NASA CR-172018

Final Report - NASA CONTRACT #NAS9-16688

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Prevention of Disuse Osteoporosis:

Effect of Sodium Fluoride During Five Weeks of Bed Rest

I. INTRODUCTION

A. OBJECTIVE

The overall objective of this research is to attempt to modify factors which promote disuse osteoporosis and thereby prevent it from occurring.

B. BACKGROUND

Disuse Osteoporosis: Bone mineral is lost when the mechanical factors present during normal ambulation are removed. Negative calcium balance and/or osteopenia have been observed during several clinical and experimental conditions in people including acute and convalescent phases of paralytic anterior poliomyelitis (2), immobilization due to casting in both fracture patients (3) and normal young men (4) and in space travel (5). The mechanism of bone loss is thought to be a normal adaptive function upon exposure to hypogravic states (7). A reproducible model of disuse osteopenia in studies of healthy young males during prolonged bed rest without immobilization has been developed (4,6,8). Using bed rest as a model to produce disuse osteoporosis, calcium loss from the whole skeleton has been measured by balance techniques and averages 0.5% of total body calcium per month (6,8). Ten fold greater rates of loss from the central portion of the calcaneus have been observed by gamma ray transmission scanning (6,8).

Mineral loss during bed rest is probably due to a reduction in the forces which are applied to the skeleton during normal activity (4,6,8). These one "G" homeostatic forces are absent also in the hypogravic environment of space flight. Loss of bone mineral during space flight is expected on theoretical grounds and has been confirmed in the Skylab experiments (5,9). This factor might prove hazardous to astronauts on flights of long duration, not only because hypercalciuria might lead to the formation of renal calculi during flight, but axial skeletal fractures may occur upon re-entry to earth's gravity.

The need to reduce these hazards has led to a series of experiments. Various therapeutic attempts to prevent the negative

(NASA-CR-172018) PREVENTION OF DISUSE OSTEOPOROSIS: EFFECT OF SODIUM FLUORIDE DURING FIVE WEEKS OF BED REST Final Report (Texas Univ.) 64 p Avail: NTIS HC A04/MF A01 CSCL 06E G3/52
N88-10483
Unclas
0104953

calcium balance and loss of calcaneal density during prolonged bed rest have met with only limited success. Other studies designed to apply either compressive and/or tensile forces to the skeleton during bed rest have been performed. Unfortunately these studies were not able to demonstrate a direct effect of either in preventing disuse osteoporosis. Mechanical methods tried were: 1) Use of the Exergenie apparatus (6) which consisted of a rope which was pulled back and forth through a pulley, the friction of which was preset to provide 8 lbs of resistance. An exercise program was performed in the supine position for 80 minutes per day. This program failed to diminish any of the metabolic changes of bed rest and did not prevent mineral loss from the calcaneus. 2) Longitudinal compression was attempted using the gravitational acceleration simulating suit (@GASS). This was tested in two ways: (@a) static compression applying 80% of the body weight from the shoulders to the soles of the feet for 3 hours daily (6,10); and (@b) intermittent longitudinal compression at a rate of 45 compressions/min for 200 min/day (6). This treatment did not prevent the negative calcium balance nor the usual loss of calcaneal mineral. 3) Impact loading of the axial skeleton to create piezoelectrical forces was tested (6). Thirty-five lbs of impact load to each heel and compression of 80% of body weight to the axial skeleton was performed 6 hours daily. Although calcaneal mineral density remained the same or increased during this therapy, overall calcium loss was equal to that in untreated bed rest. 4) Quiet standing was studied; i.e., the subject stood without lifting either foot for 3 hours each day (11). Neither calcaneal mineral density nor calcium balance was protected. 5) Three hours of quiet standing plus 20 min. of bicycle ergometry exercise daily did not provide any protection (11). 6) Three hours of normal ambulation plus 21 hours of bed rest started after 6 weeks of total demonstrated some protection from the usual negative calcium balance (11).

Five biochemical regimens have been studied: 1) synthetic salmon calcitonin (10), a hormone which inhibits bone resorption (@100 MRC U), was given daily by injection during 8 weeks of bed rest; 2) phosphate supplements in order to reduce urinary calcium excretion was given in divided doses as a neutral potassium salt (12); 3) oral calcium and phosphate with the hope that the former would increase calcium absorption from the intestine while the latter would decrease calcium excretion in the urine was given in divided doses (6,12); and 4) the diphosphonate EHDP either as a 5 mg/kg/day dose or as a 20 mg/kg/day dose (13). Little or no protection was afforded by the first three methods during long-term bed rest. Low dose diphosphonate showed no beneficial effect.

The high dose EHDP appeared to have a protective effect starting in the 16th of 20 weeks of bed rest. The effects of the 20 mg/kg/day dose was assessed by three largely independent techniques: 1) metabolic balance; 2) 125I gamma ray transmission scanning of the calcaneus; and 3) 47Ca kinetic studies. In weeks 2-12, the usual patterns of hypercalciuria, hyperphosphaturia and negative calcium and phosphorus balances were seen. During the last 8 weeks of bed rest, a shift towards positive calcium and phosphorus balance occurred. Urinary hydroxyproline excretion decreased in distinct contrast to the rise which is usually seen. The serum phosphorus level rose promptly, persisted at levels about 3 mg/dl above baseline during EHDP therapy and fell to normal levels promptly upon discontinuation of the drug. Serum alkaline phosphatase values tended to decline throughout the treatment period. Serum total and ionized calcium concentrations remained unchanged during the 20 weeks of bed rest. The subjects lost significant amounts of mineral from the calcaneus during the first 17 weeks of bed rest. During the last 3 weeks of bed rest, the usual progression of calcaneal mineral loss was no longer observed. Calcium kinetic studies during therapy revealed that bone accretion and resorption rates fell progressively and in parallel fashion to levels 50% below baseline by the end of bed rest.

Clodronate, another diphosphonate, prevented disuse osteoporosis during 17 weeks of bed rest (6); however, this drug has been withdrawn from clinical investigation.

Fluoride is currently used to enhance bone formation in the treatment of low turnover osteoporosis. In previous short term bed rest (@5 weeks), 20 mg F given as a sodium fluoride divided into three doses was not effective in reducing calcium balance loss. Fluoride balance was found to be positive suggesting that fluoride in small doses and given for a short period of time could not change the usual disuse osteoporosis of bed rest. Concern was voice that high levels of fluoride ion may have been available for only short periods of time and therefore was not able to change bed rest induced calcium changes. We hypothesized that if the fluoride ion was available over a much longer period of time, e.g. as could now be accomplished by a slow release wax matrix preparation, fluoride would slow the loss of calcium by 1) inhibiting bone resorption and 2) enhancing bone formation.

EFFECT OF SODIUM FLUORIDE ON BONE MINERAL LOSS DURING BED REST

A. HYPOTHESIS

To determine whether low levels of sodium fluoride can prevent bone mineral loss during five weeks of bed rest.

B. INTRODUCTION

Industrial workers exposed to moderate doses of compounds containing fluoride and people who ingest higher than usual F in their daily water may develop asymptomatic increased skeletal radiodensity (14,20). In 1961, F treatment for osteoporosis was tried by Rich and Ensinck (15) in hopes that the induction of sub-clinical fluorosis might strengthen an osteopenic skeleton. They reported that calcium retention ensued.

F substitutes for the hydroxyl group in the hydroxyapatite crystal which leads to a less soluble crystal system (36). F also stimulates osteoblastic activity (34,35), and therefore, with adequate calcium intake, calcium retention is enhanced (16).

High dose F has been known to cause a crippling bone disease characterized by dense bones, exostoses and neurological complications due to bony overgrowth and ligamentous calcification. When given in small doses (@less than 25 mg F ion), little or no problems have been reported in the literature (16). The side effects from low dose F include gastric irritation (@which is usually obviated when the F is given with meals, by enteric coated tablets or in a slow release was matrix form); transient arthralgia and stiffness of the joints may rarely occur.

To determine whether smaller doses of F would increase calcium balance without causing severe side effects, we studied ambulatory (18) and bed rested subjects receiving 5 or 10 mg F daily. These low doses of F did not cause changes in calcium balances in the ambulatory subjects and did not protect against bed rest induced calcium loss. Therefore the effects of 20 mg F daily were studied (xx). This is the minimal dose usually used therapeutically. We were not able to show any decrease in calcium loss by balance technique. However, since fluoride has been shown in other studies to increase bone mass, we felt that there must be an incremental fluoride effect in both its bone resorption protection and bone formation stimulation. The fluoride in the previously reported study was given to the research subjects as fast absorbing sodium fluoride in divided doses an hour before each meal. This would have caused extremely high blood levels of flouride for short periods followed by long periods of time without additional fluoride. Therefore slow release wax matrix embedded sodium fluoride was given so a constant increase of fluoride ion would be absorbed.

C. SPECIFIC AIMS

1. To determine whether oral medication with sodium F will modify or prevent 5 weeks of bed rest induced disuse osteoporosis as assessed by standard metabolic balance, lumbar vertebrae and calcaneus, and Tc99m MDP kinetic techniques.

2. To determine the longitudinal effects of 5 weeks of bed rest on PTH, CT and calcitriol on controls and treated subjects.

3. To measure muscle volume changes and metabolic activity by magnetic resonance imaging and magnetic resonance spectroscopy techniques during prolonged bed rest.

4. To measure changes in peak muscle strength and

muscle fatigability during prolonged bed rest.

5. To measure bone turnover in bone biopsies during prolonged bed rest.

D. METHODS OF PROCEDURE

Subjects were studied during 1 week of equilibration, 4 weeks of control ambulation, 5 weeks of bed rest, and 1 week of reambulation. Progress was monitored by: (@a) calcium, phosphorus, and nitrogen balance studies and urinary hydroxyproline and creatinine; (@b) gamma ray transmission scanning of the calcaneus, and lumbar vertebrae; (@c) Tc99m MDP kinetic studies; (@d) fasting hormonal responses during ambulation and bed rest; (@e) magnetic resonance imaging of the leg (@f) Cybex muscle strength testing; and (@f) bone biopsy.

A. RESEARCH SUBJECTS

Eighteen subjects were studied during 11 weeks of continuous metabolic ward living; 12 received F and 6 served as untreated controls. Random assignment of therapeutic choices occurred.

The subjects were males between the ages of 22-61, who respond to a request for research subjects from the general population. The volunteers were screened by the PI and members of the Clinical Research Center staff. Routine laboratory screening was done prior to acceptance to rule out any ongoing health problems which would be cause for subject exclusion. The research subjects were made employees of Krug International, Houston, Tx 77058 and were entitled to worker's compensation for any untoward effects during the study. No ill effects were reported nor could we determine that any had occurred from this study.

Each subject participating in the study provided the investigator with signed consent, which gave the investigator permission to study the volunteer. The consent form indicated that the volunteer had been informed about the objectives of the study, procedures to be used, and of all known possible problems the volunteer may experience as a study participant.

Subjects were housed on the Metabolic Wards of the Clinical Research Centers at Methodist or Hermann Hospital in Houston, in private or semi-private rooms. During the equilibration week, all respective research subjects underwent a prestudy examination as outlined below. All tests were carried out according to standard techniques in the clinical laboratories of NASA-Johnson Space Center, Houston. These examinations provided baseline observations and, in addition, served to detect and eliminate volunteers who did not fulfill subject selection criteria.

1. Characteristics Which Excluded a Volunteer from the Study Include

a. Acute disease other than acute upper respiratory infections and minor skin diseases, e.g., dermatophytosis

b. Chronic diseases other than minor skin diseases, e.g., acne

c. Medications which by their action interfere with the interpretation of results, e.g., fluoride, estrogen

d. Recent sub-standard nutritional status which may have altered the metabolic milieu

2. Medical History and Physical Examination

A medical history was taken and physical examination performed and recorded. In addition to the routine examination, additional tests included:

a. Neurologic evaluation
b. Dental, ear, nose and throat examination
c. Eye examination
d. Standard 12 lead electrocardiogram
e. Urinalysis
f. Stool for occult blood
g. Complete blood count
h. Fasting blood glucose
i. Serologic test for syphilis
j. Serum total protein/albumin and globulin
k. Serum uric acid
l. Serum total bilirubin
m. Serum SGOT
n. Serum creatinine
o. Serum blood urea nitrogen
p. Serum alkaline phosphatase
q. Serum sodium
r. Serum potassium
s. Serum chloride
t. Serum carbon dioxide
u. Serum calcium
v. Serum phosphorus
w. Serum hepatitis antigen, and as soon as it was available, HIV antigen
x. A screen for addicting drugs
y. Serum cholesterol and triglyceride

3. <u>Study Design</u>

The 11-week study was divided into three parts and involved a total of 18 normal test subjects. Each part of the study was divided into five phases:

a. Phase I (@week 1) consisted of orientation. The subjects started the metabolic diet. The subjects also received polyethylene glycol 4000, underwent metabolic equilibration, and received a complete physical examination.

b. Phase II (@week 2) was the ambulatory control period during which the subjects continued on the metabolic diet. Baseline measurements of calcium, phosphorus and nitrogen balance, blood PTH, CT, calcitriol, urine hydroxyproline and densitometric scans of the calcaneus, and lumbar spine were obtained.

c. Phase III (@weeks 3-5) was the ambulatory load period during which the subjects received F, or no therapy. Baseline metabolic balance and hormonal and densitometric measurements continued during this period. Tc99m MDP kinetics were done in some subjects. Magnetic resonance imaging and spectroscopy were done in some subjects. Cybex muscle testing was performed.

d. Phase IV (@weeks 6-10) was the bed rest period, during which the subjects were at strict bed rest and received F or no therapy. Metabolic balance continued and hormonal and densitometric measurements obtained. Tc99m MDP kinetics were done in some subjects. Bone biopsies were taken at week 5 of bed rest in six subjects (three controls and three treated) who had been labeled with tetracyline and doxicyline once during the ambulatory phase and once toward the end of bed rest.

e. Phase V (@week 11) was the reambulation period. The F and balance studies were discontinued at the end of bed rest. Densitometry, magnetic resonance imaging and spectroscopy and Cybex testing were performed as soon as feasible after the end of bed rest.

No. of Subjects	Ambulatory (@weeks 3-5)	Bed Rest (@weeks 6-10)
12	25 mg/d F	25 mg/d F
6	no therapy	no therapy

The studies were done on an ongoing basis over the course of several years. Two or more subjects were allowed to begin a study as soon as they were identified and additional subjects were added as they were identified.

4. <u>Medications Studied:</u>

Study Drug: Sodium Fluoride U.S.P. (@Package Insert) Sodium fluoride occurs as an odorless, white, crystalline powder prepared from a naturally occurring fluoride such as fluorospar (@CaF_2) or cryolite (@Na_3AlF_6). It contains approximately 45% fluoride ion and is soluble in water and insoluble in alcohol. Solutions of sodium fluoride have a pH of 7 and are stable but should be stored and dispensed in plastic, or in paraffin-lined glass, or U.S.P. type I borosilicate glass containers.

The mechanism of action of sodium fluoride in reducing tooth decay is not fully understood, but it appears that the most important effect is upon the formation of tooth structure before the teeth erupt. Fluorides are known to be incorporated into the teeth by occupying sites otherwise occupied by hydroxyl, and perhaps carbonate, groups in the apatite structure of the tooth enamel. The reaction, resulting in the formation of fluorapatite, is apparently irreversible. Fluorapatite is formed from ingested fluoride while the enamel is calcifying, during the pre-eruptive period and after the teeth have erupted. When concentrated fluoride solutions are applied topically to the teeth, calcium fluoride as well as fluorapatite is formed and a part of the calcium fluoride is slowly converted to additional fluorapatite. Fluoride also diffuses into the partly demineralized enamel of initial carious lesions and reacts with residual apatite structures. Fluorapatite is less soluble in an acid medium than is hydroxyapatite, and fluoride has been shown to increase the resistance of enamel to acid. During the calcification process, fluorides may exert a catalytic action upon enamel crystallization which results in a more perfect crystalline apatite. It has been postulated also that fluoride catalyze remineralization. Fluorides may, in addition, inhibit the growth of acid-forming organisms in the mouth.

Fluorides are readily and almost completely absorbed from the gastrointestinal tract following oral administration of soluble fluoride salts. If administered as a less soluble salt such as calcium fluoride or in bone meal, absorption is slow and variable. Absorption of high doses of fluorides may be decreased by simultaneous ingestion of calcium compounds (@such as those present in milk), but these compounds probably have little effect on absorption of small amounts of fluorides found in drinking water. A physiological, storage-mobilization mechanism maintains a low level of fluoride ion in the body and may be important in providing a constant supply of fluoride for developing teeth; very little fluoride accumulates in non-calcified tissues. Fluorides have been demonstrated to cross the placental barrier of animals and humans. They are excreted primarily in the urine; lesser amounts are excreted in the feces, sweat, saliva, and milk.

Cautions (@Package Insert)

Prolonged uses of water containing fluorides in concentrations of 4 to 8 parts per million may increase the density of bone mineral to a degree detectable by roentgenographic studies and apparent fluoride osteosclerosis has been reported. Concentrations representing over 2 parts per million of fluoride ion in drinking water may cause dental fluorosis (@mottling of tooth enamel) during the period of tooth development. (@Not all "white enamel opacities" are signs of dental fluorosis but may be the result of numerous hypoplastic conditions of unrelated origin). Dental fluorosis is the most sensitive index of chronic fluoride poisoning; the color of the teeth in this type of fluorosis may range from white to brown.

Acute toxicity is not likely to result from the small amounts of fluorides present in drinking water, but is possible with concentrated solutions or tablets. It has been recommended that no more than 264 mg of sodium fluoride (@119 mg fluoride ion) be dispensed at one time, and that each container should be labeled "Caution: Store out of reach of children." Doses of 230 mg of sodium fluoride have caused toxic symptoms and lesser amounts may cause poisoning or death in children. The oral dose of sodium fluoride which may be fatal to an adult is not known with certainty, but it is estimated to be about 2 to 5 grams.

Symptoms of acute fluoride poisoning include epigastric pain, nausea, vomiting, diarrhea, and local paralysis in the legs and face. Epileptiform convulsions may occur. The respiratory center is initially stimulated and then depressed, and blood pressure falls. Death results from cardiac failure or respiratory paralysis.

In the event of acute poisoning, dextrose and sodium chloride injection is given intravenously to maintain blood sugar levels. The stomach is washed with 1 to 5% calcium chloride solution or with calcium hydroxide solutions. If systemic calcium deficiency becomes apparent, calcium gluconate injection is administered intravenously. A high urine volume should be maintained by administration of intravenous fluid.

Dosage (@Package Insert)

Sodium fluoride may be administered orally or topically. To reduce the incidence of dental carries, 1.5 to 3 parts per million of sodium fluoride (@0.7 to 1.3 parts per million of fluoride ion), or another suitable fluoride representing approximately 1 part per million of fluoride ion, may be added to municipal water supplies which contain little or no fluoride. In warm climates, where more water is ingested, the concentration of fluoride in municipal supplies should be at the lower end of this range.

As an alternative to community fluoridation, fluoride may be added to family or individual water supplies under the direction of a dentist or physician. The amount of prescribed fluoride must be adjusted in proportion to the amount of fluoride provided in drinking water. Supplementary fluoride should be prescribed only when the concentration of fluoride ion in drinking water is known to be less than 0.7 parts per million (@0.7 mg of ion per 1000 ml). When the water is devoid of fluoride, supplements providing approximately 0.5 mg of fluoride ion per day for children two to three years of age, or 1 mg per day for children over three years of age, may be administered. Tablets or concentrated solutions of sodium fluoride are suitable for this purpose and may be used to prepare small quantities of fluoridated water for administration to infants (@specific daily dosage for infants has not been established) or may be added to drinking water or other food for older children. One 2.2 mg tablet of sodium fluoride provides approximately 1 mg of fluoride ion.

A 2% solution of sodium fluoride may be applied by a dentist to teeth which have been thoroughly cleaned, isolated with cotton rolls, and dried with jet of air. The maximal protective effect appears to be obtained with a treatment series of four applications with intervals of several days following a single prophylaxis. A series of treatments may be given at age three to provide protection to the deciduous teeth. The series of four applications is repeated at intervals in accordance with the pattern of tooth eruption of the individual patient so that the teeth may receive protection as soon as possible after eruption. It has been recommended that treatments might be given at three, seven, eleven, and thirteen years of age. There is some evidence, however, that annual treatments provide better protection than is obtained from less frequent applications.

5. Other Medications:

All subjects received a Hexavitamin tablet once daily which, with the diet, provided approximately 14,000 I.U. of vitamin A, 630 I.U. of vitamin D, 3 mg thiamin, 5 mg riboflavin, 42 mg niacin, and 192 mg ascorbic acid. Dioctyl sodium sulfosuccinate (@Colace) was given orally in a dose of 100 mg twice daily to prevent constipation. Polyethylene glycol 4000 was used as a fecal marker and was given in an oral dose of 500 mg three times daily.

6. Test Procedures:

a. Bone Densitometry

Bone mineral of the calcaneus and lumbar spine were measured before and after bed rest.

1. Instrumentation

Rectilinear 125I scanning was done by the method of Vogel (19) for the calcaneus; and rectilinear 153Gd scanning was done by the method of Mazess (22) for the lumbar spine.

b. **Calcium Kinetics**

Modified calcium kinetics were measured in some of the subjects by determining the urinary output of Tc99m MDP after the oral administration of 100 microcuries of the labeled MDP.

c. **Bone Biopsy**

The bone biopsies were performed during bed rest week 5.

All six subjects who had a bone biopsy took the appropriate bone marking agents four times during the 10 week study; twice during the ambulatory treated phase, and twice during the bed rest phase. The bone markers were tetracycline and demeclocycline which were alternated each time. Demeclocycline was given (orally 250 mg TID) for three days and the tetracycline was then given 10 days later (orally 300 mg TID) for three days. The labeling was done starting week 3 of ambulation and week 3 of bed rest.

The iliac bone biopsy was taken through the lateral body wall using the appropriate bone biopsy trephine. The procedure was performed on the selected day. Meperidine hydrochloride 75 mg and diazepam 10 mg were used as premedication for the biopsy. The patient was placed in the supine lateral position, the skin was prepared with the usual aseptic precautions and local anesthesia, buphercaine 0.5% was used. A 2 cm incision was made 2 cm behind the anterior superior iliac border and 2 cm below the iliac crest. Blunt dissection separated the muscle and fascia to the periosteum and the trephine was rotated with a power hand drill to cut evenly through the outer cortex, the trabecular bone and the inner cortex. One or two 7 mm bone cores were obtained. Normal lesion repair was made and an elastic pressure dressing was applied. The subject was required to lie on the site of the wound for one hour and then was allowed usual activity.

Undecalcified bone were cut using the special bone microtome and standard histomorphometry was performed.

d. **Magnetic Resonance**

MRI scans were performed over the lower leg spine of some of the subjects. Magnetic Resonance Spectroscopy was performed over the muscles of the lower legs of some of the subjects.

Each scan consisted of 5 slices, 2 cm apart, starting at the lower calf. Spectroscopy was performed for the leg. Before the start of the first scan, the desired start point was determined as the distance in centimeters from the bottom of the heel to a position on the calf where the gastrocnemius muscle mass is negligible. This is an approximate distance which, however, is constant for all subsequent scans.

e. Muscle Strength Testing

Before and after bed rest tests for muscle strength and muscle fatigue were performed using the Cybex.

f. Lean Body Mass Determination

Lean body mass was determined using skin calipers, underwater weighing and 40Potassium (@40K) standard methods. The 40K is a naturally occurring radioactive isotope found in muscle tissue. This low level natural marker of lean body mass will be measured in the NASA-Johnson Space Center whole body counter. The detectors are housed in a room 60 feet underground specially constructed for low-level counting.

13. Safety:

a. Bed Rest

In previous studies, in which longer bed rest periods were used than those for the present study, no adverse effects were recorded. None of subjects in this study have developed hypercalcemia, renal stones, renal damage, decubitus ulcers, thrombophlebitis, syncope, fractures of the spine or long bones, or psychiatric problems.

b. Radiation Hazard

(1) ^{125}I - radiation dose to the bone is less than 5 millirem per scan at the speeds and counting rate used. Six determinations were performed.

(@3) ^{153}Gd - radiation dose to the bone is less than 20 millirem per scan. Six such determinations were performed.

(@4) Tc^{99m} MDP - the dose of Tc^{99m} was 100 microcuries administered two times. This delivered approximately 20 mr to the bladder, 6 mr to the bone, and 1 mr to the whole body.

The cumulative radiation dose received during the 11-week experiment was within the acceptable limits outlined for people who work with radiation and is within FDA guidelines for experimental procedures in research subjects.

c. Polyethylene Glycol 4000

This substance is a wax-like material which is colorless and tasteless and has been found to have low toxicity. It has been studied extensively in animal and human subjects and has been available for many years as a solubilizer for use in lotions, creams, and suppositories. In addition, it is used by humans internally as a food additive, pill excipient, and as a solubilizer for toothpaste. In recent years, it has become the standard fecal marker for metabolic balance studies. We have administered this drug to 80 subjects who have participated in our studies over the last six years without any observed side effects.

d. Bone Biopsy

Bone biopsy is usually performed as an outpatient procedure and the patient is allowed to leave the procedure room to return to his/her normal activities within 60 to 90 minutes of the finish of the biopsy. Pain experienced during the procedure is usually mild. Minor analgesics are usually needed for one to two days and some increased sensitivity may persist at the biopsy site for several weeks. No serious side problems developed in any of the six subjects who underwent a bone biopsy.

e. MR Imaging and Spectroscopy

No side effects occurred.

f. Muscle strength testing

Muscle soreness occurred after the muscle testing because of presumed strain on the muscles in several subjects.

g. Underwater Weighing

No side effects occurred.

h. Sodium Fluoride

The normal intake of elemental fluoride has been estimated as high as 5.4 mg which is derived from both water and food. Water supplies range from 0.1 ppm to 3 or 4 ppm and occasionally higher in United States communities (@i.e., an intake up to 3.8 mg fluoride daily).

Fluorosis, a disease of skeletal abnormalities associated with large intake of fluoride, has been reported and consists of (@a) osteosclerosis, a radiological diagnosis; (@b) exostosis; and (@c) calcification of ligaments with signs and symptoms referable to bones, ligaments and joints. Non-skeletal complaints and signs include chronic respiratory disease and a number of common non-specific disorders. The daily fluoride exposure necessary to bring about bony changes was estimated fluoride to range from 20-80 mg of elemental fluoride taken into the body daily for 10-20 years (49).

Twenty five mg of elemental fluoride was given daily to all the fluoride treated subjects. A wax matrix tablet containing 12.5 mg fluoride was given twice daily. The fluoride preparation was sodium fluoride. The dose size and duration of extra elemental fluoride did not cause any ill effects to the research subjects.

12. Side-effects and Adverse Reactions

No unexpected reactions, illnesses or behavior occurred during the period of study.

13. Documentation of the Study

a. Record Keeping and Disposition of Case Reports and Other Documentation

(@1) Copies of the data and other study documentation will be retained in the investigator's file for a period of at least two years. The NASA will have access if they so wish to the identifiers.

14. Balance Diet

The diet was prepared in the same fashion as in previous studies (6,8,10,12,13). The solid food diet was composed of 7 daily menus, each consisting of three meals and an evening snack. All foods except some staples, soft drinks, and meats were purchased in common lots prior to the study to assure maximal constancy. Fresh fruits were avoided and canned whole milk and frozen homogenized eggs were used. Deionized water was used for food preparation, drinking, and utensil cleaning. The subjects were required to eat all food, lick their plates, and drink a distilled water rinse of their glassware. On the average, the diet contained 1 g of calcium and 1.7 g of phosphorus. To determine the exact mineral and nitrogen content of the diet, each month duplicates of the menus for one week were weighed and homogenized separately, pooled, and a aliquot stored frozen for subsequent digestion and analysis.

15. Serum, Stool, and Urine Collections

Approximately 35 ml of blood was drawn every two weeks for complete blood count, ionized calcium, total serum calcium, phosphorus, creatinine, and alkaline phosphatase determinations. Parathyroid hormone, and calcitonin were assessed. An additional 30 ml of blood were drawn every 4 weeks for a partial thromboplastin time, erythrocyte sedimentation rate, lupus cell preparation, serum sodium, potassium, chloride, and carbon dioxide, total serum protein and albumin, serum bilirubin, SGOT, and BUN. Urinary protein, sugar, and sediment were checked weekly by the research technician.

Urine and stools were collected between week 1 and 10, inclusive. Twenty-four hour urines were collected daily, acidified with 1 ml of 12 normal HCL/100 ml urine, and stored at 4 C. At the end of each 7-day period, total creatinine content of the daily urines were determined. For each subject the 7 creatinine values were averaged and any value which was more than 20% from the mean was discarded and a new mean obtained; any value which is more than 10% from the mean was assumed to represent a collection error and discarded. For each subject, the remaining urines were combined into a pool representing the seven-day period, and an aliquot stored at -22 C for subsequent analysis of calcium, phosphorus, nitrogen, and hydroxyproline. Seven-day collections of stools were obtained beginning and ending 24 hours after the 7-day urines to provide a partial correction for the intestinal transit time. Stools were collected in epoxy-lined 1 gallon canisters and frozen. Upon completion of the 7-day collections, the stools were diluted with distilled water to a final weight approximately 3 times the initial weight. They were homogenized and an aliquot stored at -22 C for subsequent analysis of calcium, phosphorus, and nitrogen. Urine sample collected from volunteers receiving F will be analyzed for total F (not yet completed). Fecal samples collected from volunteers receiving F will also be analyzed for total F (not yet completed).

16. Laboratory Determinations:

Laboratory methods are referenced in Appendix A.

Stool and diet specimens were digested in nitric acid for calcium determinations and in sulfuric acid for phosphorus and nitrogen determinations. Calcium was determined by atomic absorption spectrophotometry on an automated Perkin-Elmer Model 303. Phosphorus was analyzed by a modification of the Fiske and SubbaRow method, using standards adjusted to the pH of the samples. Creatinine was determined using the adaptation of the Folin Wu method. Nitrogen was determined after Kjeldahl digestion by the amino acid analyzer. Hydroxyproline was determined by the method of Kivirikko and Prockop, and alkaline phosphatase was determined by the automated modification of the Bessey-Lowry-Brock method. All methods have been validated by recovery studies which were repeated periodically, and quality control was maintained by including standards in all runs. All assays were carried out in duplicate and results accepted only when the disparity between the two determinations was less than 5%.

II. RESULTS

add results here!

III. DISCUSSION

The human skeleton goes through two major phases during life; (@1) growth (@modeling) and (@2) repair of micro-defects (@remodeling). Major growth stops when the skeletal epiphyses close and the human reaches their maximal height. Modeling continues along the periosteal and cortical-endosteal bone surfaces; however, it is thought to be insignificant and rarely is involved in the pathophysiology of metabolic bone disease acquired during adult life.

Remodeling in the human begins at birth and continues throughout life. The metabolic bone diseases in the adult are because of remodeling activity. Remodeling occurs in all areas of the skeleton, i.e., periosteal, haversian, cortical-endosteal and trabecular. Bone remodeling directly determines the speed of bone tissue turnover, the quantity of unmineralized osteoid, the total and relative amounts of resorption or formation surfaces and the net gain or loss of bony tissue on a particular skeletal surface.

Frost has defined the actions of bone remodeling by describing the happenings thus; a "packet" of bone (@Basic Multicellular Unit, BMU) is activated by some messenger (25). This causes proliferation and then differentiation of mesenchymal cells in the affected region of bone. The cells, which now can be identified as osteoclasts, begin bone resorption by solubilizing both the organic and inorganic components of pre-existing bone. (@Osteoclastic activity stops and the osteoclasts disappear.) Osteoblasts, derived from the marrow, appear on the resorbed surface and proceed to make new organic bone matrix and in some manner initiate the matrix's mineralization. The quantity of new bone is equal to the old bone being replaced. The duration of remodeling events is thought to take about 3 to 4 months with resorption phase lasting about 1 month and the formation phase lasting 2 to 3 months (37).

The following parameters can be measured using histomorphometry: presence of woven bone, extent of resorption, depth of resorption, extent of formation, extent of osteoid, thickness of osteoid, extent of mineralization front, mineral appositional rate and surface cell morphology.

Disuse osteoporosis is postulated to occur during space flight. Net bone loss occurs because bone resorption is grater than bone formation. This theory for osteoporosis has been confirmed in Earth-bound paraplegics, an extreme disuse state, by bone biopsy (24). Although the activation factor initiating disuse osteoporosis is not known, specific changes in bone histomorphometry would be expected to occur in untreated bed rest.

F therapy may cause profound changes in the histological pattern of a bone biopsy. F is known to stimulate osteoblastic activity (34,35) which can increase the number of osteoid sites as well as osteoid thickness (38). Additionally during F therapy appositional woven bone may be formed instead of the normal development of lamellar bone (37).

Since relatively low dose F will be given to the research subjects participating in this experiment, it will be very important to evaluate the bone directly as well as with metabolic balance and bone densitometry techniques.

Measurement of Bone Loss

In addition to the usual measurement of bone mineral by 125I photon absorptiometry rectilinear scanning of the calcaneus (19), measurement of the lower lumbar vertebrae was done using the dual photon 153Gd (22). This allowed a direct comparison among these two techniques and the metabolic calcium balance method. Bone turnover was measured by calcium kinetic studies using Tc99m MDP.

Bone histomorphometric changes during bed rest induced osteoporosis have not been reported. We have obtained bone biopsies in 6 bed rested subjects, 3 controls and 3 treated with 20 mg F, at 5 weeks of bed rest. Preliminary data is not yet available. Bone biopsies have been performed in paraplegics who were untreated or who received clodronate (24).

Measurement of Muscle Volume and Strength

The long term bed rest protocol allows investigation into the nature and extent of muscular atrophy. Magnetic Resonance Imaging (@MRI), a new technique, to measure both muscle volume and metabolic consequences of inactivity can be compared to the standard methodology for determining muscle peak strength and maximal duration of muscular activity during exercise. A separate proposal has been submitted to NASA for the MRI technique to be used in this study.

Hormonal Mechanisms in Disuse Osteoporosis

Hormonal responses to (@1) activity and nutrient intake during ambulation and recumbency were monitored longitudinally to measure the variation of parathyroid hormone (@PTH), calcitonin (@CT), calcitriol, and cortisol.

Nephrolithiasis

Nephrolithiasis is a definite potential complication of space flight (31). The limited data available suggest that the metabolic changes during space flight could lead to renal stone formation.

Hypercalciuria develops soon after space flight and calcium excretion may approach 500 mg/day (32). The excessive renal loss of calcium is probably skeletal in origin, since it is correlated with the development of negative calcium balance (5,32,33) and loss of bone mass (9) and occurs despite probable reduced intestinal calcium absorption. Urinary phosphate excretion is also increased during space flight probably by the same mechanism (5,32,33). These changes would place the astronaut at an increased risk for stone formation by increasing urinary saturation of stone-forming calcium salts (@calcium oxalate and calcium phosphate) (39).

Two other factors may contribute to stone formation during space flight. Potassium deficiency, resulting from an exaggerated renal loss of potassium (48), may reduce renal excretion of citrate (40), a well recognized inhibitor of the crystallization of calcium salts (39). Moreover, urinary uric acid may be high because of increased availability of purine substrate (@due to muscle degradation or use of a high protein diet). The resulting hyperuricosuria may predispose to uric acid lithiasis or to calcium nephrolithiasis via monosodium urate-induced crystallization of calcium salts (41). The exaggerated renal loss of sodium (48) may further promote the latter mechanism.

The risk factors which may primarily predispose astronauts to renal lithiasis in addition to those discussed above include dehydration and high animal protein intake. It has been impossible to determine the water balance of astronauts during the initial stages of flight for a number of reasons. However, it can be postulated that sweating, early limited access to water, and space motion sickness causes decreased appetite-thirst and therefore increased urine concentration. As previously mentioned, an apparent dietary preference for a high meat diet may accentuate a tendency toward stone formation. There is substantive epidemiological and biochemical data suggesting that an excessive consumption of animal protein confers an important risk for stone formation (42). A high animal protein diet has been shown to increase urinary calcium and uric acid (42) and lower urinary citrate (43).

From the data generated in this study, it may be possible to formulate an effective preventive program for nephrolithiasis. Reliable techniques are now available to quantitate various steps in the stone-forming salts (@uric acid, monosodium urate, calcium phosphate and calcium oxalate) may be reliably measured from the activity product ratio or relative saturation ratio (44,45). The inhibitor activity against spontaneous nucleation of calcium phosphate and calcium oxalate may be determine in whole urine from the formation product ratio (45). The propensity for spontaneous nucleation may be estimated from the formation product ratio minus the activity product ratio discriminant scores (39) or permissible increments (46).

The above physicochemical measures were utilized to quantitate the response in any proposed treatment program to reduce urinary saturation and/or increase inhibitor activity. A separate NASA research grant was submitted for this part of the experiment and will be reported in another communication.

IV. SIGNIFICANCE OF THE RESEARCH

Sodium fluoride has received attention because of its potential therapeutic usefulness in a wide variety of skeletal disorders. It has been shown to retard the dissolution of hydroxyapatite crystals in vitro.

Previous space missions have used only distilled water and a low fluoride diet. The average intake of fluoride from the usual community water supply is 2.35 mg/day (@1 ppm) compared to all other dietary intake of 2 mg/day. Studies in the PI's laboratory have shown fluoride balances, reflecting fluoride intake from distilled water and a whole food diet, to be slightly negative. This may have played a role in the developement of disuse osteoporosis which occurred during the Skylab mission and in the early bed rest studies.

In addition, during the last few years, the use of fluoride has been tried as therapy to increase bone mass and reverse osteoporotic disease. It has been stated that the fluoride ion is the only pharmaceutical that appears to be capable of the dual effects of increasing bone mass at the same time it stops disease progression. This mode of therapy is extensively used in many areas, and this study has produced additional information regarding fluoride balance in normal people and its role in the prevention of disuse osteoporosis.

A number of physiological changes have been demonstrated in bone, muscle, and blood after exposure of humans and animals to microgravity. Determining mechanisms and the development of effective countermeasures for long-duration space missions is an important NASA goal. Historically, NASA has had to rely on tape measures, x-ray, and metabolic balance studies with collection of excreta and blood specimens to obtain this information. The advent of tomographic magnetic resonance imaging (@MRI) offers the possibility of greatly extending these early studies in ways not previously possible; MRI is also noninvasive and safe, i.e., no radiation exposure. MRI provides both superb anatomical images for volume measurements of individual structure and qualification of chemical/physical changes induced in the examined tissues. Results of this aspect of the study will be reported later.

Data Records

name	code no	date	rx	week	red bc	retic
Carpenter		9/01/83	FL 20			
Carpenter		9/15/83	FL 20			
Carpenter		8/22/83	FL 20	1	4.59	1.5
Carpenter		9/08/83	FL 20	3	4.81	0.9
Carpenter		9/22/83	FL 20	5	4.57	1.1
Carpenter		10/06/83	FL 20	7	4.68	1
Carpenter		10/20/83	FL 20	9	4.82	1
Carpenter		11/03/83	FL 20	11	4.96	0.8
Caruthers		8/22/83	FL 20	1	4.87	1
Caruthers		9/08/83	FL 20	3	4.66	0.8
Caruthers		9/22/83	FL 20	5	4.48	1
Caruthers		10/06/83	FL 20	7	4.9	0.9
Caruthers		10/20/83	FL 20	9	4.9	0.7
Caruthers		11/03/83	FL 20	11	5.09	1
Clanton A			NO			
Crandal R		3/05/84	NO	1	5.6	0.5
Crandal R		3/19/84	NO	3	4.68	0.7
Crandal R		4/02/84	NO	5	4.92	0.5
Crandal R		4/16/84	NO	7	5.13	0.7
Crandal R		4/30/84	NO	9	5	0.8
Crandal R		5/14/84	NO	11	5.05	0.9
Fitzpatric		3/05/84	NO	1	3.49	0.5
Fitzpatric		4/16/84	NO	7	4.33	0.6
Fitzpatric		4/30/84	NO	9	4.33	1
Fitzpatric		5/14/84	NO	11	4.18	0.4
Fitzpatric		3/19/84	NO	3	4.01	0.5
Fitzpatric		4/02/84	NO	5	4.01	0.8
Huftel S			NO			
Lewis W		9/08/86	NO	2	4.93	0.9
Meynen R		9/08/86	NO	2	5.13	0.4
Slocum D			NO			
Williams J		7/16/86	NO	1		
Williams J		7/21/86	NO	2	4.53	0.5
Williams J		8/04/86	NO	4	4.58	0.7
Williams J		8/11/86	NO	5		
Williams J		7/18/86	NO	6	4.48	0.5
A A A	0			0		
A Z A	0			0		
Chase C	1	1/16/84	FL 10	1	5.15	0.8
Chase C	1	2/06/84	FL 10	3	5.25	1.1
Chase C	1	2/21/84	FL 10	5	4.98	0.7
Chase C	1	3/06/84	FL 10	7	5.16	0.9
Chase C	1	3/19/84	FL 10	9	5.19	0.6
Chase C	1	4/02/84	FL 10	11	5.29	1
Sommervill	2	1/23/84	FL 10	1	5.12	0.7
Sommervill	2	2/06/84	FL 10	3	4.82	1

name	code no	date	rx	week	red bc	retic
Sommervill	2	2/21/84	FL 10	5	4.68	0.7
Sommervill	2	3/06/84	FL 10	7	4.95	1.4
Sommervill	2	3/19/84	FL 10	9	5.01	1
Sommervill	2	4/02/84	FL 10	11	5.15	0.6
Broussard	3	4/09/84	FL 10	1	4.55	1.2
Broussard	3	4/23/84	FL 10	3	4.69	1
Broussard	3	5/07/84	FL 10	5	4.66	1
Broussard	3	5/21/84	FL 10	7	4.6	0.8
Broussard	3	6/04/84	FL 10	9	4.67	0.7
Broussard	3	6/18/84	FL 10	11	4.54	2
Hughes J	4	4/09/84	FL 10	1	5.51	0.8
Hughes J	4	4/23/84	FL 10	3	5.5	0.6
Hughes J	4	5/07/84	FL 10	5	5.49	1.1
Hughes J	4	5/21/84	FL 10	7	5.41	1
Hughes J	4	6/04/84	FL 10	9	5.61	0.9
Hughes J	4	6/18/84	FL 10	11	5.67	1.7
Ashley S	5	4/29/85	FL 20	1	4.59	1
Ashley S	5	5/13/85	FL 20	3	4.59	0.5
Ashley,S	5	6/10/85	FL 20	7		
Baker C	6	6/03/85	FL 20	1	5	0.4
Baker C	6	6/17/85	FL 20	3	4.92	0.6
Baker C	6	7/01/85	FL 20	5	4.87	0.4
Baker C	6	7/15/85	FL 20	7	5.07	0.4
Baker C	6	7/29/85	FL 20	9	4.95	0.8
Baker C	6	8/12/85	FL 20	11	5.08	0.6
Illig G	7	9/30/85	FL 20	1	4.4	0.8
Illig G	7	10/15/85	FL 20	3	5	0.3
Illig G	7	10/28/85	FL 20	5	5.02	1.2
Illig G	7	11/12/85	FL 20	7	5.32	0.5
Illig G	7	11/25/85	FL 20	9	5.06	0.8
Illig G	7	12/09/85	FL 20	11	4.89	0.5
Wahl M	8	9/30/85	FL 20	1	5.06	0.6
Wahl M	8	10/15/85	FL 20	3	5	0.4
Wahl M	8	10/28/85	FL 20	5	5.32	0.9
Wahl M	8	11/12/85	FL 20	7	5.31	0.5
Wahl M	8	11/25/85	FL 20	9	5.01	0.5
Wahl M	8	12/09/85	FL 20	11	5.06	0.8
Douglas J	9	9/30/85	FL 20	1	5.2	0.5
Douglas J	9	10/15/85	FL 20	3	4.7	0.4
Douglas J	9	10/28/85	FL 20	5	5.01	1
Douglas J	9	11/12/85	FL 20	7	4.67	0.7
Douglas J	9	11/25/85	FL 20	9	4.81	0.9
Douglas J	9	12/09/85	FL 20	11	5.02	0.4
Morin J	10	7/21/86	FL 20	2	4.97	0.6
Morin J	10	8/04/86	FL 20	4	5.13	0.6
Morin J	10	8/18/86	FL 20	6	5.03	0.7
Morin J	10	9/02/86	FL 20	8	5.26	0.9
Morin J	10	9/15/86	FL 20	10	4.98	0.5
Morin J	10	9/29/86	FL 20	12	5.1	0.9
Will A	11	7/21/86	FL 20	2	4.92	0.6
Will A	11	8/04/86	FL 20	4	4.8	0.5
Will A	11	8/18/86	FL 20	6	4.71	0.9
Will A	11	9/02/86	FL 20	8	5.18	0.7
Will A	11	9/15/86	FL 20	10	5.07	0.2
Will A	11	9/29/86	FL 20	12	5.2	0.8
Brinson R	12	9/08/86	FL 20	2	4.78	0.8

**ORIGINAL PAGE IS
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name	code no	date	rx	week	red bc	retic
Brinson R	12	9/22/86	FL 20	4	4.66	0.3
Brinson R	12	10/06/86	FL 20	6	4.53	0.4
Brinson R	12	10/20/86	FL 20	8	4.78	0.9
Brinson R	12	11/03/86	FL 20	10	4.73	1.2
Brinson R	12	11/17/86	FL 20	12	4.7	0.9

retic no	rpi	hct	hbg	oxyhb	cohb	methb
68.9	1.5	0.44	15.1	66.4	3	0.5
43.3	0.8	0.47	15.4	92	3.5	0.4
50.3	1.1	0.45	15.4	86.9	3.5	0.4
46.8	1	0.46	15.2	78.7	3	0.4
15.8	1	0.47	15.8	85.2	3.8	0
39.7	0.8	0.48	15.9	88.2	2.9	0.3
48.7	1	0.44	14.9	32.6	7.1	1.3
37.3	0.9	0.42	13.9	80.1	7.7	0.3
44.8	1	0.4	14	77.3	7.3	0.1
44.1	0.9	0.44	14.6	85.7	7.7	0
34.3	0.7	0.45	14.7	93.1	6.6	0
50.9	1	0.46	15.1	88.7	9.2	0.1
28	0.4	0.51	15			
32.8	0.7	0.44	14.5	81.6	2	0.1
24.6	0.5	0.45	15.2	97.8	1.8	0.4
35.9	0.7	0.47	15.8	90	2	0.1
40	0.8	0.46	15.4	98	2.8	0
45.5	0.9	0.46	15.5			
17.5	0.6	0.35	11.8			
26	0.6	0.42	14.3	73.4	2.4	0.2
43.3	1	0.41	14.1	98.1	1.9	0.4
15.7	0.4	0.4	13.8			
20.1	0.6	0.4	13.5	73.8	1.6	0.5
32.1	0.9	0.39	13.1	97.8	2	0.2
44.4	1	0.41	13.8	40.3	2.6	1.2
20.5	0.4	0.44	15.2	86.6	2.7	3.7
22.7	0.5	0.43	15	56.5	5.1	3.2
32	0.7	0.43	14.9	52.3	8.2	0.5
22.4	0.5	0.42	14.9	68.2	4.8	0.8
41.2	0.8	0.47	15.3	97.8	1.5	0.4
57.8	1	0.48	16	98.8	0.4	0.6
34.9	0.7	0.46	15.5	97.3	2.1	0.3
46.4	0.9	0.47	15.9	96.8	1.9	0.4
31.1	0.6	0.48	15.6	97.8	2	0.3
52.9	1	0.48	15.9	89.4	2.2	0.5
35.8	0.6	0.47	16.9	87.1	2	0.4
48.2	1	0.46	15.5	98	1.9	0.1

retic no	rpi	hct	hbg	oxyhb	cohb	methb
32.8	0.7	0.44	15.2	97.7	2.5	0.3
69.3	1.4	0.46	16	97.6	2.6	0.3
50.1	1	0.46	16.1	98	2	0.1
30.9	0.5	0.47	16	80.9	2.2	0.2
54.6	1.2	0.45	14.8			
46.9	1	0.45	15.4			
46.6	1	0.45	15.3			
36.8	0.8	0.44	15.2			
32.7	0.7	0.44	15.1			
90.8	2	0.44	14.9			
44.1	0.7	0.49	17.1			
33	0.5	0.5	17			
60.4	0.9	0.5	17.1			
54.1	0.8	0.5	17.5			
50.5	0.7	0.52	17.4			
96.4	1.4	0.52	17.9			
45.9	1	0.43	14.6			
23	0.5	0.43	14.9	92.8	1.6	0.5
20	0.4	0.43	14.6	46.3	1.8	0.1
29.5	0.6	0.43	14.2			
19.5	0.4	0.42	13.6			
20.3	0.4	0.43	14.4			
39.6	0.8	0.42	13.7			
30.5	0.6	0.43	14.2	68	6	0.1
35.2	0.8	0.42	14.5	56.6	9.4	0.1
15	0.3	0.48	16.5	87.5	10.3	0.1
60.2	1.1	0.48	16.6	92.1	6.5	0.1
26.6	0.5	0.5	16.8	90.3	7.4	0.1
40.5	0.8	0.48	16.7			
24.5	0.5	0.46	15.4			
30.4	0.6	0.46	15.3	48.4	0.9	0.1
20	0.4	0.45	15.4	97.8	1.9	0.2
47.9	0.8	0.48	16.5	72.9	2.1	0.1
26.6	0.5	0.48	16.3	85.7	2	0.3
24.1	0.5	0.45	15.7			
40.5	0.8	0.45	15.6			
26	0.5	0.48	16.1	50.2	1.3	0.2
18.8	0.4	0.42	14.3	76.6	1.8	0.1
50.1	1	0.45	16.3	71.6	0.1	0.3
32.7	0.7	0.42	13.9	80.8	3.8	0.1
43.3	0.9	0.43	14.6			
20.1	0.4	0.45	14.1			
20.4	0.7	0.41	14	77.3	0.5	0.5
30.7	0.6	0.42	14.1	57.4	1.5	1
35	0.8	0.41	13.8	79.4	0	0
47.3	0.9	0.43	14.6	78.3	0.2	0.2
24.9	0.5	0.41	13.9	84.5	0	2.1
45.9	1	0.41	13.6			
29.5	0.6	0.43	14.2	93.8	0.7	1.8
24	0.5	0.41	13.7	84.7	0.5	0.9
42	1	0.4	13.7	67.3	0.3	0
36.3	0.8	0.44	15.1	74	0.7	0.4
21.8	0.2	0.43	14.8	86.9	0	4.3
41.6	0.8	0.42	14.5			
38.2	0.8	0.44	15.2	89.5	2.1	8.3

retic no	rpi	hct	hbg	oxyhb	cohb	methb
19.6	0.3	0.42	14.8			
18.1	0.4	0.42	13.9			
43	1	0.44	14.6	56.5	7.4	1.9
56.8	1.2	0.43	15.1			
42.3	0.9	0.42	14.9			

mcv	mch	mchc	zsr	platelet	rbc's morp	white bc
97	33	34	0.5	282		5.4
98	32	33	0.55	312		4.8
98	34	35	0.52	297		4.7
98	32	33	0.57	279		4.5
98	33	33	0.55	305		5.6
97	32	33	0.55	338		7.1
90	31	34	0.52	440		11.2
91	30	33	0.54	310		7.6
89	31	31	0.49	335		8.4
91	30	33	0.52	358		8.7
91	30	33	0.56	348		8.4
91	30	33	0.58	372		11.2
92	27	29	0.54	315		6.7
93	31	33	0.5	196		5.9
91	31	34	0.5	236		6.6
91	31	34	0.51	220		6
91	31	34	0.5	237		6.8
91	31	34	0.49	213		6
100	34	34	0.53	272		4.5
96	33	34	0.56	235		4.9
96	33	34	0.51	252		4.9
95	33	35	0.52	244		5.2
100	34	34	0.56	265		6
97	33	34	0.54	264		4.4
84	28	33	0.48	246	normal	5
85	30	34	0.47	240	normal	5.8
96	33	35	0.55	385	normal	12.2
94	33	34	0.55	402	normal	10.2
95	33	35	0.52	311	normal	7.6
92	30	32	0.57	211		8.2
92	31	33	0.62	219		6.5
92	31	34	0.56	217		7.5
91	31	34	0.57	198		7.1
92	30	33	0.6	217		7.5
91	30	33	0.62	217		7.8
93	33	36	0.54	341		6.7
95	32	34	0.55	322		6.8

mcv	mch	mchc	zsr	platelet	rbc's morp	white bc
95	33	34	0.52	348		6
92	32	35	0.54	329		6.6
92	32	34	0.55	351		7.5
91	31	34	0.55	344		6.9
98	32	33	0.56	299		7.8
97	33	34	0.55	241		6.2
96	33	34	0.58	287		9.2
95	33	35	0.56	284		10.9
95	32	34	0.59	299		9.7
97	33	34	0.6	287		10.9
89	31	35	0.53	198		6.3
91	31	34	0.53	224		6.7
92	31	34	0.54	207		6.5
93	32	35	0.52	186		6.5
93	31	33	0.54	186		6.5
92	32	34	0.54	194		6.5
93	32	34	0.48	351		8.5
93	33	35	0.55	303	normal	4.9
87	29	34	0.53	204		7.3
87	29	33	0.54	207		6.8
86	28	32	0.5	212		7.2
85	28	33	0.49	198		7.1
86	28	32	0.48	199		7.5
85	28	33	0.51	206		8.7
96	33	34		288		6.7
95	33	34	0.6	308		8.8
95	33	35	0.56	280		8.6
95	32	33	0.66	294		9.1
94	33	35	0.59	295		8.2
94	32	34	0.5	336		9.5
91	30	33		229		4.3
90	31	34	0.49	200		4.9
91	31	34	0.51	205		4.8
91	31	34	0.51	208		5.2
90	31	35	0.5	198		4.7
89	31	35	0.56	191		4.9
92	31	34		375		8.1
90	30	34	0.48	356		7.1
90	31	34	0.6	382		7.4
90	30	33	0.49	334		9.2
89	30	34	0.51	341		8.2
89	30	34	0.51	408		9
83	28	34	0.48	264	normal	6.8
83	27	33	0.48	255	normal	6.8
82	28	34	0.46	270	normal	6.2
82	28	34	0.48	266		7.6
82	28	34	0.48	255	normal	7
81	27	33	0.51	208	normal	6.7
87	29	33	0.55	243	normal	6.5
86	29	33	0.51	217	normal	4.8
85	29	34	0.47	223	normal	5.5
85	29	34	0.51	228	normal	5.9
85	29	34	0.52	247	normal	6.4
80	28	35	0.51	210	normal	5.6
92	32	34	0.56	268	normal	10.7

mcv	mch	mchc	zsr	platelet	rbc's morp	white bc
						11.8
						11.9
91	31	34	0.65	302		12.7
						12.9
						13.1

neut	lymph	mono	eo	baso	bands	neut no
50	43	3	2	0	0	2.7
49	46	4	1	0	0	2.352
48	41	8	3	0	0	2.256
54	38	8	0	0	0	2.43
58	34	7	1	0	0	3.248
53	40	6	1	0	0	3.763
66	28	3	1	1	1	7.392
54	37	9	0	0	0	4.104
66	26	5	3	0	0	5.544
57	32	6	5	0	0	4.959
52	36	5	5	0	1	4.368
48	37	10	5	0	0	5.376
64	32	3	0	0	1	4.288
55	39	4	2	0	0	3.245
53	42	4	1	0	0	3.498
57	40	2	1	0	0	3.42
57	33	5	5	0	0	3.876
54	39	3	4	0	0	3.24
66	29	5	0	0	0	2.97
50	41	4	5	0	0	2.45
47	43	8	2	0	0	2.303
56	38	2	2	0	2	2.912
53	38	7	2	0	0	3.18
58	36	3	3	0	0	2.552
50	47	3				2.5
58	35	5	2			3.364
58	39	1	2			7.076
55	42	3	0	0	0	5.61
49	44	5	2			3.724
76	21	3	0	0	0	6.232
61	35	3	1	0	0	3.965
63	27	5	5	0	0	4.725
51	40	7	2	0	0	3.621
65	32	3	0	0	0	4.875
54	43	1	2	0	0	4.212
79	20	0	0	0	1	5.293
73	24	1	2	0	0	4.964

neut	lymph	mono	eo	baso	bands	neut no
64	28	5	3	0	0	3.84
65	26	5	4	0	0	4.29
67	28	4	1	0	0	5.025
56	39	3	2	0	0	3.864
52	48	0	0	0	0	4.056
44	53	3	1	0	0	2.728
60	37	2	1	0	0	5.52
53	40	4	2	0	1	5.777
54	41	4	1	0	0	5.238
58	37	4	1	0	0	6.322
60	36	1	3	0	0	3.78
56	39	3	2	0	0	3.752
56	35	3	4	0	1	3.64
58	29	5	7	0	1	3.777
60	33	3	4	0	0	3.9
65	27	2	6	0	0	4.225
79	19	1	0	0	1	6.715
65	32	0	3	0	0	3.185
72	27	1	0	0	0	5.256
69	28	2	1	0	0	4.692
64	33	0	3	0	0	4.608
71	28	1	0	0	0	5.041
66	34	0	0	0	0	4.95
67	30	3	0	0	0	5.829
59	34	4	2	0	1	3.953
63	36	0	1	0	0	5.544
64	34	2	0	0	0	5.504
76	23	2	0	0	0	6.916
65	29	1	5	0	0	5.33
69	29	1	0	0	0	6.55
51	41	5	2	0	1	2.193
60	39	0	1	0	0	2.94
62	36	2	0	0	0	2.976
66	33	0	1	0	0	3.432
58	42	0	0	0	0	2.726
56	41	2	1	0	0	2.744
73	23	1	1	0	2	5.913
60	36	0	2	0	2	4.26
65	32	2	1	0	0	4.81
67	27	5	1	0	0	6.164
65	35	0	0	0	0	5.33
60	39	1	0	0	0	5.4
63	31	3	3			4.284
63	32	2	3			4.284
61	33	4	2			3.782
63	31	3	3			4.788
53	39	2	6			3.71
62	32	0	5		1	4.154
49	47	2	2	0	0	3.185
62	35	2	1			2.976
51	44	2	3			2.805
49	44	5	2			2.891
54	41	3	1	1		3.456
42	56		2		0	2.352
58	39	3	0	0	0	6.206

neut	lymph	mono	eo	baso	bands	neut no
69	26	1	3	0	1	8.142
78	21	1	0	0	0	9.282
65	35	0	0	0	0	8.255
74	19	0	3	0	4	9.546
71	27	1	1	0	0	9.301

lymph no	mono no	eo no	baso no	band no	wbc morph	sp gr
						1.017
						1.015
2.322	0.162	0.108	0	0.108		1.014
2.208	0.192	0.048	0	0		
1.927	0.376	0.141	0	0		
1.71	0.36	0	0	0		1.013
1.904	0.392	0.056	0	0		1.01
2.84	0.426	0.071	0	0		
3.126	0.336	0.112	0.112	0.112		
2.812	0.684	0	0	0		
2.184	0.42	0.252	0	0		
2.784	0.522	0.435	0	0		
3.024	0.42	0.42	0	0.084		
4.144	1.12	0.56	0	0		
2.144	0.201	0	0	0.067		
2.301	0.236	0.118	0	0		
2.772	0.264	0.066	0	0		
2.4	0.12	0.06	0	0		
2.244	0.34	0.34	0	0		
2.34	0.18	0.24	0	0		
1.305	0.225	0	0	0		
2.009	0.196	0.245	0	0		
2.107	0.392	0.098	0	0		
1.976	0.104	0.104	0	0.104		
2.28	0.42	0.12	0	0		
1.584	0.132	0.132	0	0		
2.35	0.15				normal	1.013
2.03	0.29	0.116	0		normal	1.007
						1.012
4.758	0.122	0.244			normal	1.02
4.284	0.306	0	0	0	normal	1.009
						1.01
3.344	0.38	0.152				1.008
1.722	0.246	0	0	0		
2.275	0.195	0.065	0	0		
2.025	0.375	0.375	0	0		
2.84	0.497	0.142	0	0		
2.4	0.225	0	0	0		

name	code no	date	rx	week	red bc	retic
Sommervill	2	2/21/84	FL 10	5	4.68	0.7
Sommervill	2	3/06/84	FL 10	7	4.95	1.4
Sommervill	2	3/19/84	FL 10	9	5.01	1
Sommervill	2	4/02/84	FL 10	11	5.15	0.6
Broussard	3	4/09/84	FL 10	1	4.55	1.2
Broussard	3	4/23/84	FL 10	3	4.69	1
Broussard	3	5/07/84	FL 10	5	4.66	1
Broussard	3	5/21/84	FL 10	7	4.6	0.8
Broussard	3	6/04/84	FL 10	9	4.67	0.7
Broussard	3	6/18/84	FL 10	11	4.54	2
Hughes J	4	4/09/84	FL 10	1	5.51	0.8
Hughes J	4	4/23/84	FL 10	3	5.5	0.6
Hughes J	4	5/07/84	FL 10	5	5.49	1.1
Hughes J	4	5/21/84	FL 10	7	5.41	1
Hughes J	4	6/04/84	FL 10	9	5.61	0.9
Hughes J	4	6/18/84	FL 10	11	5.67	1.7
Ashley S	5	4/29/85	FL 20	1	4.59	1
Ashley S	5	5/13/85	FL 20	3	4.59	0.5
Ashley,S	5	6/10/85	FL 20	7		
Baker C	6	6/03/85	FL 20	1	5	0.4
Baker C	6	6/17/85	FL 20	3	4.92	0.6
Baker C	6	7/01/85	FL 20	5	4.87	0.4
Baker C	6	7/15/85	FL 20	7	5.07	0.4
Baker C	6	7/29/85	FL 20	9	4.95	0.8
Baker C	6	8/12/85	FL 20	11	5.08	0.6
Illig G	7	9/30/85	FL 20	1	4.4	0.8
Illig G	7	10/15/85	FL 20	3	5	0.3
Illig G	7	10/28/85	FL 20	5	5.02	1.2
Illig G	7	11/12/85	FL 20	7	5.32	0.5
Illig G	7	11/25/85	FL 20	9	5.06	0.8
Illig G	7	12/09/85	FL 20	11	4.89	0.5
Wahl M	8	9/30/85	FL 20	1	5.06	0.6
Wahl M	8	10/15/85	FL 20	3	5	0.4
Wahl M	8	10/28/85	FL 20	5	5.32	0.9
Wahl M	8	11/12/85	FL 20	7	5.31	0.5
Wahl M	8	11/25/85	FL 20	9	5.01	0.5
Wahl M	8	12/09/85	FL 20	11	5.06	0.8
Douglas J	9	9/30/85	FL 20	1	5.2	0.5
Douglas J	9	10/15/85	FL 20	3	4.7	0.4
Douglas J	9	10/28/85	FL 20	5	5.01	1
Douglas J	9	11/12/85	FL 20	7	4.67	0.7
Douglas J	9	11/25/85	FL 20	9	4.81	0.9
Douglas J	9	12/09/85	FL 20	11	5.02	0.4
Morin J	10	7/21/86	FL 20	2	4.97	0.6
Morin J	10	8/04/86	FL 20	4	5.13	0.6
Morin J	10	8/18/86	FL 20	6	5.03	0.7
Morin J	10	9/02/86	FL 20	8	5.26	0.9
Morin J	10	9/15/86	FL 20	10	4.98	0.5
Morin J	10	9/29/86	FL 20	12	5.1	0.9
Will A	11	7/21/86	FL 20	2	4.92	0.6
Will A	11	8/04/86	FL 20	4	4.8	0.5
Will A	11	8/18/86	FL 20	6	4.71	0.9
Will A	11	9/02/86	FL 20	8	5.18	0.7
Will A	11	9/15/86	FL 20	10	5.07	0.2
Will A	11	9/29/86	FL 20	12	5.2	0.8
Brinson R	12	9/08/86	FL 20	[illegible]	4.78	0.8

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name	code no	date	rx	week	red bc	retic
Brinson R	12	9/22/86	FL 20	4	4.66	0.3
Brinson R	12	10/06/86	FL 20	6	4.53	0.4
Brinson R	12	10/20/86	FL 20	8	4.78	0.9
Brinson R	12	11/03/86	FL 20	10	4.73	1.2
Brinson R	12	11/17/86	FL 20	12	4.7	0.9

retic no	rpi	hct	hbg	oxyhb	cohb	methb
32.8	0.7	0.44	15.2	97.7	2.5	0.3
69.3	1.4	0.46	16	97.6	2.6	0.3
50.1	1	0.46	16.1	98	2	0.1
30.9	0.5	0.47	16	80.9	2.2	0.2
54.6	1.2	0.45	14.8			
46.9	1	0.45	15.4			
46.6	1	0.45	15.3			
36.8	0.8	0.44	15.2			
32.7	0.7	0.44	15.1			
90.8	2	0.44	14.9			
44.1	0.7	0.49	17.1			
33	0.5	0.5	17			
60.4	0.9	0.5	17.1			
54.1	0.8	0.5	17.5			
50.5	0.7	0.52	17.4			
96.4	1.4	0.52	17.9			
45.9	1	0.43	14.6			
23	0.5	0.43	14.9	92.8	1.6	0.5
20	0.4	0.43	14.6	46.3	1.8	0.1
29.5	0.6	0.43	14.2			
19.5	0.4	0.42	13.6			
20.3	0.4	0.43	14.4			
39.6	0.8	0.42	13.7			
30.5	0.6	0.43	14.2	68	6	0.1
35.2	0.8	0.42	14.5	56.6	9.4	0.1
15	0.3	0.48	16.5	87.5	10.3	0.1
60.2	1.1	0.48	16.6	92.1	6.5	0.1
26.6	0.5	0.5	16.8	90.3	7.4	0.1
40.5	0.8	0.48	16.7			
24.5	0.5	0.46	15.4			
30.4	0.6	0.46	15.3	48.4	0.9	0.1
20	0.4	0.45	15.4	97.8	1.9	0.2
47.9	0.8	0.48	16.5	72.9	2.1	0.1
26.6	0.5	0.48	16.3	85.7	2	0.3
24.1	0.5	0.45	15.7			
40.5	0.8	0.45	15.6			
26	0.5	0.48	16.1	50.2	1.3	0.2
18.8	0.4	0.42	14.3	76.6	1.8	0.1
50.1	1	0.45	16.3	71.6	0.1	0.3
32.7	0.7	0.42	13.9	80.8	3.8	0.1
43.3	0.9	0.43	14.6			
20.1	0.4	0.45	14.1			
20.4	0.7	0.41	14	77.3	0.5	0.5
30.7	0.6	0.42	14.1	57.4	1.5	1
35	0.8	0.41	13.8	79.4	0	0
47.3	0.9	0.43	14.6	78.3	0.2	0.2
24.9	0.5	0.41	13.9	84.5	0	2.1
45.9	1	0.41	13.6			
29.5	0.6	0.43	14.2	93.8	0.7	1.8
24	0.5	0.41	13.7	84.7	0.5	0.9
42	1	0.4	13.7	67.3	0.3	0
36.3	0.8	0.44	15.1	74	0.7	0.4
21.8	0.2	0.43	14.8	86.9	0	4.3
41.6	0.8	0.42	14.5			
38.2	0.8	0.44	15.2	89.5	2.1	8.3

retic no	rpi	hct	hbg	oxyhb	cohb	methb
19.6	0.3	0.42	14.8			
18.1	0.4	0.42	13.9			
43	1	0.44	14.6	56.5	7.4	1.9
56.8	1.2	0.43	15.1			
42.3	0.9	0.42	14.9			

mcv	mch	mchc	zsr	platelet	rbc's morp	white bc
95	33	34	0.52	348		6
92	32	35	0.54	329		6.6
92	32	34	0.55	351		7.5
91	31	34	0.55	344		6.9
98	32	33	0.56	299		7.8
97	33	34	0.55	241		6.2
96	33	34	0.58	287		9.2
95	33	35	0.56	284		10.9
95	32	34	0.59	299		9.7
97	33	34	0.6	287		10.9
89	31	35	0.53	198		6.3
91	31	34	0.53	224		6.7
92	31	34	0.54	207		6.5
93	32	35	0.52	186		6.5
93	31	33	0.54	186		6.5
92	32	34	0.54	194		6.5
93	32	34	0.48	351		8.5
93	33	35	0.55	303	normal	4.9
87	29	34	0.53	204		7.3
87	29	33	0.54	207		6.8
86	28	32	0.5	212		7.2
85	28	33	0.49	198		7.1
86	28	32	0.48	199		7.5
85	28	33	0.51	206		8.7
96	33	34		288		6.7
95	33	34	0.6	308		8.8
95	33	35	0.56	280		8.6
95	32	33	0.66	294		9.1
94	33	35	0.59	295		8.2
94	32	34	0.5	336		9.5
91	30	33		229		4.3
90	31	34	0.49	200		4.9
91	31	34	0.51	205		4.8
91	31	34	0.51	208		5.2
90	31	35	0.5	198		4.7
89	31	35	0.56	191		4.9
92	31	34		375		8.1
90	30	34	0.48	356		7.1
90	31	34	0.6	382		7.4
90	30	33	0.49	334		9.2
89	30	34	0.51	341		8.2
89	30	34	0.51	408		9
83	28	34	0.48	264	normal	6.8
83	27	33	0.48	255	normal	6.8
82	28	34	0.46	270	normal	6.2
82	28	34	0.48	266		7.6
82	28	34	0.48	255	normal	7
81	27	33	0.51	208	normal	6.7
87	29	33	0.55	243	normal	6.5
86	29	33	0.51	217	normal	4.8
85	29	34	0.47	223	normal	5.5
85	29	34	0.51	228	normal	5.9
85	29	34	0.52	247	normal	6.4
80	28	35	0.51	210	normal	5.6
92	32	34	0.56	268	normal	10.7

mcv	mch	mchc	zsr	platelet	rbc's morp	white bc
						11.8
						11.9
91	31	34	0.65	302		12.7
						12.9
						13.1

neut	lymph	mono	eo	baso	bands	neut no
64	28	5	3	0	0	3.84
65	26	5	4	0	0	4.29
67	28	4	1	0	0	5.025
56	39	3	2	0	0	3.864
52	48	0	0	0	0	4.056
44	53	3	1	0	0	2.728
60	37	2	1	0	0	5.52
53	40	4	2	0	1	5.777
54	41	4	1	0	0	5.238
58	37	4	1	0	0	6.322
60	36	1	3	0	0	3.78
56	39	3	2	0	0	3.752
56	35	3	4	0	1	3.64
58	29	5	7	0	1	3.777
60	33	3	4	0	0	3.9
65	27	2	6	0	0	4.225
79	19	1	0	0	1	6.715
65	32	0	3	0	0	3.185
72	27	1	0	0	0	5.256
69	28	2	1	0	0	4.692
64	33	0	3	0	0	4.608
71	28	1	0	0	0	5.041
66	34	0	0	0	0	4.95
67	30	3	0	0	0	5.829
59	34	4	2	0	1	3.953
63	36	0	1	0	0	5.544
64	34	2	0	0	0	5.504
76	23	2	0	0	0	6.916
65	29	1	5	0	0	5.33
69	29	1	0	0	0	6.55
51	41	5	2	0	1	2.193
60	39	0	1	0	0	2.94
62	36	2	0	0	0	2.976
66	33	0	1	0	0	3.432
58	42	0	0	0	0	2.726
56	41	2	1	0	0	2.744
73	23	1	1	0	2	5.913
60	36	0	2	0	2	4.26
65	32	2	1	0	0	4.81
67	27	5	1	0	0	6.164
65	35	0	0	0	0	5.33
60	39	1	0	0	0	5.4
63	31	3	3			4.284
63	32	2	3			4.284
61	33	4	2			3.782
63	31	3	3			4.788
53	39	2	6			3.71
62	32	0	5		1	4.154
49	47	2	2	0	0	3.185
62	35	2	1			2.976
51	44	2	3			2.805
49	44	5	2			2.891
54	41	3	1	1		3.456
42	56		2		0	2.352
58	39	3	0	0	0	6.206

neut	lymph	mono	eo	baso	bands	neut no
69	26	1	3	0	1	8.142
78	21	1	0	0	0	9.282
65	35	0	0	0	0	8.255
74	19	0	3	0	4	9.546
71	27	1	1	0	0	9.301

lymph no	mono no	eo no	baso no	band no	wbc morph	sp gr
1.68	0.3	0.18	0	0		
1.716	0.33	0.264	0	0		
1.5	0.3	0.075	0	0		
2.691	0.207	0.138	0	0		
3.744	0	0	0	0		
3.286	0.186	0.062	0	0		
3.404	0.184	0.092	0	0		
4.36	0.436	0.218	0	0.109		
3.977	0.388	0.097	0	0		
4.033	0.436	0.109	0	0		
2.268	0.063	0.189	0	0		
2.613	0.201	0.134	0	0		
2.275	0.195	0.26	0	0.065		
1.885	0.325	0.455	0	0.065		
2.145	0.195	0.26	0	0		
1.755	0.13	0.39	0	0		
1.615	0.085	0	0	0.085		1.031
1.568	0	0.147	0	0		1.01
1.971	0.073	0	0	0		
1.904	0.136	0.068	0	0		
2.376	0	0.216	0	0		
1.988	0.071	0	0	0		
2.55	0	0	0	0		
2.61	0.261	0	0	0		
2.278	0.268	0.134	0	0.067		
3.168	0	0.088	0	0		
2.924	0.172	0	0	0		
2.093	0.182	0	0	0		
2.378	0.082	0.41	0	0		
2.755	0.095	0	0	0		
1.763	0.215	0.086	0	0.043		
1.911	0	0.049	0	0		
1.728	0.096	0	0	0		
1.716	0	0.052	0	0		
1.974	0	0	0	0		
2.009	0.098	0.049	0	0		
1.863	0.081	0.081	0	0.162		
2.556	0	0.142	0	0.142		
2.368	0.148	0.074	0	0		
2.484	0.46	0.092	0	0		
2.87	0	0	0	0		
3.51	0.09	0	0	0		
2.108	0.204	0.204			normal	1.012
2.176	0.136	0.204			normal	1.008
2.046	0.248	0.124				1.007
2.356	0.228	0.228				1.01
2.73	0.14	0.42			normal	1.008
2.144	0	0.335		0.067	normal	1.008
3.055	0.13	0.13	0	0	3% aty lym	1.01
1.68	0.096	0.048			normal	1.007
2.42	0.11	0.165				1.008
2.596	0.295	0.118			normal	1.011
2.624	0.192	0.064	0.064		normal	1.008
3.136		0.112			normal	1.008
4.173	0.321	0	0	0	1+toxic gr	1.009

lymph no	mono no	eo no	baso no	band no	wbc	morph	sp gr
3.068	0.118	0.354	0	0.118			1.008
2.499	0.119	0	0	0			
4.445	0	0	0	0			1.008
2.451	0	0.387	0	0.516			1.01
3.537	0.131	0.131	0	0			

urine ph	nitrite	glu	urobilin	blood	wbc
5	0	0	0	0	0
6	0	0	0	0	0
7	0	0	0	0	0
7	0	0	0	0	.2
7	0	0	0	0	0-1
7	0	0	0	0	0-1
6.5	0	0	0	0	0
6.5	0	0	0	0	0
6	0	0	0	0	.2
6.5	0	0	0	0	0
6.5	0	0	0	0	0
6	0	0	0	0	0
6.5	0	0	0	0	0
6	0	0	0	0	0
6	0	0	0	0	0-1

urine ph	nitrite	glu	urobilin	blood	wbc
6.5	0	0	0	0	0
6.5	0	0	0	0	0
6	0	0	0	0	.2

epith 1	mucous	amt 1	type 1	am 1	ty 1
0	1	1	3		
0	0	0	0	0	0
1-2 sq	1				
0-1 sq		2	1		
0-1 squam		1	1		
0-1 sq					
0-3 sq	0	2	1	0	0
0	0	0	0	0	0
2-3 sq	1				
0	1				
0-1 squam		0	0		
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	0				

epith 1	mucous	amt 1	type 1	am 1	ty 1
.2	.5	0	0	0	0
0	0	0	0	0	0
0	0	0	0		

1 amt	1 type	color	appearance	prot	keto
		yellow	clear	0	0
0	0	yellow	clear	0	0
		yellow	clear	0	0
		straw	clear	0	0
		yellow	clear	0	0
		yellow	clear	0	0
		yellow	clear	0	0
0	0	yellow	clear	0	0
		yellow	clear	0	0
		yellow	clear	0	0
		straw	clear	0	0
0	0	yellow	clear	0	0
0	0	yellow	clear	0	0
0	0	yellow	clear	0	0
		yellow	clear	0	0

1 amt	1 type	color	appearance	prot	keto
0	0	yellow	clear	0	0
0	0	yellow	clear	0	0
		yellow	clear	0	0

bili	rbc	epith 2	bacteria	amt 2	type 2	am 2
0	0	0	0			
0	0	0	0	0	0	0
0	0	0	0.5			
0			1			
0	0		1			
0	0					
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0.2			
0	0	0	0			
0	0	0	0	0	0	
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0			

bili	rbc	epith 2	bacteria	amt 2	type 2	am 2
0	0	0	2	0	0	0
0	0	0	0	0	0	
0	0	0	1	0	0	

ty 2	2 amt	2 type	glucose	bun	uric aci	creat
			72	15	6.1	1.2
			89	17	4.7	1.1
			87	15	5.7	1.2
			59	12	4.6	1.2
			103	9	4.5	0.9
			79	9	4.6	0.9
			70	12	4.4	1
			71	11	4.6	0.9
			72	14	5	1
			76	11	4.8	1
			83	8	6	0.8
			78	7	5.6	0.9
			86	11	5.9	1
			76	11	5.5	0.9
			79	11	5.6	1
			79	10	5.5	0.9
			103	15	8.3	1.3
0	0	0	78	11	7.3	1.1
			64	13	7.1	1.1
			77	13	6.2	0.9
			88	13	6.3	0.8
			77	11	6.1	0.8
			73	13	4.9	0.8
			70	12	5.7	0.9
			80	12	6.2	0.8
			65	10	5.9	0.9
			74	16	6.3	0.9
			66	14	5.9	1
			66	16	5.7	1.1
			68	15	5.8	1.1
			75	13	6.1	1.1
			79	13	5.9	0.9
			73	13	6.2	0.8
			69	11	6.4	0.8
			67	14	5.7	0.9
			69	12	5.7	0.9
			71	13	5.6	0.9
			83	12	6.1	0.9
			88	9	6.1	0.9
			81	10	5.1	0.8
			77	15	5.3	0.8
0	0	0	83	11	6.8	0.7
0	0	0	78	12	6.1	0.9
			78	15	6.8	0.9
			74	14	7	0.9
			75	14	7.3	0.9
0	0	0	68	15	7.2	0.9
0	0	0	76	14	7	0.8
0	0	0	72	13	7	0.8
			69	11	5.2	0.8

ty 2	2 amt	2 type	glucose	bun	uric aci	creat
0	0	0	66	10	5	0.9
			71	9	4.9	0.9
			66	12	4.5	1
			71	12	5	0.9
			66	11	4.4	0.9

bili t	chol	trigly	hdl	LDL	vldl	chol:hdl
0.8	163	51	37	115.8	10.2	4.4
0.6	189	105	34	134	21	5.6
0.6	218	162	33	152.6	32.4	6.6
0.6	191	139	33	130.2	27.8	5.8
0.9	126	44	35	82.2	8.8	3.6
0.3	131	57	35	84.6	11.4	3.7
0.7	188	70	24	150	14	7.8
0.5	175	101	35	119.9	20.2	5
0.7	196	86	27	151.8	17.2	7.3
0.6	202	98	28	154.4	19.6	7.2
0.5	112	65	29	70	13	3.9
0.6	104	67	45	45.6	13.4	2.3
0.9	137	66	26	97.8	13.2	5.3
0.8	117	64	62	44.4	10.6	1.9
0.7	109	59	28	69.2	11.8	3.9
0.6	129	72	34	80.6	14.4	3.8
0.1	184	189	22	124.2	37.8	8.36
0.3	180	129	20	134.2	25.8	9
0.2	170	126	18	126.8	25.2	9.44
0.9	174	143	30	115.4	28.6	5.8
0.7	201	152	22	148.6	30.4	9.13
0.7	223	123	24	174.4	24.6	9.29
0.8	187	162	14	140.6	32.4	13.35
0.4	217	168	17	166.4	33.6	12.76
0.4	203	150	23	150	30	8.83
0.1	147	97	34	93.4	19.4	4.32
0.4	166	95	25	122	19	6.64
0.8	182	93	32	131.4	18.6	5.68
0.6	151	101	18	112.8	20.2	8.38
0.3	161	115	20	118	23	8.05
0.3	174	107	31	121.6	21.4	5.61
	203	124	63	115.2	24.8	3.22
0.4	175	74	34	126.2	14.8	5.14
0.5	209	76	45	103.8	15.2	4.64
0.3	139	93	22	98.4	18.6	6.31
0.1	169	66	29	112	28	5.82
0.2	178	60	40	126	12	4.45
0.2	257	117	37	197	23	6.9
0.2	264	124	40	199	25	6.6
0.1	238	130	38	174	26	6.3
0.2	240	139	35	177	28	6.8
0.1	239	146	32	177.8	29.2	7.46
0.1	250	146	25	196	29	10
0.2	270	231	35	189	46.2	7.7
0.2	262	213	29	190	43	9
0.1	250	250	35	165	50	7.1
0.2	270	292	39	173	58	6.9
0.1	263	240	36	179	48	7.3
0.1	263	214	32	188	43	8.2
0.3	192	179	37	119	36	5.2

bili t	chol	trigly	hdl	LDL	vldl	chol:hdl
0.4	182	168	33	115	34	5.5
0.3	186	167	33	120	33	5.6
0.1	192	196	29	124	39	6.6
0.2	179	161	31	116	32	5.8
0.1	193	197	33	121	39	5.8

ldh:hdl	fe	uibc	tibc	ferritin	sgot	sgpt
3.1	94	281	375	6	18	15
3.9	86	250	336	6	15	18
4.6	92	237	329	7	17	20
3.9	112	236	348	49	15	16
2.3	119	320	439	53	19	16
2.4	50	333	383	52	11	8
6.3	115	375	490	52	10	10
3.4	114	365	479	32	12	14
5.6	94	312	406	48	12	13
5.5	86	332	418	59	13	14
2.4	230	400	630	242	67	149
1	110	333	443	167	72	158
3.8	150	335	485	179	75	164
0.7	140	323	463	185	64	154
2.3	111	286	397	111	62	135
2.4	91	265	356	53	61	137
5.64	40	310	350		32	45
6.71	85	371	456		19	30
7.04	80	337	417		15	20
				73		
				44		
				34		
				40		
				47		
				51		
3.85	180	365	545	67	17	13
6.75	106	312	418	36	16	19
7.26	66	280	346	30	19	24
10.04	96	379	475	32	13	23
9.78	79	309	388	32	12	19
6.52	53	288	341	23	16	21
2.75	83	325	408	213	17	8
4.88	99	421	520	154	11	7
4.1	103	350	453	190	10	9
6.27	142	407	549	96	12	11
5.9	86	361	447	99	9	9
3.92	93	354	447	108	12	11
1.88	178	355	533	96	20	18
3.71	129	356	485	70	17	16
2.3	115	310	425	89	17	19
4.47	112	355	467	80	17	22
3.86	84	320	450	76	16	18
3.15	90	303	393	81	19	21
5.3	106	173	279	91	13	11
5	88	174	262	83	15	11
4.6	64	196	260	77	12	18
5.1	106	154	260	86	14	10
5.55	98	156	254	83	14	14
7.8	100	155	255	96	15	13
5.4	77	179	256	90	15	13
6.6	62	172	234	78	14	15
4.7	40	204	244	70	13	18
4.4	86	182	268	72	15	18
4.97	76	174	250	74	18	27
5.9	58	202	260	78	26	44
3.2	68	242	310	32	22	19

ldh:hdl	fe	uibc	tibc	ferritin	sgot	sgpt
3.5	37	224	261	22	18	16
3.6	40	225	265	22	52	28
4.3	35	241	276	20	21	18
3.7	40	208	248	16	22	21
3.7	44	255	299	28	25	25

alk phos	alk ptas	Alk ptas	cpk	LDH	ggtp	amy
45			185	140	14	74
55			90	105	10	73
55			142	131	13	77
53			123	118	13	68
56			256	122	11	43
49			50	104	11	45
53			55	121	13	45
59			58	116	16	53
60			60	119	16	49
56			55	110	17	27
51			75	142	43	133
46			40	124	41	136
44			57	129	38	125
51			53	122	40	142
50			62	126	36	148
47			69	117	37	131
103			136	182	28	34
79			63	147	32	24
83			49	120	30	21
64			153	154	19	38
64			54	125	25	54
65			72	148	26	47
65			59	145	27	63
70			66	154	28	57
64			82	114	28	54
62			157	156	10	48
50			65	95	14	41
53			57	107	12	42
52			53	104	13	52
53			70	110	13	48
53			56	96	15	47
42			95	150	16	93
32			56	103	15	83
36			63	130	13	83
32			104	117	12	97
36			93	140	14	97
36			93	118	15	97
56			105	146	12	73
56			108	132	13	82
70			66	126	14	73
68			52	139	14	97
61			59	116	14	94
59			114	123	17	97
40			66	120	13	100
37			43	104	14	100
42			33	103	18	86
46			45	108	19	102
48			39	97	22	98
48			101	109	26	98
76			68	144	32	128

alk phos	alk ptas	Alk ptas	cpk	LDH	ggtp	amy
78			93	150	27	112
89			1625	182	26	115
96			67	156	26	127
97			63	168	30	134
98			94	174	32	127

na	k	cl	co2	po4	ca	ion ca
141	3.8	105	26.2	2.5	9.2	
138	3.9	103	26.2	2.6	9.3	2.3
143	4.4	101	28.5	2.5	10.1	
140	3.6	101	28.4	2.6	9.5	
138	4.1	105	22.9	3.4	9.2	
140	4.1	108	24.6	2.6	8.8	
142	3.6	104	25.8	3.6	9.4	1.99
140	4.3	104	25.9	3.7	9.3	
139	4	105	25.9	3.7	9.6	
140	4	104	27.2	4.1	9.2	2.19
139	4.2	103	21.8	3.9	9.7	
142	4.2	104	28.5	2.3	9.3	
142	3.8	104	24.6	3.2	9.8	2.02
140	3.8	101	24.4	3.2	9.6	
141	3.7	103	26.2	3.4	9.6	
141	4.1	103	27.7	3.5	9.7	2.21
143	3.8	103	26.2	2.5	9.6	2.15
141	3.7	104	30.2	2.6	9	
142	3.5		29.6	3.6	8.9	2.08

140	4		27	3	10.1	1.19
139	4.4		22.6	3	10	1.15
140	4.2		24.6	3.4	9.9	1.15
141	3.9		23.4	2.9	9.7	1.14
142	4.2		28.9	3	9.6	1.18
141	4.7		27.4	3.2	10.9	1.26
141	4.1		29.2	2.9	10.1	1.22
141	3.8		28.4	3.6	9.8	1.19
141	3.5		30.6	3.6	10.3	1.18
142	3.6		25.9	3.4	9.9	1.19
142	3.7		31.2	3.4	10	1.21
140	4.4		33.9	3.7	10.7	1.29
140	4.3		27.4	2.6	10.2	1.14
141	4.3		29	3.9	9.3	1.15
141	4.2		27	4	9.9	1.12
142	3.9		27.7	3.8	9.2	1.12
142	4		27.4	3.5	9.2	1.15
143	4.5		29.6	2.4	10.2	1.23
141	3.8	106	27	3.2	9.8	1.21
140	4	104	29	3.2	10.5	1.15
143	3.7	103	27	3.8	9.2	1.23
141	4.2	105	27	3.6	10.6	1.25
139	3.9	102	27	4	9.8	1.2
142	4.1	105	28	3.9	9.2	1.23
140	4.3	104	28	3.1	9.6	1.17
140	4.2	105	29	3.4	10.2	1.11
142	4.3	102	30	3.7	9.1	1.21
140	4.2	103	28	4.2	10.4	1.21
139	4.4	101	27	4.3	9.9	1.18
104	4.2	103	28	3.7	9.6	1.19
140	4	104	28	2.9	8.8	1.15

na	k	cl	co2	po4	ca	ion ca
136	4	102	26	3.3	8.9	1.2
144	4.2	105	30	3.3	9.6	1.2
143	4.6	104	28	3.2	10	1.18
142	4.3	105	31	3	8.8	1.12
139	4.1	101	30	3.4	8.9	1.12

mg	osmo	tot prot	albumin	A1	A2	Beta
2.1	288	6.6	4.6	0.2	0.4	0.7
2	286	6.7	4.6	0.2	0.5	0.7
2.2	289	7	4.7	0.3	0.6	0.7
1.8	290	7	4.7	0.2	0.5	0.8
2	283	7.2	4.6	0.3	0.8	0.6
1.9	283	7	3.9	0.4	0.9	0.8
2.1	286	6.9	3.9	0.3	0.9	0.9
2.1	283	6.8	3.7	0.4	0.9	0.8
2	284	7	4.3	0.3	0.7	0.8
2	285	6.9	4.1	0.3	0.8	0.8
1.9	282	7	4.2	0.4	0.5	0.7
1.9	284	6.9	4.2	0.5	0.5	0.7
2	283	7.1	4.5	0.3	0.5	0.7
2.1	283	7	4	0.5	0.6	0.8
1.7	285	6.9	4.6	0.4	0.5	0.6
2	288	7.2	5.1	0.3	0.4	0.5
2.3	292					
2.3	290					
2.2	284					

2	288	7.1	4.8	0.2	0.7	0.6
2.1	285	7.3	4.6	0.2	0.8	0.8
2	290	7	4.6	0.2	0.6	0.8
2	282	7.2	4.7	0.1	0.7	0.8
2.3	289	7.6	5	0.3	0.7	0.8
1.9	285	7.5	5.5	0.2	0.6	0.6
2.2	285	6.9	5.2	0.2	0.4	0.5
2.1	286	6.6	4.9	0.2	0.4	0.5
2.1	289	6.9	4.9	0.1	0.5	0.6
2	285	6.6	4.9	0.2	0.5	0.5
2.2	286	6.5	4.8	0.1	0.5	0.5
1.9	288	6.8	4.8	0.2	0.5	0.6
2.1	287	7.1	4.9	0.4	0.5	0.7
2.1	288	6.3	4.4	0.3	0.4	0.6
2.1	286	7.2	5.1	0.3	0.5	0.6
1.9	285	6.4	4.5	0.2	0.5	0.6
2.2	286	6.8	4.7	0.2	0.5	0.6
1.9	286	7.3	5.1	0.2	0.5	0.7
2.2	285	6.6	4.7	0.1	0.4	0.7
2.3	285	6.8	4.7	0.2	0.4	0.7
2	279	6.6	4.6	0.2	0.4	0.7
2	288	6.7	4.6	0.2	0.4	0.8
1.9	289	6.6	4.5	0.2	0.4	0.7
2.1	289	6.2	3.9	0.2	0.4	0.8
2.1	286	6.9	4.7	0.2	0.5	0.8
2.2	287	6.6	4.4	0.2	0.5	0.8
1.9	289	6.3	4.2	0.2	0.5	0.7
1.9	287	6.7	4.4	0.2	0.5	0.8
2	287	6.7	4.4	0.2	0.5	0.8
2.1	287	6.3	4.1	0.2	0.5	0.8
2.1	284	6.8	4	0.3	0.6	0.7

mg	osmo	tot prot	albumin	A1	A2	Beta
2	285	6.3	3.7	0.3	0.6	0.7
2.1	290	6.6	3.8	0.3	0.6	0.8
2.1	292	6.6	3.7	0.3	0.7	0.7
2.1		6.5	3.7	0.2	0.7	0.8
2	292	6.7	3.7	0.3	0.8	0.8

Gamma	A:G
0.7	2.3
0.7	2.2
0.7	2.1
0.8	2
0.9	1.8
1	1.3
0.9	1.3
1	1.2
0.9	1.5
0.9	1.4
1.2	1.5
1	1.5
1.1	1.7
1.1	1.4
0.8	2.1
0.9	2.4

0.8	2.1
0.9	1.7
0.8	1.9
0.9	1.9
0.8	2
0.6	2.8
0.6	3.1
0.6	3
0.7	2.5
0.5	3
0.6	2.8
0.7	2.5
0.6	2.2
0.6	2.2
0.7	2.4
0.6	2.3
0.8	2.3
0.8	2.3
0.8	2.4
0.8	2.3
0.7	2.4
0.8	2.2
0.8	2.1
0.9	1.7
0.7	2.1
0.7	2
0.7	2
0.8	1.9
0.8	2
0.7	1.8
1.2	1.4

Gamma	A:G
1	1.4
1.1	1.4
1.2	1.3
1.1	1.3
1.1	1.3