree of depression occurred at the third or sixth week post-vaccination test in these individuals. Several subjects were skin tested at 9 and 12 weeks following measles vaccinations and in all cases the degree of skin sensitivity to poison ivy had either returned to or was approaching baseline values. None of the control subjects demonstrated significant suppression.

+ The study was planned to determine whether two doses of measles vaccine gave greater depression than one dose. The small number of subjects in our study does not permit evaluation of this.

* Measles Virus Vaccine, Live, Attenuated (Schwarz Strain). Lyophilized, from Pitman-Moore Division of the Dow Chemical Company, Indianapolis, Ind., Lot No. 185-210.

A crude quantitation of the reactivity of a set of skin tests to poison ivy can be obtained by numerically adding the degree of positivity (0 to 4+) of the four dilutions of antigen. On this basis, all test subjects receiving the measles vaccine had a reduction to 50% or less of their control values (Table 1). The average reduction for the group was to 33% of the control value.

DISCUSSION

Transient depression of tuberculin skin reactivity following measles[1] or influenza[8] virus infections and following administration of a number of vaccines[2-7] has been well documented. An attempt to extend these observations to the delayed hypersensitivity of contact dermatitis to poison ivy was undertaken. In this study, even though the number of subjects is small, a significant degree of depression occurred in all individuals given the Schwarz strain measles vaccine. Maximum depression occurred at three and six weeks post-immunization and in all subjects the degree of reactivity was returning toward control values by the ninth to twelfth week. The depression, therefore, as in most similar studies, appears to be temporary.

Our results indicate that allergic contact dermatitis to poison ivy antigen is depressed transiently by the administration of live, attenuated measles virus vaccine. The mechanism of this depression is unknown. The effect may be on skin reactivity, or on the cells that mediate delayed hypersensitivity, presumably lymphocytes and plasma cells, or on both.

The effect on poison ivy reactivity was dramatic enough to suggest that live measles virus immunization might be useful if given to poison ivy sensitive individuals who anticipate exposure to the Rhus family: poison ivy, oak and sumac. The fact that the person has had naturally occurring measles should not negate this effect as all our test subjects had had measles.

SUMMARY

The degree of sensitivity to varying dilutions of a poison ivy antigen was established by patch tests in seven individuals. Administration of the Schwarz strain measles vaccine to this small group of subjects resulted in a temporary reduction of sensitivity most marked (33% of control values) between the third to sixth weeks post-immunization. At nine weeks the sensitivity was returning to pre-immunization levels. Five control subjects showed no change in their degree of sensitivity.

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Table 1

96-HOUR SKIN TEST RESULTS TO POISON IVY FOLLOWING MEASLES VACCINE

Control Reading			Post-Injection Readings			Units Change Between Control and Lowest Value	Lowest Value as % of Control
Subject	abcd		1 week abcd	3 weeks abcd	6 weeks abcd		
D.M.	4443	Measles Vaccine	4441	3220	4440	-8	47%
J.P.	4330		3332	4220	3100	-6	40%
D.G.	3100		2100	2100	2000	-2	50%
J.H.	2220		2100	2000	2200	-4	33%
W.C.	4440		4220	3000	4200	-9	25%
R.B.+	2220		----	1000	2220	-5	17%
J.M.+	3222		----	2000	2000	-7	22%
						Avg. -5.9*	Avg.33%
R.B.	2220	Saline	2210	2210	2222	-1	83%
J.M.	3332		3330	3320	3222	-3	73%
B.P.	4200		----	4200	3321	0	100%
D.R.	2000		2100	2100	2100	+1	150%
B.P.	3320		4220	----	----	0	100%
						Avg. -0.6	Avg.101%

+ - Individual used as control prior to receiving measles vaccine.
Acetone dilutions of poison ivy antigen: a=1:10, b = 1:50, c = 1:100 and d = 1:500.
* $p < .01$ by t test.

HOSPITAL DISPENSED FREE MILK SAMPLES: THEIR EFFECT ON INFLUENCING PARENTAL USE FOR INFANT FEEDING

LTC Robert G. Scherz, MC
CPT Richard D. Landes, MC

An attempt has been made to determine some of the factors involved in the choosing of an infant formula by a parent.

Two groups of infants were collected with 200 infants in each group. In both groups Similac was used in the nursery. No effort was made to hide this fact if mothers asked although they were told that any of the proprietary formulas or evaporated milk formulas were satisfactory. It is our custom to give samples of formula to mothers and infants at discharge. Hence, one group was given samples of Bakers formula at the time of discharge from the hospital. The other was given samples of either SMA, Enfamil or Similac. At the time of their six weeks check, the mothers were told of the study and asked for comments upon why they chose a particular formula. Our initial goal was to determine the effect of distribution of samples upon mothers' final choice of formula for their infant. Several interesting sidelights became evident during the course of the study and are included. The accumulated data is tabulated in Tables 1 and 2.

Other trends revealed by the study are as follows:

1. Of 111 infants in the study on whom we have records of three month checkups, 81 were receiving prepared formula, 30 whole milk. Our advice has been to continue prepared formula until 5 to 6 months of age. At six months of age 18 of 22 infants were on whole milk with four being still on prepared formula.

2. Sixty-four of 200 mothers in one group and 62 of 200 mothers in the other group attempted to breast feed their infants (approximately 32%). Of these only 29 of one group and 27 of the other breast fed their infants six weeks or more (14% of all mothers or one-half of those attempting. Of the 111 infants seen at 3 months of age only 9 (approximately 8%) were still being breast fed.

We present this data because we found it helpful in looking at our own attitudes toward choice of formulas for newborn infants. We realize that the number of infants in some of the groups is very small but feel that the trends are worth mentioning.

TABLE 1

	Breast Only	Bakers	SMA	Enfamil	Similac	Modilac	Skim or Whole Milk	Pet	Carnation	Lactum
Bakers at Discharge (200)	8% (15)	16% (33)	1% (2)	8% (17)	50% (99)	2% (3)	2% (5)	4% (8)	8% (17)	L 1% (1)
Similac at Discharge (144)	6% (8)		2% (3)	3% (5)	72% (103)	L 1% (1)	6% (9)	L 1% (1)	7% (10)	
SMA at discharge (27)	24% (6)		36% (9)	4% (1)	4% (1)		12% (3)	8% (2)	16% (4)	
Enfamil at Discharge (26)	16% (4)		4% (1)	76% (19)					8% (2)	

TABLE 2

Major comments - Reasons for choosing a formula:

1. Other children (or grandmother's children) did well on it.
2. Available at commissary.
3. Used in hospital.
4. Friends recommended it.
5. Baby prefers it.

Second Group

1. Convenience of mixing and of disposable simple feeding containers.
2. "Closest to breast feeding".
3. Suggested in pamphlet given to mother.
4. Friend or parent picked it up at store.
5. Less expensive (or most expensive!).
6. Ease of mixing.
7. Recommended by Dr. or Nurse.

Reasons for avoiding:

1. Spit up
2. Diarrhea
3. Constipation
4. "Too rich"
5. Upset stomach
6. Hunger not satisfied
7. Infant wouldn't drink it
8. "Hocus pocus"- vague reasons!

ANHIDROTIC ECTODERMAL DYSPLASIA: AUTOSOMAL DOMINANT INHERITANCE WITH PALATE AND LIP ANOMALIES

CPT Robert S. Rapp, MC
CPT William E. Hodgkin, MC

INTRODUCTION

Ectodermal dysplasia involves faulty development of embryonic ectoderm and its subsequent derivatives. Cochayne (1933) described 200 defects of ectodermal origin. Two categories of ectodermal dysplasia can be formed based on the capacity to sweat (Weech, 1929). The hidrotic form is autosomal dominant and characterized by thick, short, slow growing nails and fragile sparse hair. The anhidrotic variety manifests hypotrichosis, hypodontia and hypohidrosis. This paper reports a kindred including an affected mother, daughter and son manifesting hypohidrotic ectodermal dysplasia with palate and lip anomalies. In this family genetic transmission is most likely autosomal dominant.

CASE REPORTS

Case 1. B.R. is a thirty year old caucasian female with a history of inability to sweat, slow hair growth and poor dental development. An unexplained temperature elevation was noted at three days of age. This established a pattern of frequent headaches, dizziness and fatigue whenever environmental temperature increased or vigorous physical activity was required.

Considerable coarse, wiry scalp hair was present at birth. Subsequent hair growth was slow with little improvement in quality and a wig was purchased at age thirteen for cosmetic purposes. General body hair has been sparse with the exception of normal pubic hair.

At age eleven a full set of dentures was obtained due to numerous caries and a decreased number of teeth. Only one-half the number of expected teeth were present. No mention is made of abnormally shaped or positioned teeth. A unilateral (left) cleft palate with no lip involvement and disfigured nails on all digits were noted at birth. A poorly defined thyroid disorder requiring "up to six grains of thyroid per day" was described during adolescence. It has been of no consequence since and no further information is available regarding it.

Physical Examination: This is an obese, middle age female in apparent good health. Her head shows mild frontal bossing with minimal depression of the nasal bridge. Pseudorhages are noted at the mouth corners but none are noted at the naso-labial fold. The scalp is shaved as a wig is being worn. Eyebrows are absent laterally and sparse growth is present medially. Eyelashes are sparse and the tarsal plate is red and inflamed. No axillary or pubic hair is present. Little hair growth is present on the remaining body. A full set of dentures and evidence of a repaired (left) cleft palate are noted in the mouth. Dystrophic nails with distal soft tissue

tufting is noted on all digits. The nails are disfigured, small and have no longitudinal fissuring. The breasts are multiparous and fully developed. The remaining physical examination is within normal limits. Laboratory data is non-contributory except for an audiogram which showed a thirty decibel conductive type hearing loss.

Case 2. J.R., age six, the oldest of three siblings is the product of a normal pregnancy and delivery. Since birth she has had short, slow growing, wiry hair which has been difficult to manage. Dental development has been slow and she possesses only seven teeth all of which are carious. The incisors are short and square shaped. Sweat production has been noted over her back and posterior neck. Little difficulty with hyperthermia has been encountered in warm weather and she has no limitation of her activities. Disfigured nails are present on all fingers and toes. Plastic surgeons have described a short soft palate with no uvula and a marked limitation of motion. This has been documented with cinefluoroscopic examination.

Physical Examination: Examination of the head reveals minimal frontal prominence with a mildly depressed nasal bridge. No pseudorhages are present at the mouth or naso-labial fold. The uvual is absent and soft palate tissue is scant. Square shaped, worn upper canine teeth are present. Four lower incisors are carious and worn. Her hair is coarse, short and wiry. Eyebrows are scant and eyelashes sparse. All nails are small and misshapened. There are no fissures or soft tissue tufting.

Case 3. K.R., age 20 months, is the product of a normal pregnancy and delivery. Hair growth has been slow on the scalp, eyelashes and eyebrows. Dental development is slow as only seven teeth are present. He sweats on his back, forehead, and neck and hyperthermia has been a minimal problem. Episodes of purulent conjunctivitis have been frequent.

Physical Examination: The examination revealed a well nourished child in good health. The forehead is prominent with mild depression of nasal bridge. A left cleft lip (repaired) and bilateral cleft palate (repaired) are present. Seven teeth have erupted, all are normally placed and shaped. The hair is coarse and wiry. Eyebrows are sparse laterally. The tarsal plate shows evidence of chronic inflamation. All nails are dystrophic with marked soft tissue tufting.

METHOD FOR DETERMINATION OF HYPOHIDROSIS

Affected family members were subject to three parameters of testing to document hypohidrosis and to delineate the functional capacity of the sweat gland.

Sweat Test (Iontophoresis method): A sweat test was performed on the right and left forearm of all family members. This area normally contains 150-200 sweat glands per cubic centimeter (Kuno, 1956). Pilocarpine was the stimulating agent and the patient was subjected to 1.5 milliamperes current for a total of five minutes. Total weight of sweat produced was measured.

Skin Biopsy: A four millimeter skin biopsy was taken on B.R. from an area adjacent to that previously stimulated by iontophoresis to determine if sweat glands were absent or merely atrophic and non-functioning.

Elevated Environmental Temperature: B. R. and J. R. were then compared to a control in their ability to produce sweat in an elevated environmental temperature. K. R. was not challenged. The indicator system chosen is described by Wagner (1952) and consisted of a solution containing 15 gram of iodine, 100 ml castor oil and 900 ml of alcohol. This was painted on the skin and allowed to dry. A fine powdered potato starch was then carefully applied to the skin. Each individual was placed in a Sauna bath at a temperature of 180°F and a relative humidity of 5%. Oral temperatures were recorded before and after exposure. The time required for sweat to appear was recorded for each individual. Exposure was terminated when onset of symptoms consistent with hyperthermia appeared. Photographs of involved members were taken before and after exposure.

RESULTS OF TESTING

The skin biopsy from the left forearm of B.R. disclosed no hair follicles, sweat gland tubules or abnormalities of collagen fibers. Lack of sweat glands and hair follicles is not pathognomonic of the syndrome but their absence in an area normally endowed with a plentiful supply is consistent with the clinical observation.

Stimulation of eccrine secretion with a routine sweat test yielded total secretion weighing less than 30 mg in affected members. B.R. produced 20 mg, J.R. 20 mg and K.R. 26 mg of sweat. J.R., the unaffected member, produced 90 mg of total sweat. Failure to produce adequate sweat volume following chemical stimulation represents another area in which physiologic response is suboptimal.

Eccrine stimulation by increasing environmental temperature showed marked contrast in response as compared to a normal control. The control experienced a temperature increase from 97°F to 99°F, B.R. from 99°F to 100°F and J.R. from 99°F to 99.7°F. After three minutes exposure the control showed fine, black, pinpoint areas of sweat production followed in one to two minutes by larger coalescing areas. At seven minutes beads of sweat rolled down his face, neck and chest, washing away the chemical indicator.

B.R. showed twenty-five to fifty black pinpoint areas of color change on the posterior neck at 3 1/2 minutes. After four minutes of stimulation a fine black semicircle, 1/2 x 4 cm, developed in the intertriginous area of her left breast and a sharply circumscribed oval 1 x 1.5 cm was noted at the medial aspect of her left wrist. This area exhibited the most intense color change. At no time did coalescing areas develop.

J.R. showed several areas of sweat production. Most noticeable was that over the right and left paravertebral masculature. Additionally, sweat activity was apparent on the extensor surface of her hands and very minimally over her brow. Exposure was concluded for all persons at ten minutes when B.R. complained of occipital headache, dizziness and fatigue.

DISCUSSION

Many excellent reviews are available regarding the clinical characteristics of anhidrotic ectodermal dysplasia (Helwig-Larsen, 1946; Upshaw-Montgomery, 1949; Marshall, 1959; Butterworth, 1962).

Hypohidrosis during raised environmental temperature, low sweat volume during pilocarpine stimulation, and lack of sweat glands in skin biopsy places this kindred in the hypohidrotic category. The exact mode of inheritance of anhidrotic ectodermal dysplasia is difficult to delineate. This suggests a multifactorial causation producing similar clinical states. Cochayne (1933) described an X-linked recessive form in families with affected males and an autosomal dominant inheritance in families with affected females. Helvig-Larsen (1946) states that the anhidrotic variety with dominant inheritance exhibits only partial expression of the gene. Upshaw(1949) concluded that the syndrome can be transmitted as a sex linked recessive or autosomal dominant or recessive trait. Kerr (1966) felt that reported cases of dominant inheritance were "recorded without adequate detail or were very atypical".

In this kindred no family history of anomalies consistent with ectodermal dysplasia or palatal anomalies could be elicited. Palatal and lip anomalies have not been previously reported with anhidrotic ectodermal dysplasia. Setlies (1963) reports a family with a midline scar beneath the lower lip. By description it was not a cleft lip and no mention is made of palatal anomalies.

B.R., J.R. and K.R. (by history and pilocarpine stimulation) show full expression and concordance of the mutant gene or genes and probably represent an autosomal dominant form of inheritance. From available information, no definitive statement can be made regarding ectodermal dysplasia and palate anomalies stemming from a single mutant gene or two genes.

SUMMARY

A family manifesting hypohidrotic ectodermal dysplasia and anomalies of palate and lip is described. Females in the family exhibit full expression of the trait. An autosomal dominant form of transmission is postulated. Palate and lip anomalies appear concurrent with extodermal defects.

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BACKGROUND INCIDENCE OF MYCOPLASMA PNEUMONIAE INFECTIONS IN BASIC COMBAT TRAINEES

LTC Joseph A. Ionno, MC, et al

The primary purpose of this particular study is to determine factors which may be associated with poor resolution and/or complications thereof. As this particular study develops, it is apparent that there may be a significant incidence of non-clinical infections due to mycoplasma pneumoniae in the basic combat trainee. As far as is known to the investigators, a study of this type has not been accomplished in the past and is sorely needed to truly appreciate the incidence of clinical or overt disease due to this organism.

A basic combat training unit was studied from its inception to the time of completion of training period and at suitable time intervals; blood specimens were obtained as well as a simple questionnaire filled out by each subject. In addition, 50 of these individuals were selected on a random basis to be followed for culture of the mycoplasma pneumoniae organism. The results of this study have recently been completed and there is an incidence of positive complement fixation test to the organism under study in 11.5% with a smaller percent showing a fourfold rise in titer during the time period under study. In addition, there were a number of individuals who were seen at the dispensary and/or hospitalized, the results of which are being tabulated and quantified. The results of this study are being prepared for submission for publication.

EFFECT OF LIVE MEASLES VIRUS IMMUNIZATION ON CIRCULATING ANTIBODIES

LTC Donald G. Moyer, MC

Live measles virus immunization has been shown to cause a decrease in subject reactivity to PPD (1-2) and to poison ivy antigen (3). In these studies the skin has been used as the indicator. A direct effect of measles virus on skin has not been eliminated as an explanation for the results. A study of the effect of measles virus on circulating antibodies may indicate whether the skin itself or antibodies are affected.

Initially, a group of 30 adult volunteers had H and O typhoid and paratyphoid B titers to establish the presence of significant titer. Three weeks later a second specimen was drawn and 15 were given a live measles virus immunization and 15 saline. The specimen sera was frozen. Three and six weeks following the shot, specimens were drawn and frozen. All specimens had titers run at the same time. The results were studied for significance.

The typhoid-paratyphoid antibody titers on all subjects have been determined. There was no consistent change in the antibody titers as a result of measles vaccination. No further studies are planned.

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THE EFFECT OF HEPARIN ON HYALINE MEMBRANE FORMATION

CPT William E. Hodgkin, MC, et al

INTRODUCTION

Idiopathic respiratory distress syndrome has been estimated to cause 25,000 deaths per year in the United States. The majority of infants who live for several hours prior to death develop an eosinophilic membrane composed of fibrin [1], benzidine positive material[2] and cellular debris in the alveoli and alveolar ducts.

Predisposing factors include prematurity, delivery by cesarean section (especially if there has been vaginal bleeding) and maternal diabetes.

The pathogenesis of the respiratory distress syndrome is not completely clear. Systemic hypotension [3] and pulmonary hypoperfusion [4] are well documented. Precipitating and complicating factors are hypoxemia, acidemia, hypothermia and hypovolemia. Low plasma proteins and decreased fibrinolytic enzymes have been associated with respiratory distress syndrome. Recommended and clinical trial therapies have included delayed clamping of the cord, oxygen administration, maintaining body temperature and correcting acid-base imbalance. Less common therapies have utilized serum albumin, aerosols to reduce surface tension, fibrinolysins by aerosol and acetylcholine given into the right atrium to decrease pulmonary vasoconstriction.

This study was designed to explore the hypothesis that pulmonary intravascular thrombosis is a major factor in the development of hyaline membranes just as intravascular thrombosis appears to be a major component of purpura fulminans [5] and some cases of meningococcal sepsis.

If this hypothesis is correct, the pathogenesis for the premature infant might then be as follows:

1. Reflex vasoconstriction resulting from hypoxemia, hypothermia and in some cases hypovolemia.

2. Acidosis and hypoxemia increase with arteriovenous admixture due to increased right to left shunt thereby causing increased vasoconstriction and hypoperfusion.

3. The vasoconstriction and hypoperfusion allow thrombosis in capillaries and other small vessels with subsequent capillary damage and transudation of blood products into the alveoli.

4. Hypofibrinogenemia and thrombocytopenia develop as thrombi form.

5. With lysis, vascular continuity is reestablished.

6. There is then resorption of water and low molecular weight substances leaving fibrin and other blood products in the alveoli.

By heparinizing the patient one should be able to interrupt this cycle and prevent the full development of hyaline membranes.

This study was designed to determine if disseminated intravascular coagulation plays a significant role in the development of hyaline membrane disease in the fetal lamb.

METHODS

Results are summarized in Tables 1 and 2.

In the human with generalized, consumptive coagulopathy, one of the earliest laboratory findings is a marked thrombocytopenia. Table 1 shows concordance or discordance of platelet levels between the treated and control lambs. Nonconcordance with the controls platelet level decreased and the heparin's platelet level stable would favor the hypothesis. All others would suggest that disseminated intravascular coagulopathy does not play a significant part in the formation of hyaline membrane disease. Only four of thirteen matched pairs showed decreased platelets in the control but not in the heparinized animal. Of seven control animals which developed hyaline membranes four or 57% showed significantly decreased platelets. Of five heparinized animals which developed hyaline membrane disease three or 60% showed significantly decreased platelet levels.

Table 2 shows the results of hyaline membrane production in heparinized and control lambs. Of nine pairs in which the control animal developed hyaline membrane disease, five heparinized animals developed hyaline membranes.

Of thirteen animals delivered at 136 days gestation or less and lived 1 hour or more, eleven (89%) developed hyaline membranes. All five heparinized animals that developed hyaline membranes were 136 days gestation or less and received the 300 u/Kg/4 hour dosage of heparin.

Of ten lambs, seven heparinized and three controls, 138 days or longer gestation, and who lived one hour or more, only one (C9), a control, developed hyaline membranes.

In six lambs given 30,000 u/Kg/4 hours (age 135-144 days gestation) none developed hyaline membranes while two of the four controls (135-144 days gestation) did have hyaline membranes.

Tissue specimens from nine animals of which eight had hyaline membranes were studied by use of Pearse's PAS hematoxylin stain. No evidence of intravascular fibrin thrombi was found.

Two animals in the 30,000 u heparin per Kg/4 hour showed soft tissue, intra-alveolar and perivascular hemorrhage. One control animal showed similar findings (Appendix 1).

CONCLUSION

Hyaline membranes developed in both heparinized and control animals. Six lambs receiving heparin at 30,000 u/Kg/4 hours did not develop hyaline membranes. However, the number of lambs studied is insufficient to comment on the significance of this observation. Two of the four control animals in this group failed to develop hyaline membranes.

There was no evidence of pulmonary intravascular fibrin thrombus formation in either the control or heparinized animals who developed hyaline membrane disease.

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APPENDIX I

Effect of Heparin on Survival Rate of Lambs with Respiratory Distress Syndrome

C1 Vasodilation
Lungs - desquamation of bronchiolus epithelium
Alveolar walls - slight thickening with hyaline amorphous material

C2 Early hyaline membrane formation
Thickening of alveolar walls

C3 Liver - extramedullary hematopoiesis
Lung - good hyaline membrane disease

C4 Lung - good hyaline membrane disease
Liver - extramedullary hematopoiesis

C5 Intra-alveolar hemorrhage and moderate hyaline membrane

C6 Mild hyaline membrane - hemorrhage in respiratory atrium and respiratory bronchials

C7 Atelectasis - no hyaline membrane disease

C8 No hyaline membrane disease

C9 Mild hyaline membrane disease

H1 Lung - Slight protein membrane formation

H2 Lung - good hyaline membrane
Liver - extramedullary hematopoiesis

H3 Lung - good hyaline membrane
Liver - extramedullary hematopoiesis

H4 Liver - extramedullary hematopoiesis
Lung - no hyaline membrane

H5 Lung - early hyaline membrane - marked congestion
Liver - extramedullary hematopoiesis

APPENDIX I (Cont):

H6	Mild hyaline membrane disease
H7	Atelectasis - no hyaline membrane disease
H8	Soft tissue hemorrhage in lung Intra-alveolar and intra-vascular hemorrhage No hyaline membrane disease
H10	No hyaline membrane disease
H11	No hyaline membrane disease
H12	No hyaline membrane disease
H13	Soft tissue hemorrhage and intra-alveolar hemorrhage Hemorrhage in vessels in lung
H14	No hyaline membrane disease
H15	No hyaline membrane disease
H16	Soft tissue hemorrhage - intra-alveolar hemorrhage

TABLE 1

H SHEEP	GEST	PLATELETS ↑ ↓ →	CONTROL SHEEP	GEST	PLATELETS ↑ ↓ →	CONCORDANCE HEP.CONT.
H 1	127	↓	C 1	127	→	No ↓ →
H 2	130	↓	C 2	130	→	No ↓ →
H 3	130	↓	C 3	130	↓	Yes ↓ ↓
H 4	134	→	C 4	134	↓	No → ↓
H 5	134	→	C 4	134	↓	No → ↓
H 6	136	↓	C 5	135	↓	Yes ↓ ↓
H 7	135	→	C 6	135	↓	No → ↓
H 8	138	→	C 9	138	→	Yes → →
H 9	140	DOA	C 7	141	↑	
H 10	140	→	C 7	141	↑	No → ↑
H 11	141	→	C 7	141	↑	No → ↑
H 12	144	→	C 8	144	↓	No → ↓
H 13	138	→	C 9	138	→	Yes → →
H 14	140	↓	C 7	141	↑	No ↓ ↑
H 15	136		C 5	137		
H 16	136		C 5	137		

↑ Platelets increased to twice that level in the cord blood at sometime

↓ Platelets decreased to one-half that level in the cord blood at sometime

→ No change to twice the level of platelets or to one-half the number in the cord blood

TABLE 2

H - Sheep #	GEST	HM	HRS LIVED	CONTROL #	GEST	HM	HRS LIVED	CONCORDANCE	H	C
H1 - 5068	127	+	1	C1 - 5068	127	+	1 1/4	Yes	+	+
H2 - 0117	130	+	4 1/2	C2 - 0130	130	+	2 1/2	Yes	+	+
H3 - 5062	130	+	3	C3 - 0110	130	+	8 1/4	Yes	+	+
H4 - 5028	134	-	1	C4 - 0107	134	+	24	No	-	+
H5 - 0101	134	+	3 1/4	C4 - 0107	134	+	24	Yes	+	+
H6 - 5247	136	+	6 1/4	C5 - 5246	135	+	9 1/4	Yes	+	+
H7 - 5437	135	-	12	C6 - 2277	135	+	6 1/2	No	-	+
H8 - 5041	138	-	1	C9 - 2295	138	+	5 1/4	No	-	+
DOA H9 - 5494	140	DOA		C7 - 5497	141	-	12			
H10 - 5250	140	-	1	C7 - 5497	141	-	12	Yes	-	-
H11 - 5500	141	-	12	C7 - 5497	141	-	12	Yes	-	-
H12 - 5501	144	-	12	C8 - 5501	144	-	12	Yes	-	-
H13 - 4087	138	-	4	C9 - 2295	138	+	5 1/4	No	-	+
H14 - 2540	140	-	12	C7 - 5497	141	-	12	Yes	-	-
H15 - 3204	136	-	1/4	C5 - 5246	135	+	9 1/4			
H16 - 3204	136	-	1/4	C5 - 5246	135	+	9 1/4			

CONCENTRATION OF SODIUM METHICILLIN, AMPICILLIN AND CEPHALOTHIN IN SYNOVIAL FLUID FOLLOWING SYSTEMIC ADMINISTRATION

CPT Robert W. Lipscomb, VC

BACKGROUND AND PURPOSE OF STUDY: Penicillin administered to man and animals by the intramuscular, intravenous or subcutaneous routes has been shown to appear rapidly in the blood serum and to be excreted in the urine. Clinical observations by both Herrell and Dawson indicated that effective antibacterial amounts of penicillin may be obtained in joint fluid following administration. Administration of aqueous penicillin by the intramuscular and subcutaneous routes yield maximum blood levels in 15 to 30 minutes. It has been shown that some fractions of the penicillin lose 50% of their antibacterial activity due to binding to plasma protein. The diffusion of penicillin into tissues and fluids occurs as long as the unbound plasma concentration exceeds that of the tissues and fluids.

It has been shown that potassium penicillin G crosses into synovial fluid in therapeutic amounts. This has not been shown with the synthetic and semi-synthetic penicillins. With the exception of penicillin, the literature is sparse on the diffusion of antibiotics into synovial fluid when administered either parenterally or orally. Jacson discussed this topic after using procaine penicillin, potassium penicillin G, streptomycin, oxytetracycline, chlortetracycline, and chloramphenical in patients with hydarthrosis of the knee. He found only penicillin G diffused consistently into the knee.

Ortiz duplicated much of this work, concluding that much remained to be done in regard to diffusion of antibiotics into joints before there could be reliance on the use of systemic antibiotics alone for the treatment of joint infections.

Balboni, et al, demonstrated an equal concentration of penicillin in the synovial fluid (infected) and serum one hour after systemic injection of aqueous crystalline penicillin. The concentration in the joint fluid decreased much more slowly than it did from the serum. Morgan, et al, have shown that diffusion of antibiotics into the joint space is related to the molecular weight of the drug, and that the lower the molecular weight the more rapid and complete the diffusion.

The most common pathogens found in septic arthritis are Staphylococci Aureus and beta hemolytic streptococci. In children Hemophilus influenza arthritis seems to be quite prevalent. Other less common pathogens of the joint are Salmonella species, Neisseria species and staphylococcus albus.

Ampicillin has proven quite effective against Hemophilus influenza, hemolytic and non-hemolytic streptococci, nonpenicillinase-producing staphylococci, Neisseria and some strains of Salmonella and Shigella.

Sodium Methicillin, Ampicillin and Cephalothin - Lipscomb

Methicillin shows high efficacy against penicillinase producing staphylococci. Cephalothin has been shown to be effective against the above mentioned pathogens. This drug may be given to individuals allergic to the penicillins.

METHOD OF PROCEDURE: This study is designed to obtain answers to the following questions: a. How well does Ampicillin, Methicillin and Cephalothin penetrate the synovial membrane?

b. Is there a difference in penetration of an inflammed joint versus a normal joint?

Fifteen dogs with normal joints will be included. Each joint will be assumed normal if there has been no evidence of systemic disease for one month and no history or clinical evidence of disease in the joint.

Subjects will receive 150 mg/Kg/day of Methicillin or Ampicillin or 80mg/Kg/day Cephalothin. Two methods of administration will be used: Single intramuscular injection and single rapid intravenous injection. One quarter of the daily dose will be used for the administration in each method.

Synovial fluid samples will be obtained at 1/2 hour, 1 hour, 3 hours, 6 hours and 24 hours. Blood samples will be collected concomitantly with joint fluid samples. Cultures will be obtained on joint fluid samples as indicated. After a ten day rest period the experiment will be re-run on the same animals by a different route of administration of the antibiotic. A different joint will be used for the second trial.

The third portion of the experiment is designed to evaluate synovial fluid levels of antibiotic in inflammed joints. One or two cc's of autogenous blood injected into the synovial space will be used to develop inflammation and hydrathrosis. Subjects will then receive intramuscular and intravenous injections of antibiotic and resultant blood and synovial fluid levels ascertained.

DISCUSSION: Synovial fluid and serum samples were taken after systemic injection of each drug on 15 dogs each. These samples were collected at 1/2 hour, 1 hour, 3 hours, 6 hours and 24 hours post-injection. Attempts to bio-assay the fluids for the specific drug were made. However, the extreme variability in the results, even in paired samples taken at the same time, suggest that the bio-assay process was not reliable. Due to this fact, the project will be terminated with no statistical proof of the hypothesis.

It may be well to note, however, that both Ampicillin and Methicillin were in the blood and synovial fluid at about the same time in bactericidal levels. The intravenous route of administration resulted in higher levels than did the intramuscular route and lasted about the same time prior to a drop in the levels. Both levels and synovial fluid levels were about the same at 1/2 hour after administration and remained essentially the same for about 3 hours. Between 3 and 6 hours post-injection the intramuscular route gave slightly higher levels in both drugs after which both drugs were below therapeutic levels. Results of work with Cephalothin were inconclusive.

CONCLUSION: No statistical results are available, but from a clinical standpoint using staphococcal infection of the joint, both Ampicillin and Methicillin yielded the joint sterile within 60 hours post-injection by either the intravenous or intramuscular route.

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BLOOD GLUCOSE LEVELS IN NONCHILLED NEWBORNS

CPT Richard D. Landes, MC

This study has been designed to study the effects of early feeding of normothermic newborn infants using 5% dextrose water and to establish normal values for blood sugar levels in those infants.

Recent studies have indicated that the blood sugar of the newborn, especially premature and low birth weight infants, falls to dangerously low levels shortly after birth. Some investigators have suggested that low body temperature exaggerates this hypoglycemia.

Three groups of infants are being studied and they are:

I - Full term infants of normal birth weight .

II - Premature infants whose gestational age is less than 37.0 weeks and birth weight less than 5.5 lbs.

III - Low birth weight infants, meaning those whose birth weight is below the 25th percentile for gestational age.

To date the following number of infants have been studied:

I - Full term infants - 24
II - Premature infants - 14
III - Low birth weight infants - 16

Attached are the results obtained from those studied.

PLAN: Additional infants will be studied in the numbers as indicated below:

I - Full term - 0
II - Premature infants - 6
III - Low birth weight infants - 4

5% GLUCOSE

NORMOTHERMIC FULL-TERM INFANTS

Relationship between Blood Sugar and Age

Age (Hours)	No. of Determinations	Mean	Range	
Cord	40	87.05	163	56
1	48	48.10	80	21
2	46	46.76	80	22
4	46	47.17	71	28
6	47	45.65	64	26
12	47	46.73	70	18
18	45	52.65	85	33
24	48	53.97	83	32
48	44	54.57	75	39
72	43	61.48	86	37

5% GLUCOSE

NORMOTHERMIC PREMATURE INFANTS

Relationship between Blood Sugar and Age

Age (Hours)	No. of Determinations	Mean	Range	
Cord	28	73.5	55	106
1	28	30.65	4.2	77
2	26	30.15	2.8	63
4	25	45.69	6.5	83
6	26	52.64	4.3	85
12	24	47.32	4.7	98
18	24	41.73	4.2	89
24	24	42.25	4.3	69
48	22	47.21	4.2	71
72	22	55.05	4.2	79

5% GLUCOSE

NORMOTHERMIC TERM UNDERWEIGHT INFANTS

Relationship between Blood Sugar and Age

Age (Hours)	No. of Determinations	Mean	Range	
Cord	29	65.18	12	104
1	29	47.74	28	66
2	29	51.60	34	71
4	30	50.5	32	75
6	29	43.1	25	71
12	29	52.36	32	102
18	30	51.65	31	70
24	30	55.21	34	85
48	30	53.88	42	80
72	28	64.34	48	82

THE PATHOGENESIS OF LYMPHADENOPATHY IN CHILDREN

CPT Robert S. Rapp, MC
CPT George H. Latham, MC

A frequent diagnostic problem in the pediatric age group is cervical lymphadenopathy. Various etiologic factors have been brought to light in numerous publications (1,2,3,4,5,6). Little information is available in text or current literature regarding the role of virus as a causative factor.

The purpose of this study was to deliniate the relative importance of three considerations: (1) The relationship of virus infections to cervical lymphadenopathy. (2) The concurrence of bacterial and viral infections and (3) The frequency of pathogens other than viruses.

The patients studied were selected from the Pediatric Outpatient Service and the Emergency Room of Madigan General Hospital. Criteria for selection was patients with cervical lymphadenopathy measuring at least 2.5 x 2.5 cm and who had received no antibiotics. Patients were included on a consecutive basis and were examined by one of the investigators. Two days after the initial visit the patient was reevaluated in light of culture and skin test results. Twelve days later the CBS and sedimentation rate were repeated, a convalescent serum drawn and an antistreptolysin titer and heterophile agglutination test were performed at that time.

Needle aspiration of all nodes were performed using sterile technique and topical anesthesia. If no fluid was readily obtained, 2 ml of .9% sodium chloride solution were injected and withdrawn.

The aspirate was submitted for viral bacteriological and fungal cultures. In addition, nose and throat cultures were obtained for bacteria. A pharyngeal washing was included in the viral studies.

A total of 20 patients were included in the study with the following etiologies found:

Streptococcus	7
Staphylococcus	4
Cat Scratch	1
Infectious Mononucleosis	1
Undiagnosed	7

None of the viral cultures were productive of any viruses. One problem which may account for negative viral cultures is the fact that the materials had to be transported from Madigan General Hospital to Fort Baker, San Francisco, California. Since many viruses are quite temperature sensitive, they may have been destroyed intransit.

A more formalized evaluation of this study is presently being prepared and will be submitted to the research committee in addition to being published in a medical journal.

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RESEARCH AND TECHNOLOGY RESUME

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003500 Clinical Medicine	NA	NA	Other DA

16. PROCURE. METHOD	17. CONTRACT/GRANT a. NUMBER b. TYPE c. DATE d. AMOUNT	18. RESOURCES EST.	a. PROFESSIONAL MAN-YEARS	b. FUNDS (In thousands)
C. In-House	NA NA	PRIOR FY 68		Less than
		CURRENT FY 69	NA	$500 each

19. GOV'T LAB/INSTALLATION/ACTIVITY	20. PERFORMING ORGANIZATION
NAME Headquarters	NAME Madigan Gen Hosp
ADDRESS U.S. Army Medical Res & Dev Command Washington, D. C. 20315	ADDRESS Tacoma, Washington 98431
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TEL. 202 - OX 65472	TEL 967-6511 TYPE DA

21. TECHNOLOGY UTILIZATION	22 COORDINATION
NA	NA

23. KEYWORDS: Inflatable dorsal glove-splint; epididymitis; ampicillin; heel balance; dental erosion.

24.

1. The Relationship of Shoe Heel Height to Forefoot - Heel Balance - MAJ Marx.
2. The Efficacy of Cortisone and Butazolidin in the Treatment of Epididymitis - LTC Ceccarelli.
3. The Rash with Ampicillin - CPT Pappano.
4. Feasibility of Inflatable Dorsal Glove-Splint as an Aid to Rehabilitation of Extension to Digits of the Habd - MAJ Boggs.
5. Comprehensive Study of Dental Erosion with Particular Emphasis on Patients with Hematological, Endocrine, Gastric, Renal and Periodontal Disorder - CPT Fausett.
6. Evaluation of Multifocal Contact Lens - MAJ Barnett

25.

27. COMMUNICATIONS SECURITY	28.	29. DOD CODE	30. BUDGET CODE
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33. REQUESTING AGENCY	34. SPECIAL EQUIPMENT

35. EST. FUNDS (In thousands)	36.
CPY++	

DD FORM 1 AUG 64 1498A (Items 1 to 26 identical to NASA Form 1122)

THE RELATIONSHIP OF SHOE HEEL HEIGHT TO FOREFOOT-HEEL BALANCE

MAJ Ralph L. Marx, MC

An improper balance of the body weight on different parts of the foot produces foot strain manifested by the clinical conditions of march fracture, ligamentous strain, plantar hyperkerratosis and metatarsalgia. The weight distribution between the forefoot and heel are affected by the age of the individual, tightness of the heel cord and shoe heel height.

The normal values of forefoot-heel weight distribution in adult and child have been determined experimentally. The relationship of shoe heel height and tightness of the heel cord on forefoot-heel balance has not been studied experimentally.

Our approach to the problem was to purchase an apparatus which determined the amount of weight borne on the various parts of the foot. The heel height was then varied and a determination of the shift of weight was made. Several hundred individuals were placed on the foot balance indicator. It was determined that there was little relationship between the height of the heel and the weight distribution between the foreparts of the foot and the heel. It has been found that patients with a tight heel cord did have a foot imbalance and that most of the weight was on the forefoot. It was further learned that this weight would often be directed to either the medial or lateral aspect of the foot. Further clinical trials were discontinued as the study was terminated due to departure of principal investigator.

THE EFFICACY OF CORTISONE AND BUTAZOLIDIN IN THE TREATMENT OF EPIDIDYMITIS

LTC Frank E. Ceccarelli, MC
CPT Gordon H. Deen, MC

Estimates made during WWII and the Korean conflict have concluded that acute non-gonococcal epididymitis was a major cause of duty time lost in the military.

Personal communications have implied that Cortisone and Butazolidin have been very efficacious in reducing the hospitalization secondary to this disease.

Approximately 43 patients were studied. Preliminary evaluation of those completed show the mean days of hospitalization to be:

Control	8.0 days
Prednisone treated	9.2 days
Butazolidin treated	9.2 days

This study has been terminated due to PCS of both investigators.

THE RASH WITH AMPICILLIN

MAJ Joe D. Corless, MC, et al

A generalized, maculopapular, erythematous eruption has been noted in a number of children in association with ampicillin therapy. The eruptions are mildly pruritic and last 3 to 5 days. A 3% incidence of rash with ampicillin has been observed at this hospital as part of a study of four therapeutic regimes for acute otitis media. Other authors such as Breese, et al[1] report an incidence of rash up to 17%.

The exact etiology of this rash is unclear. Because it may be allergic, eight children were evaluated in this clinic. Negative penicilloyl polylysine, benzyl penicillin G and ampicillin skin tests plus negative penicillin hemagglutination antibody titers were obtained. Subsequent oral challenge with phenoxymethyl penicillin resulted in no allergic reaction. Three children have subsequently had ten day courses of oral penicillin without apparent hypersensitivity reaction. These results suggested that significant penicillin allergy did not occur. Therefore, it was proposed that another, larger group of children with ampicillin rash be studied. Parental consent will be obtained in writing for the oral challenges with penicillin and ampicillin. Full explanation will be given to the parents based upon the results of negative skin tests and negative penicillin hemagglutination titers.

Patients utilized were from a comparative study of phenoxymethylpenicillin and ampicillin given equally to each of 100 children with streptococcal pharyngitis and from the general clinic population. The former group was used to determine incidence. To date two patients with rash have been found from 74 included in the pharyngitis study. Four additional patients with an apparent ampicillin rash have been found. Allergy history and skin testing have been completed, all the latter being negative. Penicillin hemagglutination titers are pending prior to the final step of oral challenge.

In August 1967 three more patients with rash were added to the study. Penicillin hemagglutination titers on all patients except one were negative. On one patient the titer was 1:16 which was felt to be significant. Four patients were challenged with penicillin with no untoward reaction including the one with the elevated titer. Because that patient's skin tests were negative the challenge was advised. Two patients were challenged with ampicillin including the latter with the significant reaciton.

This study has been terminated due to PCS of the investigators. Also, the reduced number of ampicillin treated infections during the summer months did not provide patients eligible for the study.

REFERENCE

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FEASIBILITY OF INFLATABLE DORSAL GLOVE-SPLINT AS AN AID TO REHABILITATION OF EXTENSION TO DIGITS OF HAND

MAJ Grace R. Boggs, AMSG

In striving for rehabilitation of disabled hands considerable difficulty has been experienced in obtaining extension of digits of the hand. This is mainly due to the fact that grasp (flexion) is the natural activity of accomplishment while release (extension) occurs to permit further appropriate grasp.

Review of literature reveals no practical means of obtaining extension in restoration of hand function. It is known that the astronauts when wearing the inflated glove of the space suit have difficulty in grasp, thus more easily obtain extension. Therefore, through therapeutic application and use of the Inflatable Dorsal Glove-splint, it is possible that earlier return to normal function may be facilitated.

The purpose of this study is to establish the feasibility of the Inflatable Dorsal Glove-splint as a practical means of regaining digital extension of the hand.

The Inflatable Dorsal Glove-splint which has been conceived will be further developed to treat patients who through trauma or disease are unable to extend digits. The following goals will be kept in mind:

1. Materials - non-irritating and durable
2. Design - simplicity
3. Minimal weight and bulk
4. Establish controlled and appropriate means of inflation to be regulated manually and/or automatically.

When prescribed by the doctor, prototypes of the Inflatable Dorsal Glove-splint will be applied to patients with inability to obtain digital extension. An appropriate form will be used to record pertinent information including diagnosis, extent of limitation, treatment media, duration and results of application of the Inflatable Dorsal Glove-splint, recommendations for improvement, acceptability of Inflatable Dorsal Glove-splint as an aid to rehabilitation of disabled hands and so forth.

A portion of the bladder of a Sphygmomanometer with two tubes, one tube to the Manometer and the second tube to the inflation bulb, has been sealed to dorsal distal end of metacarpal area of autopsy lates glove with entrance to cuff sealed, thus permiting glove to be inflated. It is planned that additional areas of the glove will be sealed off appropriately to treat specific conditions.

The major problems contine to be to find an accurate, dependable and permanent sealant of the glove-splint material to itself and/or inclusion of tubes and other indicated parts.

As the investigator is going PCS from Madigan General Hospital, the study will be terminated at this time.

INCIDENCE OF DENTAL EROSION: EMPHASIS ON ITS INITIATION AND PROGRESSION IN PATIENTS WITH LOCAL ORAL CONDITIONS AND CERTAIN CHRONIC SYSTEMIC CONDITIONS

CPT Phillip D. Fausett, DC

The cause of erosion is involved in the utmost obscurity, Most observers have drawn their opinions of its causation from the observation of the circumstances attending a comparatively small number of cases coming under their personal observation (1), Brushing the teeth may have some role in the causation or spread of the lesion (2); neurological disturbances, bacterial, gland action and hyposaturation of the saliva with calcium and phosphorous salts have all been postulated. These opinions along with many others may be found in the literature reaching back some two hundred years. There appears to be no present theory that does not have features that seem to render it impossible (1).

The purpose of this study is to gain statistical evidence relating to the incidence of dental erosion; its prevalence and progression in patients with certain chronic systemic conditions, particularly those with renal, gastric, endocrine and hematological disorders. To compare the above information with a sample group of patients in an attempt to gain information on the etiology and progression of erosion other than mechanical abrasion by tooth brushing.

Methods and Materials:

The direct oral examination of 1,500 patients presenting to the Department of Dentistry. The patients were a random selection as they presented to the hospital for various dental complaints and routine oral examination. This was to establish a baseline for statistical purposes. In addition, selected patients seen by other practitioners were referred if they presented with erosion. This was done to compile 500 cases of erosion for detailed data collection and examination of their condition. The data collection sheet was developed to facilitate computerizing of the results. One hundred inpatients were also examined.

This study has been terminated due to PCS of the principal investigator.

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EVALUATION OF MULTIFOCAL CONTACT LENS

MAJ Howard J. Barnett, MSC

Several years ago the investigator invented a multifocal contact lens. Because there was no really successful bifocal or multifocal contact lens available and because of the success of this new lens, the Office of The Surgeon General recommended that the Department of the Army patent the lens in the name of the inventor provided only that the United States Government receive, from the inventor, an irrevocable royalty free license to use the lens for governmental purposes.

A patent application for this lens (called The Barnett Multifocal Contact Lens), the process by which it is manufactured and the instrument to manufacture it has been filed in the U.S. Patent Office.

In presbyopia and aphakia the accomodative function is either reduced or eliminated. Therefore, in those cases, a bifocal or multifocal contact lens is required if the patient is to see both far and near with the same lens and without the use of spectacles.

The bifocal contact lenses currently available are extremely difficult to fit (most require a prism ballast and/or truncation), very expensive and are seldom successful even in cases where no injury has been sustained. There are diplopia, blurring, distortion of field and objects appear curved as the division line between the two different foci passes in front of the pupil. In cases of iris loss, resulting in a larger pupil, this distortion is even more noticeable.

Since the power of the Barnett Multifocal Contact Lens changes gradually from distance to intermediate to near (i.e., a true multifocal lens; not just a smeared or blurred area separating a far and near portion) and has in the past eliminated these problems in cases of presbyopia and aphakia without iris loss, it is the purpose of this study to evaluate subject lens in these cases with varying amounts of iris loss through iridectomy and/or injury especially in monocular cases.

Here there can be no single binocular vision with a spectacle lens or lenses because of the great size disparity. Therefore, a contact lens is necessary if fusion, single binocular vision and depth perception are to be achieved.

With a single vision contact lens these objectives can be reached at 20 feet or greater. However, at distances less than 20 feet the aphakic or presbyopic eye, having lost its ability to focus within 20 feet cannot achieve fusion, single binocular vision, or depth perception due to the disparity in image clarity. Therefore, only with a true multifocal contact lens can these goals be reached at all distances.

Multifocal Contact Lens - Barnett

In monocular aphakia with iris loss we have the most difficult of situations with one eye having a normal accommodating crystalline lens requiring no contact lens and the other eye having no crystalline lens and therefore requiring a multifocal contact lens if the two eyes are to work as a team at all distances.

To date two patients have been fitted. Initially a control lens of the ordinary single vision type was fitted to these patients by the investigator to eliminate the variable of fitting technique and to have a basis for comparison between the single vision lens and the multifocal lens. The results follow:

I. Subject #1

* Visual Acuity

Unaided

Far (20 ft)
O.D. = 20/15+
O.S. = 20/L.P.
O.U. = 20/20

Near (16")
O.D. = J-1
O.S. = L.P.
O.U. = J-1-

Intermediate (O.D.)
16 ft = 16/16
12 ft = 12/12
30" = J-1
20" = J-1

O.S. Light perception only at all distances

* NOTE: American Optical Company Project-O-Chart was used and properly adjusted for correct size at the various distances. A.O. reading card was used for near point acuities.

Aided with Single Vision Contact Lens (O.S.)
Far (20 ft) 20/15
Near (16") Light perception only
Intermediate
16 ft = 16/16
12 ft = 12/12-2
30" = Light perception
20" = Light perception

Aided with the Barnett Multifocal Contact Lens (O.S. & O.U.)
Far (20 ft) = 20/15
Near (16") = J-1
Intermediate
16 ft = 16/16
12 ft = 12/12
8 ft = 8/8
30" = J-1
20" = J-1

Worth 4 Dot Test (For fusion)
Unaided = No fusion at any distance
Aided with single vision contact lens
20 ft = passed
16 ft = passed
12 ft = passed
8 ft = questionable
30" = failed
20" = failed

Aided with Multifocal Lens
20 ft = passed
16 ft = passed
12 ft = passed
8 ft = passed
30" = passed
20" = passed

Verhoeff Sterropter Test for Depth Perception
Unaided = failed
With single vision lens = failed
With Multifocal Lens = passed

II. Subject #2 - Due to illness, operations (bilateral leg amputation) and psychological problems, and refractive changes in the eye which were just discovered, subject recently has been unable to use the lens, even though initially the lens was successful.

III. Since no other subjects can be found for this pilot study and because funds are almost depleted, it is felt that this study should be terminated at this time.

RESEARCH AND TECHNOLOGY RESUME

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003500 Clinical Medicine	NA	NA	Other DA

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C. In-House	NA / NA	PRIOR FY 68	Less than
		CURRENT FY 69 NA	$500 each

19. GOVT LAB/INSTALLATION/ACTIVITY	20. PERFORMING ORGANIZATION
NAME Headquarters	NAME Madigan Gen Hosp
ADDRESS U.S. Army Medical Res & Dev Command Washington, D. C. 20315	ADDRESS Tacoma, Washington 98431
RESP. INDIV. Project Monitor	INVESTIGATORS PRINCIPAL ASSOCIATE See Below
TEL 202 - OX 65472	TEL 967-6511 TYPE DA

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1. Techniques in Experimental Hydrocephalus and Development of Ventriculo Sagittal Sinus Shunt - LTC Gallo.
2. The Influence of Surgical Excision of the Periosteum and Chemical Destruction of the Outer Dura and Bone Regeneration in Mongrel Puppies - LTC Gallo.
3. Regeneration Rates in "Oblique" Suture Anastomosis of Peripheral Nerves - LTC Gallo.
4. Accidental Poisoning of Children in a Military Setting - LTC Scherz; CPT Latham and BG Crone.
5, Clinical and Serologic Differentiation of Rubella from Other Viral Exanthems Admitted to the Rubella Ward - LTC Ionno and CPT Bybee.

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TECHNIQUES IN EXPERIMENTAL HYDROCEPHALUS WITH DEVELOPMENT OF VENTRICULO SAGITTAL SINUS SHUNT

LTC Anthony E. Gallo, Jr., MC

The purpose of this study is to design a shunting system to transport cerebral spinal fluid from the lateral ventricle to the sagittal sinus, and thus eliminate the many problems associated with the effect of growth of the shunting function.

Approach: A series of mongrel and beagle dogs are rendered hydrocephalic by the injection of Kaolin into the cisterna magna. After adequate documentation, they are treated with a Ventriculo Sagittal Shunt of special design (modification of the Pudenz Ventriculo Atrial Shunt) with a hepacone coating.

Progress: This study is essentially at a standstill since the last quarterly report due to the insufficient neurosurgical staffing. To date, two preparations have been accomplished in dogs and a single infant maintained a functioning shunt for 11 months.

THE INFLUENCE OF SURGICAL EXCISION OF THE PERIOSTEUM AND CHEMICAL DESTRUCTION OF THE OUTER DURA AND BONE REGENERATION IN MONGREL PUPPIES

LTC Anthony E. Gallo, Jr., MC

The purpose of this study is to demonstrate the influence of dura externa on skull regeneration in mongrel puppies and hopefully to get further insight into the treatment of craniosynostosis.

Approach: Bilateral trephine were performed in a series of mongrel puppies and destruction of the dura accomplished with direct application of Zenkers solution. The intact skull dura and underlying brain was then prepared for sectioning after extended intervals of x-ray documentation of bone growth.

Progress: Sectioning of these specimens continues and awaits microscopic evaluation. Some conclusions can be drawn at this time:

1. Destruction of the dura retards the rate of bone regeneration approximately 50% in puppies under the age of six weeks. Its affect is less obvious in older puppies.

2. There is invariable associated brain injury with destruction of the dura by a three minute application of Zenkers solution and this method (described in the literature) is inappropriate for clinical application in the treatment of craniosynostosis.

REGENERATION RATES IN "OBLIQUE" SUTURE ANASTOMOSIS OF PERIPHERAL NERVES

LTC Anthony E. GAllo, Jr., MC

The purpose of this study is to see if peripheral nerve regeneration across a suture anastomotic site can be improved by an oblique suture anastomosis, thus increasing the surface area of the anastomosis approximately 50%.

Approach: Seven mongrel dogs had bilateral sciatic nerve sectioning and suture anastomosis, with each dog serving as its own control having one as an anastomosis in conventional fashion and the other obliquely. The dogs were followed with serial EMG's and photographs. Movies of their gait improvement were performed to document changes objectively. The anastomotic site was harvested for microscopic sectioning and axonal counting.

Progress: All specimens have been harvested and well fixed in blocks awaiting sectioning and microscopic analysis by the pathology department.

ACCIDENTAL POISONING OF CHILDREN IN A MILITARY SETTING

LTC Robert G. Scherz, MC, et al

The purpose of this study is to evaluate the epidemiology of childhood poisoning in this area with the objective of developing preventative and treatment programs that will reduce incidence, morbidity and mortality.

The approach has been a careful review of each accidental poisoning and the tabulation of pertinent statistical information.

Important strides have been made during the last 12 months in the evaluation and use of child-resistant containers to dispense all appropriate prescription tablet and capsules from Madigan General Hospital and McChord Air Force Base pharmacies. Based on our studies here, the test container has been adapted as a standard item by DOD. It is now available for use throughout the world. The expected reduction in childhood poisonings by direct and indirect effects of 10,000,000 child-resistant containers ordered initially by DOD is 6,000 among children receiving outpatient care from the Army, Navy, Air Force and Public Health Medical facilities. It is also anticipated there will be about 1,000 fewer hospitalizations for treatment of poisoning by the same large group of children. Based on our studies here, this container has been adopted as a standard item by a large civilian drug store chain (500 company stores and 900 agencies). It is anticipated that widespread use of the test container will produce a significant decrease in childhood poisonings due to tablet and capsule prescriptions in the United States.

Studies with child-resistant containers have been productive of two papers submitted for publication and two papers presented at national meetings, plus numerous lectures to professional, lay and television audiences during the last 12 months.

Research will continue to be active in this pilot project. It is anticipated that additional short term pilot projects will be generated from this study as needs for additional funding become evident.

CLINICAL AND SEROLOGIC DIFFERENTIATION OF RUBELLA FROM OTHER VIRAL EXANTHEMS ADMITTED TO THE RUBELLA WARD

CPT Joseph D. Bybee, MC
LTC Joseph A. Ionno, MC

The purpose of this study is to determine what clinical parameters, if any, differentiates patients with rubella from patients from other viral exanthems admitted to the hospital.

A history and physical examination is recorded at the time of admission and a blood specimen for acute phase serum obtained. At a return visit three weeks later a convalescent specimen is obtained. The paired sera are tested for a change in titer by the hemagglutination inhibition test against standard rubella antigen.

A total of 46 acute and convalescent sera together with the appropriate clinical information have been obtained. Currently technical problems in performing the hemagglutination inhibition test are being resolved by consultation with other institutions where this procedure is operative.

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13. ABSTRACT

A Progress report on the research program at Madigan General Hospital, Tacoma, Washington for the fiscal year 1968 is presented.

The research projects put forth in this report are directed toward the implementation of experimental studies in the field of clinical medicine.

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