VITAMIN “D”

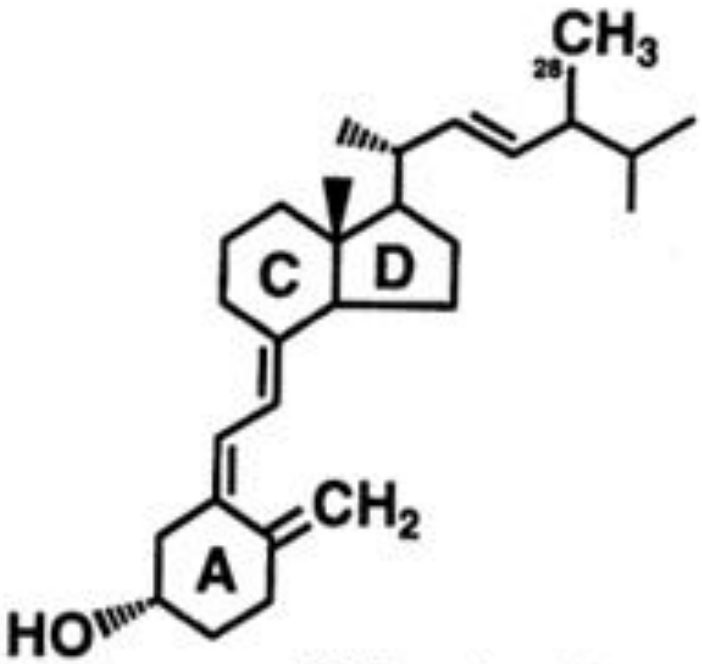
THE VITAMIN DU JOUR

VITAMIN "D"

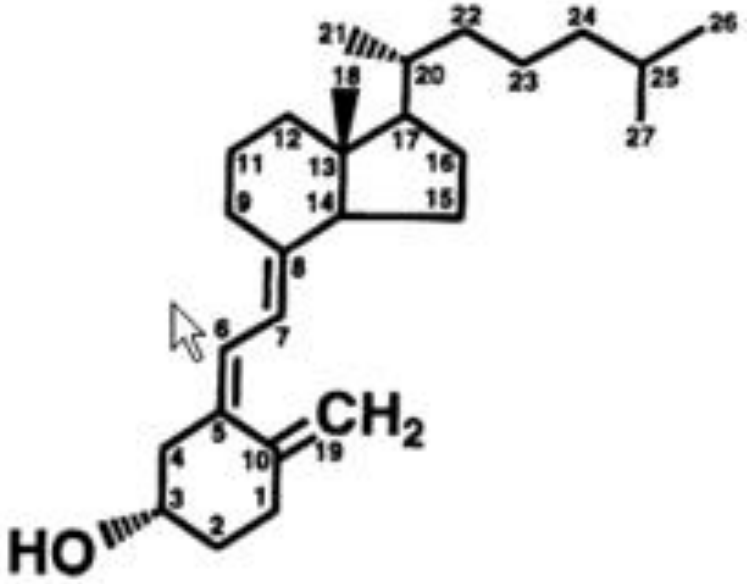
- WHAT ARE THE FACTS AND AND WHAT IS STILL FICTION ABOUT THIS VITAMIN?

VITAMIN "D"

- VITAMIN D FROM THE DIET IN THE FORM OF CHOLECALCIFEROL(D 3) OR ERGOCALCIFEROL(D 2) IS CONVERTED IN THE SKIN BY SUN EXPOSURE(UVB RADIATION) BREAKING THE B RING OF 7-DEHYDROCHOLESTEROL AND FORMING D3
- THIS IS THE MAJOR SOURCE OF VIT D



Vitamin D_2
(Ergocalciferol)



Vitamin D_3
(Colecalciferol)

VITAMIN "D"

- D3 IS BOUND TO VITAMIN D BINDING PROTEIN(DBP) AND TRANSPORTED TO THE LIVER
- HERE IT IS HYDROXYLAED TO FORM 25 HYDROXYCHOLECALCIFEROL
- THIS IS THE VITAMIN D THAT IS MEASURED BY LOCAL LABS WHEN VITAMIN D LEVELS ARE ORDERED

VITAMIN "D"

- 25 OH D IS THEN TRANSPORTED TO THE KIDNEY
- IN THE PROXIMAL TUBULES OF THE KIDNEY UNDER THE INFLUENCE OF PARATHYROID HORMONE IT IS 1 ALPHA HYDROXYLATED TO BECOME 1:25 DIHYDROXYCHOLECALCIFEROL
- THIS IS THE ACTIVE FORM OF VIT D

VITAMIN "D"

- OTHER BODY TISSUES ARE ALSO CAPABLE OF PRODUCING 1:25 DIOH D BUT NO WHERE NEAR THE KIDNEY'S CAPABILITY
- THIS KIDNEY CONVERSION IS INHIBITED BY:

  1) HIGH CALCIUM OR PHOSPHATE LEVEL

  2) FIBROBLAST GROWTH FACTOR 23

VITAMIN “D”

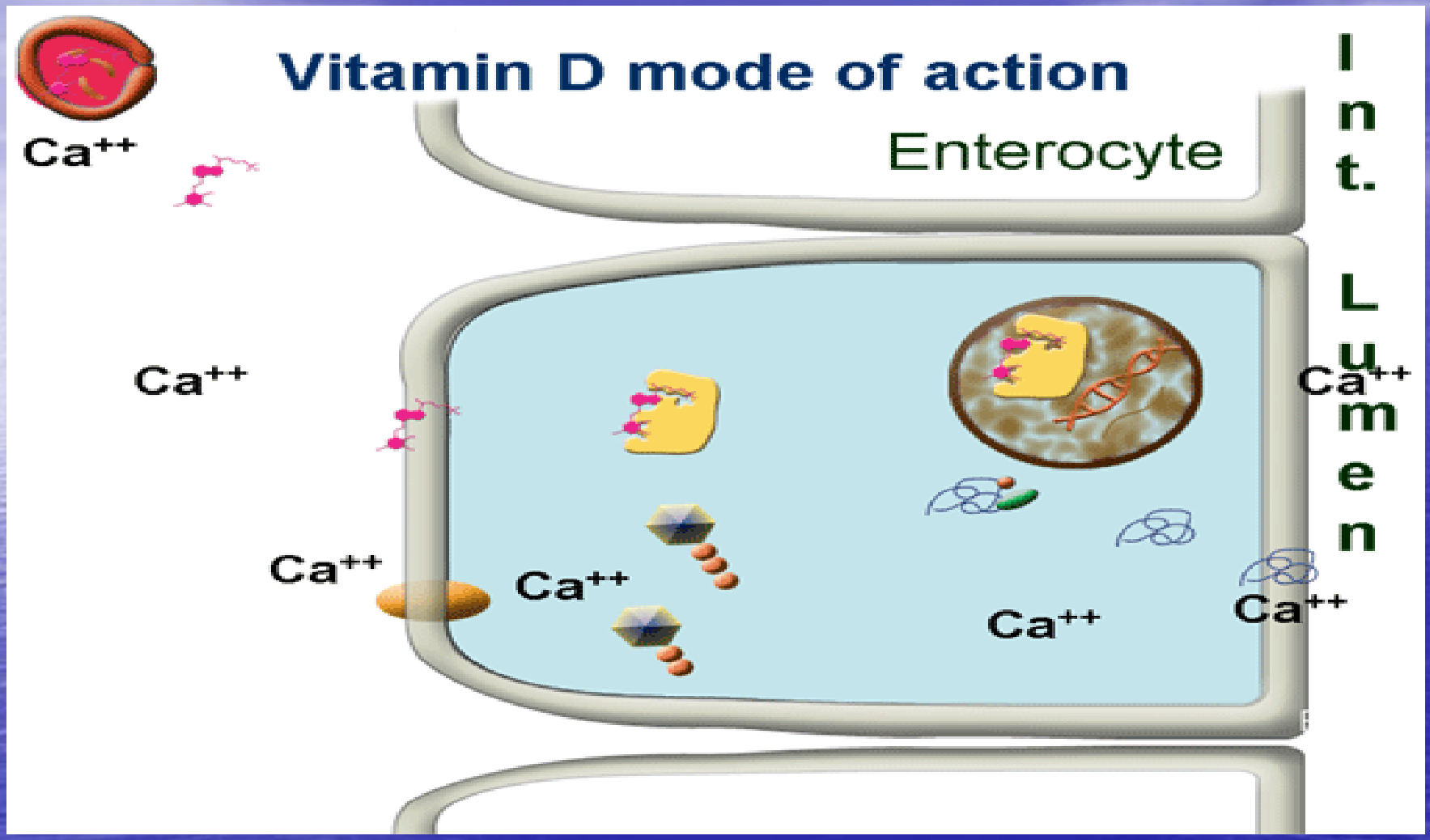
- CHONDROCYTES, OSTEOBLASTS AND OSTEOCLASTS ALL HAVE INTRA NUCLEAR VIT D RECEPTORS AND ALSO AN ENZYME CYP27B1 CAPABLE OF PRODUCING 1:25DIOH D

VITAMIN "D"

- BECAUSE VIT D IS FAT SOLUBLE IT EASILY CROSSES THE CELL MEMBRANE AND BINDS TO RETINOID X RECEPTORS ON THE CELL NUCLEUS KNOWN AS VIT D NUCLEAR HORMONE RECEPTORS (VDR)
- THIS STIMULATES RNA TRANSCRIPTION FACTORS TO PRODUCE CERTAIN PROTEINS

VITAMIN "D"

- IN THE ILEAL LUMINAL CELLS THIS PRODUCES CALBINDIN WHICH BINDS BOTH CALCIUM AND PHOSPHATE IN THE GUT LUMEN AND TRANSPORTS THEM TO THE VASCULAR SIDE TO THE LUMINAL CELL TO BE PICKED UP BY THE CIRCULATORY SYSTEM


Vitamin D mode of action
Enterocyte
Int. Lumen
Ca++
Ca++
Ca++
Ca++
Ca++
Ca++
Ca++

VITAMIN "D"

- ONE MOLECULE OF CALBINDIN CAN BIND TWO MOLECULES OF CALCIUM
- THIS IS HOW VIT D PICKS UP GUT SOURCES OF CALCIUM AND MAKES THEM AVAILABLE TO THE BODY

VITAMIN "D"

- DIRECT EFFECTS ON BONE ARE MORE CONTRAVERSIAL
- 1:25 DIOH D SEEMS TO HELP TRIGGER OSTEOCLAST REABSORPTION OF BONE IN CONJUNCTION WITH PTH
- DEFECIENCIES OF 1:25 DIOH D MAY PREVENT TERMINAL DIFFERENTIATION TO HYPERTROPHIC CHONDROCYTES AND CALCIFICATION OF BONE MATRIX

VITAMIN "D"

- DEFECIENCIES OF VIT D CLEARLY CAUSE RICKETS IN CHILDREN
  1) FIRST APPRECIATED WHEN THE INDUSTRIAL REVOLUTION CAUSED A MIGRATION FROM RURAL AREAS TO URBAN – REFLECTING A RELATIVE DEPRIVATION OF SUN EXPOSURE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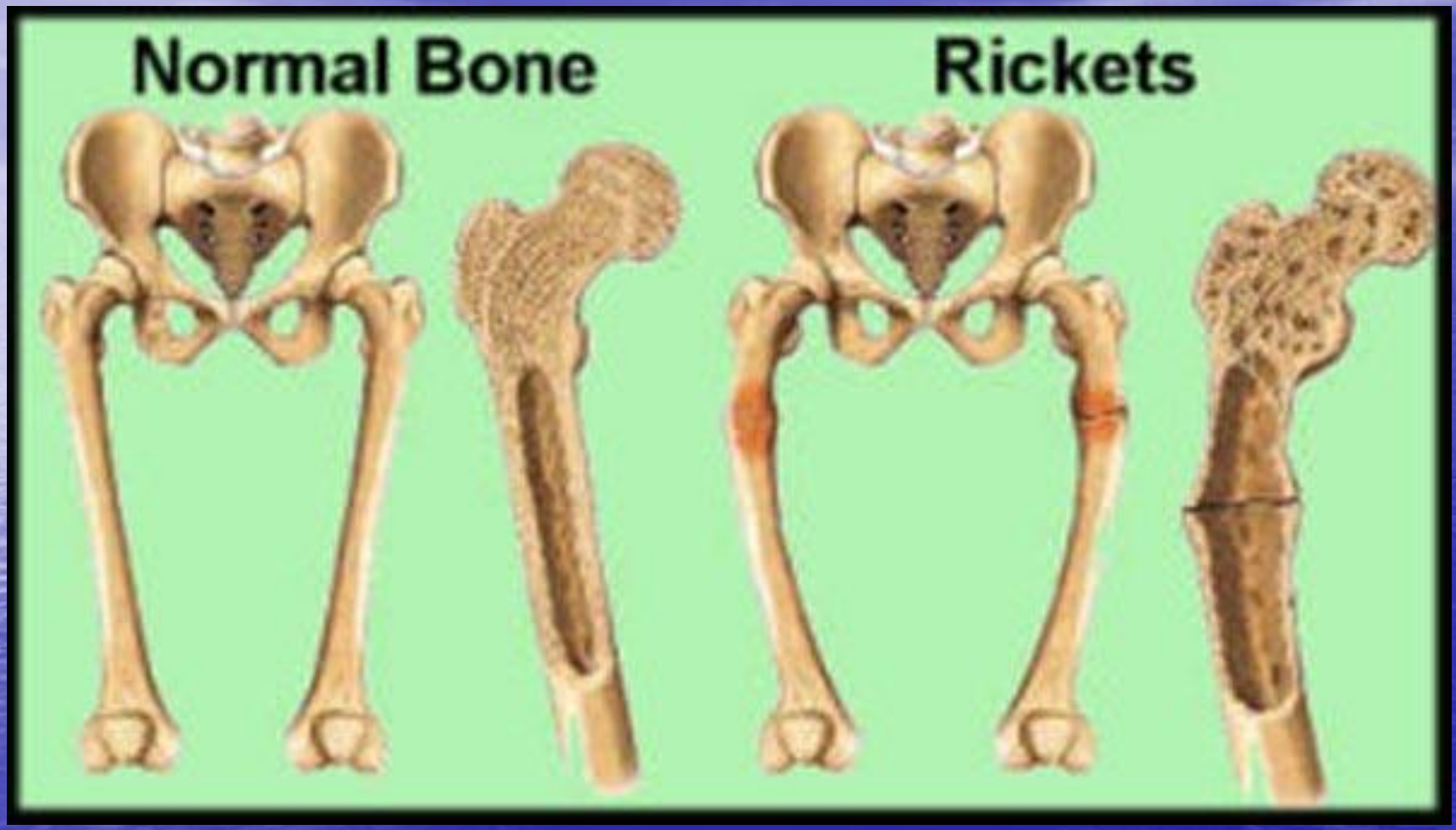
Normal Bone
Rickets

VITAMIN “D”

- OSTEOMALACIA IS MORE COMMONLY SEEN IN OLDER POPULATIONS BUT ALSO CAUSED BY A DEFICIENCY IN VIT D

Osteomalacia

- X- ray -Looser zone

VITAMIN "D"

- 99% OF TOTAL BODY CALCIUM IS STORED IN BONE AS HYDROXYAPATITE
- NORMAL DAILY REQUIREMENT FOR MOST ADULTS IS 400-500 MG/DAY
- PREGNANCY GOES UP TO 1000-1200MG/DAY
- MORE MAY BE NEEDED IN MENOPAUSE, AMENORRHEA, ATHLETES, VEGETERIANS AND LACTOSE INTOLERANT

VITAMIN "D"

- MAIN DIETARY SOURCE FOR VIT D IS FATTY FISH OR SUPPLEMENTS
- MAIN DIETARY SOURCE FOR CALCIUM IS MILK, CHEESES, YOGURT, SALMON, SARDINES AND GREEN LEAFY VEGETABLES

VITAMIN "D"

- ONGOING DEBATE AS TO WHAT THE LOWER ACCEPTABLE BLOOD LEVEL IS FOR VIT D

  1) MOST LABS LIST 30 NANOGMS/ML

  2) RECENT EXPERT OPINIONS NOW FAVOR 20 NANOGMS/ML

VITAMIN "D"

- DAILY DOSING OF VIT D CAN VARY FROM 600 IU TO 4000 IU
- ADEQUATE SUN EXPOSURE (5-10 MINUTES/DAY OF BRIGHT SUNLIGHT) EQUALS APPROXIMATELY 3000 IU/DAY

VITAMIN "D"

- TOXIC LEVELS ARE SEEN WHEN LEVELS ARE > 150 NANOGRAMS/ML

VITAMIN "D"

- OVERDOSING WITH VIT D CAUSES HYPERVITAMINOSIS D WHICH CAN RESULT IN HYPERCALCEMIA
  1) FAT SOLUBLE AND CAN BE PERSISTENT
  2) TREATMENT IS STOPPING VIT D, IV HYDRATION, LOOP DIURETICS, STEROIDS AND PAMIDRONATE

VITAMIN "D"

- HYPOVITMINOSIS D IS TREATED WITH 50,OOO IU/WEEK FOR 8 WEEKS

  1) THEN 1500 TO 2000 IU DAILY

  2) ADD CALCIUM AS WELL

VITAMIN "D"

- UNTIL THIS POINT EVERYTHING HAS BEEN FACTUAL AND ACCEPTED BY THE MEDICAL COMMUNITY
- THE NEXT COUPLE OF SLIDES ARE MUCH MORE CONTRAVERSIAL AND MAY EVEN BORDER ON FICTION

VITAMIN "D"

- POTENTIAL EFFECTS ON CANCER

  1) INHIBITS TUMOR ANGIOGENESIS

  2) STIMULATES CELL ADHESION

  3) INHIBITS CELL PROLIFERATION

VITAMIN "D"

- CANCER AND VIT D
  1) THERE HAVE BEEN ANECDOTAL REPORTS OF REDUCTIONS NOTED IN BREAST, PANCREAS AND PROSTATE CANCER
     A) SO FAR THESE ARE ALL CONJECTURAL

VITAMIN "D"

B) TO DATE THERE ARE NO DOUBLE BLINDED PROSPECT STUDIES THAT SUGGEST THIS

VITAMIN "D"

- THERE ARE SOME EPIDEMIOLOGIC STUDIES THAT SUGGEST A DECREASE IN THE INCIDENCE OF COLORECTAL CARCINOMA IN SUBJECTS TAKING VIT D
- AFTER 7 YEARS OF THE WOMEN'S HEALTH INITIATIVE STUDY WHERE WOMEN DID TAKE HIGH LEVELS OF VIT D THERE WAS NO REDUCTION IN COLORECTAL CARCINOMA

VITAMIN "D"

- WOMEN'S HEALTH INITIATIVE

  1) POST HOC STUDIES IN WOMEN

     NOT TAKING VIT D SHOWED A

     A DECREASED INCIDENCE OF

     BREAST AND COLORECTAL CANCER

VITAMIN "D"

- THE COLON POLYP STUDY IN PATIENTS WITH ALREADY PROVEN COLONIC POLYPS ON HIGH DOSES OF VIT D WILL NOT BE COMPLETED UNTIL DEC 2017
- THERE IS A NEED FOR A RANDOMIZED PROSPECTIVE STUDY TO ALSO ESTABLISH THE PROPER DOSE OF VIT D IF IT TURNS OUT TO BE PROTECTIVE

VITAMIN "D"

- DOES IT CONFER ANY CARDIOPROTECTIVE BENEFITS?
- THERE ARE VIT D RECEPTORS ON:

  1) CARDIOMYOCYTES

  2) VASCULAR SMOOTH MUSCLE CELLS

  3) ENDOTHELIAL CELLS

VITAMIN "D"

- IN SOME STUDIES HAS BEEN SHOWN TO:
  1) REDUCE INFLAMMATION
  2) ALTER CELL PROLIFERATION
  3) REDUCE APOPTOSIS
  4) REDUCE OXIDAIVE STRESS
  5) ALTER MEMBRANE TRANSPORTATION
  6) ALTER CELL ADHESION

VITAMIN "D"

- LOW LEVELS OF VIT D HAVE SHOWN:
  1) A TENDENCY TOWARD LVH
  2) VASCULAR DYSFUNCTION
  3) NEGATIVE INVOLVEMENT WITH THE RENIN-ANGIOTENSIN SYSTEM
     a) HAS BEEN SHOWN TO INCREASE BLOOD PRESSURE

VITAMIN "D"

- CARDIOVASCULAR EFFECTS:
  1) INHIBIT METALLOPROTEINASES
  2) INHIBIT RAAS SYSTEM
  3) VASCULAR WALL
     a) DECREASES VEGF SYNTHESIS
     b) IMPROVES ENDOTHELIAL DYSFUNCTION

VITAMIN “D”

- CARDIOVASCULAR BENEFITS ARE CONFERRED IN CHRONIC KIDNEY DISEASE WITH SECONDARY HYPERPARATHYROIDISM

VITAMIN "D"

- SUNLIGHT ALONE WILL DECREASE BP BY REDUCING VASCULAR RESISTANCE
  1) THIS IS CALLED PHOTORELAXATION
  2) MAY BE RELATED TO INCREASED LEVELS OF NITRIC OXIDE

VITAMIN "D"

- IN SPITE OF THE ATTRIBUTES ASCRIBED TO VIT D THERE HAVE BEEN NO STUDIES THAT CLEARLY SHOW IMPROVED EVENT RATES

VITAMIN "D"

- VITAL STUDY (VIT D AND OMEGA 3)
  1) 5 YR PROSPECTIVE STUDY TO EVALUATE EFFECT OF VIT D WITH AND WITHOUT OMEGA 3 ON CARDIOVASCULAR BENEFITS
  2) 20,000 PARTICIPANTS ARE ENROLLED

VITAMIN "D"

- COULD PROPOSED CARDIOVASCULAR BENEFITS OF VIT D BE AN EPIPHENOMENON ?

  1) THE FACT THAT HEALTHIER PEOPLE TEND TO EXERCISE MORE AND HAVE MORE SUNLIGHT EXPOSURE WOULD GIVE THEM HIGHER VIT D LEVELS

VITAMIN "D"

- SLIGHT INCREASED TENDENCY TO DEVELOP T1DM PERHAPS BY ALTERING THE IMMUNE SYSTEM
- DEFICIENCIES HAVE ALSO BEEN SHOWN TO AGGRIVATE INSULIN RESISTANCE WITH THE THEORETICAL POTENTIAL TO DEVELOP T2DM

VITAMIN “D”

- HAS NOT BEEN SHOWN TO HELP CONTROL EITHER T1DM OR T2DM

VITAMIN "D"

- IT IS A CLEAR FACT THAT VIT D PLAYS A KEY ROLE IN CALCIUM METABOLISM AND BONE HEALTH
- AT THE PRESENT TIME THERE IS STILL A LOT OF FICTION SURROUNDING THE CLAIMS THAT IT MAY REDUCE CANCER OCCURRENCE OR IMPROVE CARDIOVASCULAR HEALTH