DISCLOSURES

• WISCONSINITE

• HAPPY TO BE HERE ON SUPER BOWL SUNDAY
OVERVIEW

• EFFECTS OF EXERCISE:
  • WHITE BLOOD CELLS
  • PLATELETS
  • RED BLOOD CELLS
    • ANEMIA
      • PSEUDOANEMIA
      • EXERCISE ASSOCIATED GI BLEEDING
      • EXERTIONAL HEMOLYSIS

• OTHER HEMATOLOGIC CONDITIONS IN ATHLETES:
  • IRON-DEFICIENCY ANEMIA
  • SICKLE CELL TRAIT

• BLOOD DOPING
LEARNING OBJECTIVES

• BY THE END OF THIS PRESENTATION, THE LEARNER SHOULD BE ABLE TO:

• 1. SUMMARIZE BASIC HEMATOLOGIC CHANGES ASSOCIATED WITH EXERCISE
• 2. RECOGNIZE COMMON HEMATOLOGIC ISSUES SEEN IN ENDURANCE ATHLETES
• 3. DESCRIBE BLOOD DOPING AND BASIC TENETS AND CHALLENGES OF TESTING FOR DOPING
HEMATOLOGIC EFFECTS OF EXERCISE

WBC’S, PLATELETS, RBC’S
LEUKOCYTES

• STRENUOUS OR PROLONGED EXERCISE CAN EFFECT WBC POPULATIONS:
  • MILD LEUKOPENIA/LEUKOCYTOSIS
    • INCREASED GRANULOCYTES
  • TYPICALLY LASTS SEVERAL DAYS, RESOLVES WITH REST

• PROFOUND OR PERSISTENT LEUKOPENIA OR LEUKOCYTOSIS MAY REQUIRE FURTHER W/U FOR MALIGNANCY, HIV, ETC
THROMBOCYTES

• EXERCISE HAS NET **NEUTRAL** EFFECT ON PLATELETS & COAGULATION
  • MAY SEE BRIEF THROMBOCYTOSIS AFTER STRENUOUS EXERTION

• ANY ATHLETE WITH PETECHIAE, UNUSUAL BRUIsing OR EASY BLEEDING
  (GINGIVAL, EPISTAXIS, MENSTRUAL, HEMATURIA, HEMATOCHERZIA) SHOULD
  HAVE FURTHER INVESTIGATION
  • HEAVY MENSES, FREQUENT BRUIsing, ETC MAY BE SIGN OF COAGULOPATHY (IE VON
    WILLEBRAND DISEASE, FACTOR VIII OR IX DEFICIENCY)

• NSAIDS AND ASA-CONTAINING COMPOUNDS MAY ADVERSELY AFFECT PLATELET
  ACTIVITY
HEMATOCYTES

- **ATHLETIC PSEUDOANEMIA**
  - REGULAR AEROBIC OR ENDURANCE TRAINING → INCREASE RBC PRODUCTION & PLASMA VOLUME
    - PLASMA VOLUME TYPICALLY EXCEEDS INCREASED RBC MASS
      - → SLIGHT DECREASE IN HGB, HCT IN RESTING STATE
    - **NOT A TRUE ANEMIA**
  - **HGB CHANGES**:  
    - MODERATE INTENSITY → 0.5 G/DL LOWER  
    - ELITE-LEVEL → 1.0 G/DL LOWER

- **DIAGNOSIS**:  
  1. REST X 3-4 DAYS AND RE-TEST  
  2. **INFER FROM LABS**:  
     1. NORMAL RDW, MCV, MCH  
     2. NORMAL RETICULOCYTE  
     3. NORMAL FERRITIN
EXERTIONAL HEMOLYSIS

• AKA = FOOTSTRIKE HEMOLYSIS
  • = “MARCH HEMOGLOBINURIA”

• OCCURS IN RUNNERS, SWIMMERS, ROWERS, WEIGHTLIFTERS

• CAUSE:
  • UNKNOWN
  • THEORY: CAPILLARY COMPRESSION, INTRAVASCULAR TURBULENCE, ACIDOSIS, ELEVATED MUSCLE TEMPERATURE MAY ALL PLAY A ROLE

• ASYMPTOMATIC
EXERTIONAL HEMOLYSIS

• LABS:
  • HGB, HCT - **USUALLY NORMAL**
  • RETIC, RDW, MCV - **MAY BE SLIGHTLY ELEVATED**
  • HAPTOGLOBIN LEVELS - **MAY BE REDUCED**
  • TRANSIENT HEMOGLOBINURIA - **MAY BE SEEN**
    • *IF HEMOLYSIS EXCEEDS SERUM HAPTOGLOBIN BINDING CAPACITY ~ 20 CC BLOOD*

• TREATMENT
  • **NOT NECESSARY**
  • **MAY TRY CUSHIONED FOOTWEAR, SOFTER TERRAIN IN RUNNERS**
OTHER HEMATOLOGIC CONDITIONS IN ATHLETES
IRON-DEFICIENCY ANEMIA

- **Most Common Cause** of true anemia in athlete and non-athlete

- **Causes:**
  - Inadequate dietary intake or malabsorption
  - Excessive blood loss (menstrual, GI)
  - Combination

- More common in female athletes

- May cause symptoms depending on severity
IRON-DEFICIENCY: LABS

- **HEMOGLOBIN, HEMATOCRIT ↓**
- **MCV ↓, MCH ↓**
- **RDW – TYPICALLY ↑** (UNLESS CHRONIC)
- **RETICULOCYTE – NL/↓**
- **TIBC – TYPICALLY ↑**
- **TRANSFERRIN SATURATION (SERUM FE X 100/ TIBC)** TYPICALLY LOW (< 16%)

- **FERRITIN - NL/↓**
  - TYPICALLY LOW (<12 μg/L)
  - MAY HAVE LOW NORMAL FERRITIN (12-35 μg/L) WITH NOTED DECREASE IN ATHLETIC PERFORMANCE BUT NORMAL HCT/HGB

**RAPID BLOOD LOSS:**
- Hgb, HCT initially normal
- RBC indices initially normal
  - MCV & RDW increase after 3-5 days 2° reticulocyte response
IRON DEFICIENCY: MANAGEMENT

DETERMINE CAUSE:

- HISTORY
  - DIETARY INTAKE
  - OTHER MEDICAL CONDITIONS
  - BLEEDING HISTORY
    - MENSTRUAL:
      - FREQUENCY
      - DURATION
      - # PADS/TAMPONS
      - PASSAGE CLOTS AFTER DAY 1

- SYMPTOMS PRESENT?
  - PALLOR, FATIGUE, TACHYCARDIA, LIGHTHEADEDNESS, DECREASED ATHLETIC PERFORMANCE...

LABORATORY ANALYSIS

- INDICES
- RETICULOCYTE

TREATMENT:

- DEPENDS ON SEVERITY, CAUSE

ORAL IRON:

- FESO4:
  - RECHECK HGB IN 1 MONTH
  - RECHECK FERRITIN IN 3 MOS
  - CONTINUE X 6-12 MOS AFTER RESOLUTION

- IV IRON?
SICKLE CELL TRAIT

• HETEROZYGOUS

• PRESENT IN 8% AFRICAN-AMERICANS IN US

• TYPICALLY ASYMPTOMATIC
  • MILD, MICROSCOPIC HEMATURIA (*INDEPENDENT OF EXERCISE; INSIGNIFICANT*)

• HAS BEEN ASSOCIATED WITH INCREASED RISK OF COMPLICATIONS DUE TO SICKLING:
  • ALTITUDE: ESPECIALLY > 10,000 FT; ALSO VIGOROUS EXERCISE > 5,000 FT
  • HEAT STRESS
  • RAPID ACCELERATED CONDITIONING
  • SUSTAINED MAXIMAL EXERTION

• TESTING NOW MANDATORY IN NCAA
EXERCISE-ASSOCIATED GI BLEEDING

- **AKA:** CECAL SLAP SYNDROME
- LOW GRADE GASTRONINTESTINAL BLEEDING ASSOCIATED WITH PROLONGED ENDURANCE EVENTS

- **CAUSE:**
  - UNKNOWN; SOURCE RARELY DETECTABLE
  - THEORY: ACUTE TRANSIENT ISCHEMIA OR MECHANICAL CONTUSION

- RARELY SYMPTOMATIC
- MAY CAUSE HEME-POSITIVE STOOLS AFTER EVENT
- NO TREATMENT TYPICALLY NECESSARY
BLOOD DOPING
BLOOD DOPING

• DEFINITION
  • ARTIFICIALLY AUGMENTING RBC MASS TO IMPROVE PERFORMANCE
  • INCREASED RBC MASS
  • \(\rightarrow\) INCREASES O2 CARRYING CAPACITY
    • \(\rightarrow\) INCREASES MAXIMAL AEROBIC POWER & AEROBIC CAPACITY
    • \(\rightarrow\) INCREASED VO2 MAX \(\rightarrow\) INCREASED TIME TO EXHAUSTION
  • IMPROVED PERFORMANCE FOR DISTANCE RUNNERS, CYCLISTS
    • IN HEAT, ESPECIALLY IN ACCLIMATIZED ATHLETES

\[O2\text{max} = Q\text{max} \times \alpha - vO2\text{max}\]
DOPING: TYPES/CASES

• MODES:
  • RBC TRANSFUSION
    • ALLOGENEIC
    • AUTOLOGOUS
  • RECOMBINANT ERYTHROPOIETIN (R-EPO)
    • STIMULATE RBC PRODUCTION
  • TYPES:
    • SYNTHETIC EPO
      • EFFECTS LAST 6X LONGER THAN EPO
    • CONTINUOUS ERYTHROPOIETIN RECEPTOR ACTIVATORS (CERAS)
      • EFFECTS LAST 20X LONGER THAN EPO
      • CAN DOSE MONTHLY
    • ESA (ERYTHROPOEISIS STIMULATING AGENTS)
      • NOVEL EPO MIMETICS, EPO GENE ACTIVATORS
      • COBALT CHLORIDE – POTENT INDUCER OF EPO TRANSCRIPTION
DOPING: SAFETY

• **RISKS:**
  • TRANSFUSION REACTION (RARE)
  • INFECTION
  • HYPERVISCOSITY
    • OCCURS W/ HGB > 55%
    • VASCULAR SLUDGING, MYOCARDIAL ARTERY OCCLUSION
    • MAY LEAD TO CVA, MI
  • INCREASED BLOOD PRESSURE
    • CONTRAINDICATED IN SEVERE HYPERTENSION
• NCAA
• IOC
DOPING: TESTING

- **DETECTION:**
  - **BLOOD TRANSFUSION**
    - ALLOGENEIC → BLOOD GROUP ANTI-SERA / FLOW CYTOMETRY
    - AUTOLOGOUS → DIFFICULT
      - CO REBREATHING TEST INVESTIGATIONAL
  - **EPO ISOFORMS**
    - DETECTABLE IN BLOOD AND URINE
      - R-EPO
        - ONLY DETECTABLE FOR 12-18 HRS IN URINE,
        - FEW DAYS IN BLOOD
        - DARBEPOPROTEIN-α - 7 DAYS
      - CERA'S
        - UNCLEAR HOW LONG CAN BE DETECTED IN BLOOD
        - NO CURRENT URINE TEST
  - **EPO MIMETIC PEPTIDES – ELISA**
  - **EPO ENHANCER GENES - ?**
  - **COBALT - ?**
WADA BIOLOGIC PASSPORT

• DECEMBER 2009
• MEASURE HEMATOLOGIC PARAMETERS OVER TIME
• =LONGITUDINAL BLOOD PROFILE
• INCLUDES:
  • HCT, HGB
  • RBCS
  • RETICULOCYTE NUMBER & PERCENTAGE
  • MCV, MCH, MCHC
  • OFF-HR SCORE
KEY POINTS

• ATHLETIC PSEUDO-ANEMIA, EXERCISE-ASSOCIATED HEMOLYSIS, EXERCISE-ASSOCIATED GI BLEEDING RARELY SIGNIFICANT

• MOST COMMON ANEMIA IN ATHLETES IS IRON DEFICIENCY

• SICKLE CELL TRAIT IS RARELY SYMPTOMATIC
  • BUT MAY PREDISPOSE TO SICKLING AND DEATH IN ALTITUDE, HEAT AND EXTREME EXERTION

• BLOOD DOPING CONTINUES TO BE SERIOUS ISSUE IN INTERNATIONAL ENDURANCE SPORTS
  • NEWER FORMS OF R-EPO/ CERA'S ARE DIFFICULT TO DETECT
  • MAY LEAD TO DEATH THROUGH HYPERVISCOSITY
THANK YOU

• BIBLIOGRAPHY:

• BEUTLER E, WAALEN J; THE DEFINITION OF ANEMIA: WHAT IS THE LOWER LIMIT OF NORMAL OF THE BLOOD HEMOGLOBIN CONCENTRATION?; BLOOD; 2006

• EICHER R; THE ANEMIAS OF ATHLETES; PHYSICIAN IN SPORTS MEDICINE; 1986

• JELKMANN W, LUNDBY C; BLOOD DOPING AND ITS DETECTION; BLOOD; 2011; 118

• LIPPI G, FRANCHINI M, GUIDI GC; BLOOD DOPING BY COBALT. SHOULD WE MEASURE COBALT IN ATHLETES?; JOURNAL OF OCCUPATIONAL MEDICINE AND TOXICOLOGY; 2006; 1(18)

• ROBINSON N ET AL; ERYTHROPOIETIN AND BLOOD DOPING; BRITISH JOURNAL SPORTS MEDICINE; 2006; 40

• SOTTAS PE, ET AL; PREVALENCE OF BLOOD DOPING IN SAMPLES COLLECTED FROM ELITE TRACK AND FIELD ATHLETES; CLINICAL CHEMISTRY; 2011