AN EVIDENCE-BASED APPROACH TO CURRENT CONCEPTS IN GASTROENTEROLOGY

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***NO DISCLOSURES***
DIVERTICULITIS AND COLONOSCOPY

• IN A META-ANALYSIS (BR. J SURGERY 7/19) OF 17 OBSERVATIONAL STUDIES OF COLONOSCOPY AFTER ACUTE DIVERTICULITIS, COLORECTAL CANCER WAS DETECTED IN 2.1% (95% CI 1.5–3.1) OF PATIENTS.

• THIS RISK IS HIGHER THAN THE 0.4 TO 1.0% PREVALENCE OF COLORECTAL CANCER IN THE GENERAL POPULATION UNDERGOING SCREENING COLONOSCOPY.

• THIS DATA PROVIDES ADDITIONAL SUPPORT FOR THE RECOMMENDATION FOR COLONOSCOPY IN ALL PATIENTS AFTER AN EPISODE OF ACUTE DIVERTICULITIS, UNLESS THE PROCEDURE WAS PERFORMED IN THE PREVIOUS YEAR.
COLORECTAL CANCER

• THE EFFECTIVENESS FOR CANCER PREVENTION OR EARLY DETECTION IS AN IMPORTANT FACTOR WHEN SELECTING A COLORECTAL CANCER (CRC) SCREENING TEST

• STUDY FROM ANNALS INT MED 2018 EVALUATED PATIENTS WHO DID FECAL IMMUNOCHEMICAL TESTING (FIT) EVERY TWO YEARS:

  1. THE RATE OF DETECTION OF CRC STEADILY DECLINED IN THE LEFT COLON OVER 12 YEARS

  2. REMAINED RELATIVELY UNCHANGED IN THE RIGHT COLON
COLORECTAL CANCER

• THESE RESULTS ARE CONSISTENT WITH A LOWER SENSITIVITY OF FIT FOR PROXIMAL COLON LESIONS

• WHY?

• THE RESULT COULD BE DUE TO THE INCREASE IN THE PROPORTION OF CANCER THAT OCCURS IN THE RIGHT COMPARED WITH THE LEFT COLON (A "RIGHTWARD SHIFT") THAT OCCURS WITH AGE
COLORECTAL CANCER (CRC)

• THIRD MOST COMMON CANCER, SECOND CAUSE OF CANCER DEATH IN THE US
• THE AMERICAN CANCER SOCIETY ESTIMATED THERE WAS APPROXIMATELY 140,000 NEW CASES OF CRC AND 50,000 DEATHS BECAUSE OF CRC IN 2018
• THE MOST COMMON RISK FACTOR IS AGE: 90% OF CRCS ARE DIAGNOSED IN PEOPLE 50 YEARS OF AGE AND OLDER (1)
• THE US PREVENTIVE SERVICES TASK FORCE RECOMMENDS ROUTINE SCREENING FOR AVERAGE-RISK INDIVIDUALS STARTING AT AGE 50 (ACS 45)
• FOR INDIVIDUALS WITH ABOVE-AVERAGE RISK (AA, INDIVIDUALS WITH STRONG FAMILY OR PERSONAL HISTORY) SCREENING SHOULD BEGIN AT AN EARLIER AGE (2)
FIT (Fecal Globin by Immunochemistry or Fecal Immunochemistry Test): CRC Facts

- Screening for CRC effectively reduces incidence and mortality by $\geq 50\%$ (3)
- Early detection is crucial, as survival rates decrease dramatically with increasing cancer stage
- The 5-year survival stage I is approximately 90% vs stage IV 14% (4)
- Most CRCs begin as adenomatous polyps, which take 10 years or longer to undergo malignant transformation (5)
- This long transformation period is one of the reasons CRC screening is so effective: precancerous lesions can be identified and removed before becoming cancerous.
FECAL OCCULT BLOOD TEST VS FIT (Fecal Globin by Immunocytchemistry or Fecal Immunocytchemistry Test)

- FECAL OCCULT TESTING FALL INTO 2 MAIN CATEGORIES: GUAIALC-BASED (GFOBT) AND IMMUNOCHEMICAL

- GFOBTS DETECT HEME PEROXIDASE ACTIVITY AND ARE NOT SPECIFIC FOR HUMAN HEMOGLOBIN
  - THUS, HEMOGLOBIN FROM RED MEAT, PEROXIDASE FROM FRUITS AND VEGETABLES, AND CERTAIN MEDICATIONS CAN CAUSE FALSE+ RESULTS
  - VITAMIN C (EXCESS OF 250 MG/DAY) FROM SUPPLEMENTS OR CITRUS FRUITS MAY CAUSE A FALSE- GUAIALC TEST RESULT (5)

- NOT SPECIFIC TO LOCATION
FOBT VS FIT (Fecal Globin by Immunochemistry or Fecal Immunochemistry Test)

• **IMMUNOCHEMICAL FOBTS (Fecal Immunochemical Tests)** do not react with non-human hemoglobin or peroxidase

• Uses a simple brush

• FIT is specific for lower gastrointestinal bleeding because they target the globin portion of hemoglobin, which does not survive passage through the upper gastrointestinal tract

• FIT > FOBT Sensitivity
DIVERGENT LONG-TERM DETECTION RATES OF PROXIMAL AND DISTAL ADVANCED NEOPLASIA IN FITSCREENING PROGRAMS: A RETROSPECTIVE COHORT STUDY (6)

- AUZORZI ET AL., ANN INTERN MED. 2018;169(9):602. EPUB 2018 OCT 2

**BACKGROUND:**
- SHORT-TERM STUDIES HAVE REPORTED THAT THE FECAL IMMUNOCHEMICAL TEST (FIT) IS LESS ACCURATE IN DETECTING PROXIMAL \(^\circ\) THAN DISTAL (L) COLORECTAL NEOPLASIA

**OBJECTIVE:**
- TO ASSESS THE LONG-TERM DETECTION RATES FOR ADVANCED ADENOMAS AND CRC WITH REGARD TO ANATOMICAL LOCATION

**DESIGN AND SETTING:**
- POPULATION-BASED RETROSPECTIVE STUDY EVALUATING SCREENING PROGRAM IN THE VENETO REGION OF ITALY
DIVERGENT LONG-TERM DETECTION RATES OF PROXIMAL AND DISTAL ADVANCED NEOPLASIA IN FECAL IMMUNOCHEMICAL TEST SCREENING PROGRAMS: A RETROSPECTIVE COHORT STUDY

- PARTICIPANTS:
  - PERSONS AGED 50 TO 69 YEARS WHO COMPLETED 6 ROUNDS OF FIT SCREENING

- MEASUREMENTS:
  - AT EACH SCREENING ROUND, THE DETECTION RATES FOR BOTH ADVANCED ADENOMA AND COLORECTAL CANCER, AS WELL AS THE PROPORTIONAL INTERVAL CANCER RATE (PICR), WERE CALCULATED BY ANATOMICAL LOCATION
    - (PROXIMAL COLON, DISTAL COLON, OR RECTUM)
DIVERGENT LONG-TERM DETECTION RATES OF PROXIMAL AND DISTAL ADVANCED NEOPLASIA IN FIT SCREENING PROGRAMS: A RETROSPECTIVE COHORT STUDY

• RESULTS:

• BETWEEN 2002 AND 2014, A TOTAL OF 123,347 PARTICIPANTS HAD A TOTAL OF 441,647 FITS

• THE NUMBERS OF ADVANCED ADENOMAS AND CANCER CASES DETECTED RESPECTIVELY, WERE:
  • 1704 AND 200 IN THE PROXIMAL COLON
  • 3703 AND 324 IN THE DISTAL COLON
  • 1220 AND 209 IN THE RECTUM

• OVERALL 150 CASES OF INTERVAL CANCER WERE DIAGNOSED

• THE PROPORTIONAL INTERVAL CANCER RATE (PICR) WAS HIGHER IN THE PROXIMAL COLON (25.2% [95% CI, 19.9% TO 31.5%]) THAN THE DISTAL COLON (6.0% [CI, 3.9% TO 8.9%]) OR RECTUM (9.9% [CI, 6.9% TO 13.7%])
DIVERGENT LONG-TERM DETECTION RATES OF PROXIMAL AND DISTAL ADVANCED NEOPLASIA IN FECAL IMMUNOCHEMICAL TEST SCREENING PROGRAMS: A RETROSPECTIVE COHORT STUDY

• CONCLUSION:
  • THIS FIT-BASED, MULTIPLE-ROUND, LONG-TERM SCREENING PROGRAM DEMONSTRATED A LOWER DETECTION RATE FOR NEOPLASTIC LESIONS IN THE PROXIMAL VERSUS THE DISTAL COLON
THE IMPACT OF COLORECTAL SCREENING PROGRAM ON THE DETECTION OF RIGHT-SIDED COLORECTAL CANCER
A 5-YEAR COHORT STUDY IN THE MANTUA DISTRICT (7)

• ASTERIA, ET AL. INT J COLORECTAL DIS. 2015 DEC;30(12):1627–37

• BACKGROUND:
  • HIGH RATES OF ADVANCED COLORECTAL CANCER (CRC) ARE DIAGNOSED IN THE RIGHT SIDE OF THE COLON
  • AIM TO INVESTIGATE IF SCREENING PROGRAMS INCREASE CRC DETECTION AND IF TUMOR LOCATION IS ASSOCIATED WITH SURVIVAL OUTCOME

• METHODS:
  • PATIENTS AFFECTED BY CRC, AGED FROM 50 TO 69 YEARS AND OPERATED ON FROM 2005 TO 2009 WERE REVIEWED
  • DETECTION MODE AND TUMOR LOCATION WERE RECORDED
  • OVERALL SURVIVAL (OS) AND DISEASE–FREE SURVIVAL (DFS) WERE INVESTIGATED USING UNIVARIATE AND MULTIVARIATE ANALYSES
THE IMPACT OF COLORECTAL SCREENING PROGRAM ON THE DETECTION OF RIGHT-SIDED COLORECTAL CANCER

• RESULTS:
  • MEAN AGE OF 386 PATIENTS INCLUDED WAS 62.0 YEARS, 59 % WERE MALES
  • CRC WAS DETECTED BY:
    • SCREENING IN 17 % OF CASES
    • WORK UP OF SYMPTOMS IN 67 %
    • FOUND DURING EMERGENCY SURGERY 16 %
  • SCREENING-DETECTED CRCS WERE LOCATED IN THE LEFT COLON (59 %), THEN IN RECTUM (25 %) AND IN PROXIMAL COLON (16 %) (P = 0.02)
  • MOST OF CRC PATIENTS URGENTLY OPERATED ON HAD CANCER LOCATED IN PROXIMAL COLON (45 %), THEN IN THE LEFT COLON (36 %) AND IN RECTUM (18 %) (P = 0.001)
  • RIGHT-SIDED CRC DEMONSTRATED HIGHER TNM
THE IMPACT OF COLORECTAL SCREENING PROGRAM ON THE DETECTION OF RIGHT-SIDED COLORECTAL CANCER

• CONCLUSION:
  • LOW RATES OF RIGHT-SIDED CRC ARE DIAGNOSED FOLLOWING SCREENING PROGRAM
  • PROXIMAL CRC DEMONSTRATES AGGRESSIVE BEHAVIOR WITHOUT IMPACT ON OUTCOME
  • THESE FINDINGS PROMPT CONCERN ABOUT POPULATION AWARENESS FOR CRC SCREENING
LYNCH SYNDROME IN PATIENTS WITH MICROSATELLITE UNSTABLE TUMORS (J CLIN ONC JANUARY 2019)

• COLORECTAL (CRC) AND ENDOMETRIAL CANCERS IN LYNCH SYNDROME DEMONSTRATE HIGH LEVELS OF MICROSATELLITE INSTABILITY (MSI–H) DUE TO A LOSS OF DNA MISMATCH REPAIR

• THE PREVALENCE OF LYNCH SYNDROME IN PATIENTS WITH MSI–H SOLID TUMORS OTHER THAN CRC AND ENDOMETRIAL CANCER IS NOT KNOWN

• IN A STUDY OF APPROXIMATELY 15,000 INDIVIDUALS WITH SOLID TUMORS, THE PREVALENCE OF LYNCH SYNDROME IN PATIENTS WITH MSI–H, AND INDETERMINATE (MSI–I) TUMORS WAS 16% AND 2%, RESPECTIVELY (8)

• AMONG 66 PATIENTS WITH LYNCH SYNDROME AND MSI–H/I TUMORS, APPROXIMATELY ~50% HAD TUMORS OTHER THAN CRC/ENDOMETRIAL CANCER
  • ONLY 50% OF THESE MET CRITERIA FOR GENETIC EVALUATION FOR LYNCH SYNDROME BASED ON THEIR PERSONAL OR FAMILY CANCER HISTORY

• THE ABOVE DATA SUPPORTS CURRENT RECOMMENDATIONS FOR GERMLINE GENETIC TESTING FOR LYNCH SYNDROME IN INDIVIDUALS WITH ANY MSI–H TUMOR
  • EVEN IF THEY LACK PERSONAL OR FAMILY CANCER HISTORY CLASSICALLY ASSOCIATED WITH LYNCH SYNDROME
WHAT IS MSI–H?

• MSI–H STANDS FOR MICROSATELLITE INSTABILITY–HIGH
• IT IS A FEATURE OF CANCER’S GENETIC CODING, WHICH RESULTS IN IT BEHAVING AND “LOOKING” A CERTAIN WAY ON A MICROSCOPIC LEVEL
• DUE TO DEFECTS IN THE WAY THAT DNA IN THE CANCER CELLS REPAIRS ITSELF, IT CREATES CHANGES AND MUTATIONS TO NORMAL BODY CELLS THAT CAN EVENTUALLY LET THEM TURN INTO CANCER
• BECAUSE OF THIS FEATURE AND ABILITY OF THE CELLS TO LOOK SO ABNORMAL THE IMMUNE SYSTEM CAN CALL THE BODY’S NORMAL DEFENSES AGAINST INVADERS TO TRY TO ATTACK THE CANCER
CAUSE OF MSI–H

• GENETIC ABSENCE OF CERTAIN PROTEINS THAT HELP REPAIR DNA IN CELLS WHEN IT BREAKS

• IN THE ABSENCE OF THESE PROTEINS, OR IF THEY BREAKDOWN OVER TIME, THEN A HEALTHY CELL CAN’T REPAIR ITSELF NORMALLY AND IT STARTS MAKING MANY MISTAKES IN ITS OWN GENETIC CODE

• SUDDENLY, THE "INSTRUCTION MANUAL" ON HOW A NORMAL CELL SHOULD WORK BECOMES INCORRECT, CAUSING THE CELL TO BECOME INCREASINGLY ABNORMAL AND LEADING TO DISORDERED GROWTH, WHICH IS A HALLMARK FEATURE OF CANCER
WHAT ARE THE COMMON MALIGNANCIES ASSOCIATED WITH MSI–H STATUS, AND WHAT IS ITS SIGNIFICANCE IN THESE TUMORS?

• CRC IS MOST COMMONLY ASSOCIATED HERE, BUT ANY CANCER CAN BE IMPLICATED JUST AT VARIABLE AND RELATIVELY LOW PERCENTAGES

• THE BEHAVIOR OF MSI–H CRC IS DIFFERENT FROM SO–CALLED MICROSATELLITE STABLE (MSS, OR NON–MSI–H) CRC

• GENERALLY, MSI–H IS ASSOCIATED WITH A BETTER PROGNOSIS, ALTHOUGH THIS IS NOT UNIVERSAL

• WHILE TRADITIONAL CHEMOTHERAPY DRUGS ARE STILL USED FREQUENTLY IN MSI–H CRC, IMMUNOTHERAPY DRUGS AFFECTING THE INTERACTION OF SOMETHING CALLED PD–1 (PROGRAMMED DEATH RECEPTOR–1) HAVE SHOWN TRULY REMARKABLE PROMISE IN TREATING THESE TYPES OF CANCERS
WHAT ARE THE COMMON MALIGNANCIES ASSOCIATED WITH MSI–H STATUS, AND WHAT IS ITS SIGNIFICANCE IN THESE TUMORS?

• THEREFORE MSI–H STATUS MAY DRAMATICALLY CHANGE THE WAY WE TREAT TUMORS, BOTH IN DECISIONS TO TREAT IN A POST-SURGICAL SETTING AND THE TYPES OF DRUGS USED

• IT IS IMPORTANT TO NOTE THAT THE FDA HAS APPROVED SOME OF THESE IMMUNOTHERAPY DRUGS, KNOWN AS CHECKPOINT INHIBITORS, IN THE TREATMENT OF ALL MSI–H TUMORS REGARDLESS OF LOCATION

• THIS IS A BIG STEP FORWARD (DESPITE THAT IT AFFECTS SUCH A SMALL% OF TUMORS)
WHY IS IT IMPORTANT TO TEST FOR MSI–H STATUS FOLLOWING A PATIENT’S DIAGNOSIS?

• PEOPLE WITH LYNCH SYNDROME ARE MORE LIKELY TO GET COLORECTAL CANCER AND OTHER CANCERS AT A YOUNGER AGE (BEFORE 50) (UTERINE INCLUDING ENDOMETRIAL, STOMACH, LIVER, KIDNEY, BRAIN AND SKIN CANCER)

• LYNCH SYNDROME CAUSES ABOUT 4,000 COLORECTAL CANCERS AND 1,800 UTERINE (ENDOMETRIAL) CANCERS PER YEAR

• DUE TO INHERITED MUTATIONS IN GENES THAT AFFECT DNA MISMATCH REPAIR (A PROCESS THAT FIXES MISTAKES MADE WHEN DNA IS COPIED)

• DEFICIENCIES OF THE GENES MOST FREQUENTLY RESPONSIBLE FOR CAUSING MSI–H CANCERS ARE MOST OFTEN ASSOCIATED WITH A SYNDROME CALLED HNPCC OR HEREDITARY NON–POLYPOSIS COLORECTAL CANCER SYNDROME (LYNCH SYNDROME)

• THERE ARE A NUMBER OF OTHER CANCERS INVOLVED IN THIS SYNDROME INCLUDING UTERINE, BILE DUCT, STOMACH, PANCREATIC, BLADDER AND SMALL INTESTINE CANCER
LYNCH SYNDROME

• ORIGINALLY TERMED HEREDITARY NONPOLYPOSIS COLORECTAL CANCER (HNPCC)
• AN AUTOSOMAL DOMINANT MULTICANCER DISORDER
• MORE FREQUENT AND EARLIER THAN EXPECTED ONSET OF COLORECTAL, ENDOMETRIAL, OVARIAN, AND OTHER CANCERS
• FIRST CHARACTERIZED IN 1966 BY HENRY T. LYNCH
• SYNDROME IS CAUSED BY GENETIC DEFECTS IN ONE OR MORE DNA MISMATCH REPAIR (MMR) GENES, INCLUDING MLH1, MSH2, MSH6, AND PMS2
• THESE MMR GENES IDENTIFY AND CORRECT MISMATCHED DNA BASE PAIRS
How does MSI-H status change oncology treatment?

- It may change decisions on whether to treat a patient with chemotherapy or to use immunotherapy.
- The decisions behind this are highly applicable to each individual’s presentations.
- The immune system is more easily able to “recognize” these MSI-H tumors.
  - Meaning that they respond far more readily to the wave of immunotherapy drugs available.
ORAL SIMETHICONE ON ADENOMA DETECTION RATE
GIE MAY 2019;90:114 (9)

• ADDING SIMETHICONE INTRAPROCEDURAL MAY RESULT IN ENDOSCOPIC CONTAMINATION
  • OFSTEAD ET AL. PUBLISHED IN THE AMERICAN JOURNAL OF INFECTION CONTROL DESCRIBED RESIDUAL SIMETHICONE AND NON-PATHOGENIC BACTERIAL COLONIZATION IN ENDOSCOPES DESPITE REPROCESSING
  • THESE FINDINGS RECEIVED SIGNIFICANT MEDIA ATTENTION, IN PART BECAUSE THEY WERE RELEASED FOLLOWING A WARNING ISSUED BY THE FDA AND THE CDC REGARDING THE POTENTIAL TRANSMISSION OF MULTIDRUG RESISTANT BACTERIA ASSOCIATED WITH THE USE OF DUODENOSCOPES

• SIMETHICONE IS A FULLY METHYLATED SILICONE-BASED POLYMER USED TO DECREASE THE SURFACE TENSION OF GAS OR AIR BUBBLES, USED SINCE 1978 IN ENDO PROCEDURES

• SIMETHICONE IS FREQUENTLY MIXED IN THE WATER PUMP TO DISPERSE THE REMAINING BUBBLES DURING THE EXAMINATION, BUT THE USE WITH BOWEL PREP IS STILL NOT COMMON

• TRIAL OF 268 PATIENTS UNDERGOING COLONOSCOPY WITH BOWEL PREP CONTAINING SIMETHICONE WERE LESS LIKELY TO NEED THROUGH THE SCOPE (TTS) SIMETHICONE TO IMPROVE VISUALIZATION COMPARED TO BOWEL PREP ALONE (2% VS 49%)
BLEEDING CAN BE SERIOUS COMPLICATION FOLLOWING ENDOSCOPIC MUCOSAL RESECTION

TRIAL INCLUDING >900 PATIENTS WITH NON-PEDUNCELATED POLYPS ≥ 2 CM FOUND CLIP CLOSURE REDUCED THE POST-POLYPECTOMY BLEEDING RATE FOR PROXIMAL COLON POLYPS (3% VS 10%) BUT NOT FOR DISTAL POLYPS
BUDESONIDE VERSUS FLUTICASONE IN EOSINOPHILIC ESOPHAGITIS
GASTROENTEROLOGY APRIL 2019

• TOPICAL GLUCOCORTICOIDS ARE A FIRST-LINE TREATMENT FOR EOSINOPHILIC ESOPHAGITIS

• FIRST RANDOMIZED TRIAL COMPARED THE EFFICACY OF ORAL VISCOS BUDESONIDE 15 DAYS VS SWALLOWED FLUTICASONE FOR 8 WEEKS

• EQUALLY EFFECTIVE IN TREATMENT OF EOE

• VISCOS BUDESONIDE (PULMICORT RESPULE) 4 X .5 MG/2 ML = 8 ML BID X 15 D (NO FOOD 30 MIN AFTER)

• FLUTICASONE (ADVAIR DISCUS/INHALOR) SWALLOW 220 UG 2 PUFFS SWALLOW BID X 8 WEEKS (GOOD LUCK)
EOSINOPHILIC ESOPHAGITIS (EOE)

BACKGROUND

• IMMUNOLOGIC REACTION TO INGESTED OR INHALED ALLERGENS → ESOPHAGEAL EOSINOPHILIA → GASTROINTESTINAL SYMPTOMS

• M > W WITH A MEAN AGE OF ONSET OF 38 YEARS

• RECENT DATA SHOW THAT EOE IS INCREASING IN PREVALENCE WITH AN INCIDENCE OF 6–30 CASES/100,000 INDIVIDUALS (10)

• COMMON WITH FAMILY HISTORY OF ALLERGIES OR ASTHMA, AND SYMPTOMS OF 1 OR MORE ALLERGIC DISORDERS
  • ASTHMA, ALLERGIC RHINITIS, ATOPIC DERMATITIS (ECZEMA) AND FOOD ALLERGY

• ENVIRONMENTAL ALLERGIES TO SUBSTANCES SUCH AS DUST MITES, ANIMALS, POLLEN AND MOLDS CAN PLAY A ROLE IN EOE
  • EOE CAN BE WORSE DURING POLLEN SEASONS
  • ALLERGY TESTING FOR THESE COMMON ENVIRONMENTAL ALLERGIES IS OFTEN PART OF THE EOE EVALUATION

• FOOD ALLERGIES ARE THE MOST COMMON CAUSE OF EOE
EOSINOPHILIC ESOPHAGITIS (EOE) BACKGROUND

• DIAGNOSIS INCLUDES EGD WITH BIOPSIES 4–6 MID/PROXIMAL (> 15 EOS/HPF), ALLERGY BLOOD TEST, PRICK SKIN TEST AND FOOD PATCH TEST (ALL CAN HAVE FALSE POSITIVES)

• TREATMENT OPTIONS
  • ELIMINATION AND ELEMENTAL DIETS TO DECREASE ALLERGEN EXPOSURE
  • ACID SUPPRESSION
  • TOPICAL GLUCOCORTICOIDs TO DECREASE ESOPHAGEAL INFLAMMATION
  • FLUTICASONE 220 UG 2 PUFFS (SWALLOWED) BID X 8 WEEKS
  • VISCOS BUDESONIDE CAN BE COMPOUNDED BY MIXING TWO OR FOUR 0.5 MG/2 ML PULMICORT RESPULES WITH SUCRALOSE (SPLENDA; 10 1-GRAM PACKETS PER 1 MG OF BUDESONIDE, CREATING A VOLUME OF APPROXIMATELY 8 ML) X 8 WEEKS
  • ***NO EATING 30 MINUTES AFTER TAKING THE ABOVE

• ESOPHAGEAL DILATION TO TREAT STRICTURES
  • ALTHOUGH ESOPHAGEAL DILATION MUST ALWAYS BE PERFORMED WITH CAUTION, THE RISK FOR PERFORATION IN EOE SEEMS TO HAVE BEEN EXAGGERATED (<1%) (11)
ASA USE IN PATIENTS WITH NAFLD

• LIFESTYLE MODIFICATION CONFIRMS BENEFIT, LITTLE DATA ON MEDICATIONS EXCEPT VITAMIN E

• VITAMIN E IS THE MAJOR LIPID-SOLUBLE CHAIN-BREAKING ANTIOXIDANT FOUND IN THE HUMAN BODY THAT HAS ANTI-OXIDATIVE PROPERTIES
  • OXIDATIVE STRESS PLAYS A CRUCIAL ROLE IN PRODUCING THE LETHAL HEPATOCYTE INJURY ASSOCIATED WITH NAFLD
  • THEREFORE, BY TARGETING OXIDATIVE STRESS COMPONENTS, VITAMIN E APPEARS AS A PROMISING THERAPEUTIC APPROACH IN NASH PATIENTS

• THIS COHORT STUDY > 360 PATIENTS WITH NAFLD DAILY ASPIRIN USE
  • ASSOCIATED WITH A LOWER BASELINE RISK OF NONALCOHOLIC STEATOHEPATITIS (NASH) AND FIBROSIS
  • LOWER RISK OF DISEASE PROGRESSION OVER TIME COMPARED WITH NON-ASA USERS
NONALCOHOLIC FATTY LIVER DISEASE

• NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) IS ASSOCIATED WITH OBESITY, DIABETES, AND DYSLIPIDEMIA

• AFFECTS 20% TO 30% OF ADULTS IN WESTERN DEVELOPED COUNTRIES

• IN ITS MOST INDOLENT FORM (SIMPLE STEATOSIS) IT IS CHARACTERIZED BY THE HISTOLOGIC ACCUMULATION OF FAT WITHIN HEPATOCYTES

• IF FAT ACCUMULATION IS ACCOMPANIED BY VARYING DEGREES OF INFLAMMATION AND FIBROSIS → NONALCOHOLIC STEATOHEPATITIS [NASH]

• IN PATIENTS WITH NAFLD LIVER FIBROSIS IS AMONG THE MOST IMPORTANT PREDICTORS OF PROGRESSION TO END-STAGE LIVER DISEASE AND OUTCOME

• THE NAFLD FIBROSIS SCORE IS A VALIDATED NONINVASIVE TOOL FOR IDENTIFYING PATIENTS WHOSE NAFLD HAS ADVANCED TO LIVER FIBROSIS (12)
NONALCOHOLIC FATTY LIVER DISEASE

• RECOMMENDED BY AASLD, ACG, AGA

• PATIENTS WITH A HIGH NAFLD FIBROSIS SCORE MAY BE IN NEED OF ADDITIONAL STUDIES SUCH AS ELASTOGRAPHY OR LIVER BIOPSY

• THE PANEL ASSESSES SELECTED LABORATORY VALUES (SERUM GLUCOSE, PLATELET COUNT, ALBUMIN, AST/ALT RATIO) AND READILY AVAILABLE PATIENT CHARACTERISTICS (AGE, BMI, AND DIABETES STATUS)
  • NAFLD FIBROSIS SCORE ABOVE 0.676, THE PRESENCE OF ADVANCED LIVER FIBROSIS CAN BE DIAGNOSED WITH HIGH ACCURACY
  • NAFLD FIBROSIS SCORE BELOW −1.455, ADVANCED LIVER FIBROSIS CAN BE EXCLUDED WITH HIGH ACCURACY
  • SCORES BETWEEN −1.455 AND 0.676 ARE CONSIDERED “INDETERMINATE”

• HTTP://NAFLDSCORE.COM/
MATERIAL TENOFOVIR DISOPROXIL FUMARATE (TDF) FOR HBV INFECTION AND FETAL BONE DENSITY

CLIN INFECT DIS MAY 2019

• FOR PREGNANT WOMEN WITH HEPATITIS B VIRUS (HBV) INFECTION AND HIGH VIRAL LOAD, TENOFOVIR DISOPROXIL FUMARATE (TDF) IS RECOMMENDED DURING THE THIRD TRIMESTER TO REDUCE THE RISK OF PERINATAL HBV TRANSMISSION (IN ADDITION TO PASSIVE–ACTIVE IMMUNIZATION OF NEWBORNS)
  • POST–EXPOSURE IMMUNOPROPHYLAXIS IS ALSO AVAILABLE

• APPROXIMATELY 40% OF INFANTS BORN TO HBV–INFECTED MOTHERS IN THE UNITED STATES WILL DEVELOP CHRONIC HBV INFECTION

• APPROXIMATELY ONE–FOURTH OF WHOM WILL EVENTUALLY DIE FROM CHRONIC LIVER DISEASE
MATERIAL TDF FOR HBV INFECTION AND FETAL BONE DENSITY
CLIN INFECT DIS MAY 2019

• THERE HAVE BEEN CONCERNS ABOUT MATERNAL USE OF TDF ON FETAL GROWTH AND DEVELOPMENT SINCE TDF IS ASSOCIATED WITH DECREASED BONE MINERAL DENSITY

• DATA ARE GENERALLY REASSURING:
  • IN A RANDOMIZED TRIAL OF PREGNANT WOMEN WITH HBV MONO-INFECTION, USE OF TDF FROM 28 WEEKS GESTATIONAL AGE TO TWO MONTHS POSTPARTUM HAD NO EFFECT ON MATERNAL OR INFANT BONE DENSITY ONE YEAR AFTER DELIVERY COMPARED WITH PLACEBO (13)
  • THESE FINDINGS SUPPORT CURRENT RECOMMENDATIONS TO PREVENT PERINATAL TRANSMISSION

• ALTHOUGH A NEWER FORMULATION OF TENOFOVIR (TENOFOVIR ALAFENAMIDE) HAS LESS BONE TOXICITY COMPARED WITH TDF, WE DO NOT USE TENOFOVIR
The American Association for the Study of Liver Diseases (AASLD) has updated practice guidance on the management of PBC.

The major change addressed the role of obeticholic acid (Ocaliva), a semi-synthetic bile acid analogue:

- For patients with PBC with compensated liver disease (Child–Pugh A) who are inadequate responders to ursodeoxycholic acid (UDCA) alone, obeticholic acid can be used in combination with UDCA.
- Those with compensated liver disease (Child–Pugh A) unable to tolerate UDCA can receive obeticholic acid as monotherapy.
PRIMARY BILIARY CHOLANGITIS (PBC)

• PRIMARY BILIARY CHOLANGITIS (PREVIOUSLY CALLED PRIMARY BILIARY CIRRHOSIS) IS A CHRONIC DISEASE
• AUTOIMMUNE
• ANTI-MITOCHONDRIAL ANTIBODY
• BILE DUCTS IN LIVER SLOWLY DESTROYED
• WOMEN 30–60 YO
• AMERICAS AND NORTHERN EUROPE
• >50% DON’T DEVELOP SYMPTOMS 5–20 YEARS
PRIMARY BILIARY CHOLANGITIS (PBC)

• COMMON EARLY SYMPTOMS INCLUDE:
  • FATIGUE, ITCHY SKIN, DRY EYES AND MOUTH

• LATER SIGNS AND SYMPTOMS MAY INCLUDE:
  • PAIN IN THE UPPER RIGHT ABDOMEN FROM SWELLING OF THE SPLEEN
  • BONE, MUSCLE OR JOINT PAIN
  • EDEMA AND/OR ASCITES
  • XANTHOMAS ON THE SKIN AROUND THE EYES, EYELIDS OR IN THE CREASES OF THE PALMS, SOLES, ELBOWS OR KNEES
  • JAUNDICE AND/OR HYPERPIGMENTATION
  • OSTEOPOROSIS
  • HIGH CHOLESTEROL
  • DIARRHEA/STEATORRHEA
  • HYPOTHYROIDISM
  • WEIGHT LOSS
URSODEOXYCHOLIC ACID

- URSO 250 (URSODIOL 250 MG) IS AVAILABLE AS A FILM-COATED TABLET FOR ORAL ADMINISTRATION
- URSO-FORTE (URSODIOL 500 MG) IS AVAILABLE AS A SCORED FILM-COATED TABLET FOR ORAL ADMINISTRATION
- URSODIOL (URSODEOXYCHOLIC ACID, UDCA) IS A NATURALLY OCCURRING BILE ACID FOUND IN SMALL QUANTITIES IN NORMAL HUMAN BILE AND IN LARGER QUANTITIES IN THE BILE OF POLAR BEARS
- TREATMENT OF PBC IS 13–15 MG/KG/DAY ADMINISTERED IN TWO TO FOUR DIVIDED DOSES WITH FOOD
- SIDE EFFECTS INCLUDE: ABDOMINAL DISCOMFORT, ABDOMINAL PAIN, CONSTIPATION, DIARRHEA, DYSEPSIA, NAUSEA, VOMITING, DRUG HYPERSENSITIVITY TO INCLUDE FACIAL EDEMA, URTICARIA, ANGIOEDEMA AND LARYNGEAL EDEMA, MYALGIA, DIZZINESS, HEADACHE, COUGH, ALOPECIA, PRURITUS, RASH
URSODEOXYCHOLIC ACID

- Liver function tests should be monitored every month for three months after start of therapy, and every six months thereafter.
  - This monitoring will allow the early detection of a possible deterioration of the hepatic function.

- Bile acid sequestering agents (cholestyramine and colestipol) may interfere with the action of URSO 250 and URSO forte by reducing its absorption.

- Aluminum-based antacids (Tums) may interfere with URSO 250 and URSO forte in the same manner as the bile acid sequestering agents.

- Estrogens, oral contraceptives, and clofibrate increase hepatic cholesterol secretion → cholesterol gallstone formation → may counteract the effectiveness of URSO.
OBETICHOLIC ACID

• SYNTHETICALLY MODIFIED BILE ACID THAT IS A POTENT AGONIST OF THE FARNESOID X NUCLEAR RECEPTOR (FXR), A NUCLEAR RECEPTOR WITH MAJOR EFFECTS ON BILE ACID SYNTHESIS AND TRANSPORT AS WELL AS LIPID METABOLISM AND GLUCOSE HOMEOSTASIS

• IMPROVES ENZYMES IN NONALCOHOLIC STEATOHEPATITIS (NASH) AND PBC

• GIVEN PROVISIONAL APPROVAL FOR USE IN THE US FOR PBC IN 2016 AND IS CURRENTLY UNDER EVALUATION IN OTHER LIVER DISEASES INCLUDING PRIMARY SCLEROSING CHOLANGITIS (PSC) AND NONALCOHOLIC STEATOHEPATITIS (NASH)

• AVAILABLE AS TABLETS OF 5 AND 10 MG UNDER THE BRAND NAME OCALIVA

• THE TYPICAL INITIAL DOSE FOR PRIMARY BILIARY CHOLANGITIS IS 5 MG ONCE DAILY WHICH CAN THEN BE INCREASED TO A MAXIMUM OF 10 MG DAILY
  • PATIENTS WITH ADVANCED CIRRHOSIS (CHILD'S CLASS B OR C) ARE ADVISED TO START AT A DOSE OF 5 MG ONCE WEEKLY AND INCREASE THEREAFTER BASED UPON TOLERANCE AND EFFECT TO A MAXIMUM OF 10 MG TWICE WEEKLY
  • SIDE EFFECTS INCLUDE PRURITUS, FATIGUE, NAUSEA AND HEADACHE. SYMPTOMS OF PRURITUS APPEAR TO BE LESS IF THERAPY IS STARTED AT A LOW DOSE AND INCREASED
OBETICHOLIC ACID

• [09–21–2017] FDA IS WARNING THAT OCALIVA (OBETICHOLIC ACID) IS BEING INCORRECTLY DOSED IN SOME PATIENTS WITH MODERATE TO SEVERE DECREASES IN LIVER FUNCTION RESULTING IN AN INCREASED RISK OF SERIOUS LIVER INJURY AND DEATH

• PATIENTS WITH MODERATE TO SEVERE LIVER IMPAIRMENT (CHILD–PUGH B AND C) SHOULD BE STARTED ON THE APPROVED DOSING SCHEDULE OF 5 MG ONCE WEEKLY AND CAN BE INCREASED UP TO A MAXIMUM APPROVED DOSE OF 10 MG TWICE WEEKLY

• MONITOR PATIENTS FREQUENTLY AND REDUCE THE DOSING FREQUENCY TO ONCE– OR TWICE–WEEKLY FOR PATIENTS WHO PROGRESS TO MODERATE OR SEVERE LIVER IMPAIRMENT

• IN ALL PATIENTS TREATED WITH OCALIVA MONITOR FREQUENTLY FOR LIVER INJURY (Q1–2 MO)
THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY (ASCO) HAS ISSUED A PROVISIONAL CLINICAL OPINION ON THE EVALUATION OF GENETIC SUSCEPTIBILITY TO CANCER IN PATIENTS AND FAMILY MEMBERS OF PATIENTS WITH PANCREATIC CANCER (PC) (15).

THE GUIDELINE SUGGESTS OBTAINING A DETAILED PERSONAL AND FAMILY CANCER HISTORY IN PATIENTS DIAGNOSED WITH PC TO ASSESS RISK OF A FAMILIAL PREDISPOSITION TO CANCER.

GERMLINE GENETIC TESTING FOR PC SUSCEPTIBILITY SHOULD BE PERFORMED IN INDIVIDUALS WITH A FAMILY HISTORY OF PC MEETING CRITERIA FOR FAMILIAL PC (>5 DIAGNOSES OF PC IN SAME SIDE OF THE FAMILY) AND INDIVIDUALS MEETING CRITERIA FOR OTHER GENETIC SYNDROMES ASSOCIATED WITH INCREASED RISK FOR PC.

GERMLINE GENETIC TESTING MAY ALSO BE OFFERED TO PATIENTS WITH PC WITH AN UNREMARKABLE FAMILY HISTORY IF AN INFORMATIVE RESULT WOULD DIRECTLY BENEFIT THE PATIENT OR FAMILY MEMBERS.
EVALUATION OF GENETIC SUSCEPTIBILITY TO PANCREATIC CANCER

J CLINICAL ONCOLOGY

• THESE GUIDELINES ARE CONSISTENT WITH UP-TO-DATE CONTENTS AND RECOMMENDATIONS FROM OTHER ORGANIZATIONS, INCLUDING THE NATIONAL COMPREHENSIVE CANCER NETWORK (NCCN)
  • A GROUP OF 27 EXPERT CANCER CENTERS THROUGHOUT THE U.S. THAT PROVIDES RECOMMENDATIONS CALLED CLINICAL PRACTICE GUIDELINES FOR THE TREATMENT OF SOME 30 DIFFERENT CANCER TYPES

• JAMA RECENTLY SHOWED THAT SIX GENES CONTAIN MUTATIONS THAT MAY BE PASSED DOWN IN FAMILIES AND SUBSTANTIALLY INCREASE A PERSON’S RISK FOR PANCREATIC CANCER
  • THE GENES INCLUDE NOT ONLY BRCA1 AND BRCA2 BUT ALSO CDKN2A, TP53, MLH1 AND ATM

• THESE GENETIC MUTATIONS WERE IDENTIFIED IN 5.5% OF ALL PANCREATIC CANCER PATIENTS, INCLUDING 5.2% OF CANCER PATIENTS WITHOUT A FAMILY HISTORY OF PANCREATIC CANCER
  • THIS FINDING LED THE MAYO CLINIC RESEARCH TEAM TO RECOMMEND GENE TERT TESTING FOR ALL PANCREATIC CANCER PATIENTS AS THE NEW STANDARD OF CARE
JAMA SUGGESTS “GENETIC MUTATIONS THAT CAN BE INHERITED, KNOWN AS GERMLINE MUTATIONS, ARE MORE PREVALENT THAN PREVIOUSLY THOUGHT”

• MOST CANCER CASES BEGIN WITH A MUTATION IN THE DNA

• MOST INCIDENCES OF PANCREATIC CANCER SEEM TO BE CAUSED BY SPORADIC (NON-HEREDITARY) OR ENVIRONMENTAL FACTORS SUCH AS SMOKING, OBESITY AND INCREASED AGE

• 10% OF PANCREATIC CANCERS ARE CONSIDERED FAMILIAL OR HEREDITARY, AND THERE IS INTEREST IN THESE SPECIFIC INHERITED GENES

• THE FOLLOWING ARE DISORDERS THAT ARE CURRENTLY BEING STUDIED FOR CONNECTIONS TO PANCREATIC CANCER:
  • BRCA, CF, FAP, FAMMM, HNPCC, HP, PALN2, PJ
JAMA SUGGESTS “GENETIC MUTATIONS THAT CAN BE INHERITED, KNOWN AS GERMLINE MUTATIONS, ARE MORE PREVALENT THAN PREVIOUSLY THOUGHT”

1. BRCA MUTATION
   - BRCA 1 AND 2 MUTATIONS ARE OFTEN RELATED TO INHERITED BREAST AND OVARIAN CANCER
   - THE BRCA1 MUTATION MAY ALSO CAUSE A SMALL INCREASED RISK OF DEVELOPING PANCREATIC CANCER
   - MUTATIONS IN THE BRCA2 GENE ARE ASSOCIATED WITH A 3 TO 10 FOLD INCREASED RISK OF DEVELOPING PANCREATIC CANCER
   - PEOPLE WITH BRCA2 MUTATIONS HAVE A 10% LIFETIME RISK OF DEVELOPING PANCREATIC CANCER

2. CYSTIC FIBROSIS
   - CYSTIC FIBROSIS AFFECTS THE PANCREAS BY CAUSING PANCREATIC INSUFFICIENCY AND CHRONIC PANCREATITIS
   - THE RISK OF DEVELOPING PANCREATIC CANCER IS 5 TO 6 TIMES GREATER IN PEOPLE WHO HAVE CYSTIC FIBROSIS COMPARED TO AVERAGE RISK
JAMA SUGGESTS “GENETIC MUTATIONS THAT CAN BE INHERITED, KNOWN AS GERMLINE MUTATIONS, ARE MORE PREVALENT THAN PREVIOUSLY THOUGHT”

3. FAMILIAL ADENOMATOUS POLYPOSIS (FAP)
   - FAP IS A RARE HEREDITARY FORM OF COLON CANCER IN WHICH A PERSON DEVELOPS HUNDREDS TO THOUSANDS OF POLYPS IN THE COLON THAT EVENTUALLY BECOME MALIGNANT
   - IT IS ASSOCIATED WITH HIGHER RATES OF THYROID, SMALL BOWEL, STOMACH AND PANCREATIC CANCERS

4. FAMILIAL ATYPICAL MULTIPLE MOLE MELANOMA (FAMMM)
   - FAMMM IS CHARACTERIZED BY YOUNGER AGE OF MELANOMA DIAGNOSIS AND MULTIPLE SKIN MOLES PEOPLE WITH FAMMM HAVE A 13 TO 22 FOLD INCREASED RISK OF DEVELOPING PANCREATIC CANCER

5. HEREDITARY NONPOLYPOSIS COLORECTAL CANCER (HNPCC) OR LYNCH SYNDROME
   - IT IS AN INHERITED CONDITION THAT IS ASSOCIATED WITH 5% OF COLON CANCER CASES
JAMA SUGGESTS “GENETIC MUTATIONS THAT CAN BE INHERITED, KNOWN AS GERMLINE MUTATIONS, ARE MORE PREVALENT THAN PREVIOUSLY THOUGHT”

6. HEREDITARY PANCREATITIS
   - HEREDITARY PANCREATITIS IS A RARE, INHERITED CONDITION THAT USUALLY STARTS BEFORE AGE 20
   - IT IS CHARACTERIZED BY RECURRENT EPISODES OF SEVERE INFLAMMATION OF THE PANCREAS THAT CAN LEAD TO CHRONIC PANCREATITIS AND APPROXIMATELY A 40–55% LIFETIME RISK OF DEVELOPING PANCREATIC CANCER
   - INDIVIDUALS WITH HP WHO ALSO SMOKE MAY DEVELOP EARLIER ONSET PANCREATIC CANCER
   - 80% D/T MUTATION OF PRSS1 (CFTR, CTRC, PRSS1, SPINK1)

7. PALB2 MUTATION
   - ABOUT 1–3% OF PATIENTS WITH FAMILIAL PANCREATIC CANCER HAVE INHERITED MUTATIONS IN THE PALB2 GENE
   - MUTATIONS IN THE PALB2 GENE HAVE ALSO BEEN ASSOCIATED WITH AN INCREASED RISK OF BREAST CANCER

8. PEUTZ–JEGHERS SYNDROME
   - PEUTZ–JEGHERS SYNDROME IS CHARACTERIZED BY POLYPS IN THE SMALL INTESTINE AND
THE AMERICAN GASTROENTEROLOGICAL ASSOCIATION HAS PUBLISHED A CLINICAL PRACTICE UPDATE ON THE ROLE OF SEROLOGY AND HISTOLOGY IN MONITORING CELIAC DISEASE

THEY SUGGEST CELIAC-SPECIFIC SEROLOGY MONITORING 6 AND 12 MONTHS AFTER THE INITIAL DIAGNOSIS OF CELIAC DISEASE AND ANNUALLY THEREAFTER (16)

THEY ALSO CAUTION AGAINST USING NEGATIVE SEROLOGY AS A RELIABLE INDICATOR OF MUCOSAL HEALING AND SUGGEST ENDOSCOPIC BIOPSIES TO EVALUATE HEALING IN PATIENTS WITH CELIAC DISEASE WHO HAVE PERSISTENT SYMPTOMS
CELIAC DISEASE TESTING

• SEROLOGIC TESTS LOOK FOR THREE ANTIBODIES COMMON IN CELIAC DISEASE:
  1. ANTI–TISSUE TRANSGLUTAMINASE (TTG) ANTIBODIES
  2. ENDOMYSIAL ANTIBODIES (EMA)
  3. DEAMIDATED GLIADIN PEPTIDE (DGP) ANTIBODIES

• THE MOST SENSITIVE ANTIBODY TESTS ARE OF THE IMMUNOGLOBULIN A (IGA) CLASS; HOWEVER, IMMUNOGLOBULIN G (IGG) TESTS MAY BE USED IN PEOPLE WITH IGA DEFICIENCY
CELIAC DISEASE TESTING

- **TTG–IGA** Test is an Enzyme-Linked Immunosorbent Assay (ELISA) Test
- Is the preferred screening method and has a Sensitivity (TP) of 93%, yielding few false negative results and has a Specificity (TN) of more than 98%
- The performance of the TTG–IGA test may depend on the degree of intestinal damage, making the test less sensitive among people with milder celiac disease
- TTG test may be used to assess initiation and maintenance of a gluten-free diet
- The TTG–IGG test is only useful in those subjects who have IGA deficiency 5% population
CELIAC DISEASE TESTING

- The test for EMA–IGA is highly specific for celiac disease, with 99% accuracy.
- The reason the test has a variable sensitivity of 70 to 100% may be due in part to the high technical difficulty in performing this test.
- EMA are measured by indirect immunofluorescent assay, a more expensive and time-consuming process than ELISA testing.
- In addition, the EMA test is qualitative, making the results more subjective than those for TTG.
- EMA is often used as an adjunctive test to the routine TTG–IGA test where positive EMA make celiac disease more certain.
CELIAC DISEASE TESTING

- A NEW GENERATION OF TESTS THAT USE DGP (DEAMINATED GLIADIN PEPTIDE) ANTIBODIES HAS SENSITIVITY AND SPECIFICITY THAT IS SUBSTANTIALLY BETTER THAN THE OLDER GLIADIN TESTS

- HOWEVER, BASED ON A META-ANALYSIS OF 11 STUDIES, INSUFFICIENT EVIDENCE EXISTS TO SUPPORT THE USE OF DGP OVER TTG OR EMA TESTS (17)

- THE TTG TEST IS LESS EXPENSIVE THAN THE DGP TEST AND OFFERS BETTER DIAGNOSTIC PERFORMANCE

- IF ORDERING TTG–IGA OR EMA–IGA TOTAL IGA SHOULD BE MEASURED TO IDENTIFY SELECTIVE IGA DEFICIENCY, WHERE TTG–IGG OR DGP–IGG SHOULD BE MEASURED INSTEAD
CELIAC DISEASE TESTING

• MOST PEOPLE WITH CELIAC DISEASE HAVE GENE PAIRS THAT ENCODE FOR AT LEAST ONE OF THE HUMAN LEUKOCYTE ANTIGEN (HLA) GENE VARIANTS, OR ALLELES, DESIGNATED HLA-DQ2—FOUND IN 95% OF PEOPLE WITH THE DISEASE—AND HLA-DQ8

• THESE ALLELES ARE FOUND IN ABOUT 30 TO 35% OF CAUCASIANS AND MOST PEOPLE WITH THE VARIANTS DO NOT DEVELOP CELIAC DISEASE

• NEGATIVE FINDINGS FOR HLA-DQ2 AND HLA-DQ8 ESSENTIALLY RULES OUT DISEASE

• AN INCREASED RISK OF DEVELOPING CELIAC DISEASE HAS RECENTLY BEEN DESCRIBED IN INDIVIDUALS WHO CARRY A NEW HLA-G1 ALLELE IN ADDITION TO HLA-DQ2
Fecal Microbiota Transplantation (FMT) may be an effective and safe treatment for ulcerative colitis. Optimal dosing schedule, stool processing regimen, and delivery method are unclear. A trial comparing multi-donor anaerobically prepared FMT with standard autologous FMT in over 70 patients with ulcerative colitis resulted in higher rates of glucocorticoid-free remission at eight weeks. Further studies on stool processing methods and long-term efficacy are needed before FMT can be routinely used for treating ulcerative colitis.
FMT IN THE NEWS
JUNE 2019

• A PATIENT DIED AFTER CONTRACTING A DRUG RESISTANT BACTERIA THAT WAS TRANSMITTED BY AN EXPERIMENTAL FECAL MICROBIOME TRANSPLANT (FMT)

• ANOTHER PATIENT ALSO FELL ILL AFTER RECEIVING A FECAL TRANSPLANT
  • BOTH ADULTS HAD COMPROMISED IMMUNE SYSTEMS
FMT IN THE NEWS
JUNE 2019

• FDA ISSUED A SAFETY WARNING FOLLOWING THE DEATH OF A PATIENT AND SEVERE ILLNESS IN ANOTHER WHO BOTH CONTRACTED A DRUG RESISTANT BACTERIA THAT WAS TRANSMITTED DURING AN EXPERIMENTAL FMT

• THE STOOL USED FOR BOTH PATIENTS’ TRANSPLANTS WAS OBTAINED FROM THE SAME DONOR, ACCORDING TO THE FDA, AND WAS NOT TESTED FOR E.COLI BACTERIA THAT PRODUCED THE BETA-LACTAMASE ENZYME

• “WHILE WE SUPPORT THIS AREA OF SCIENTIFIC DISCOVERY, IT’S IMPORTANT TO NOTE THAT FMT DOES NOT COME WITHOUT RISK,” DR. PETER MARKS, DIRECTOR OF THE FDA’S CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

• THE FDA SAID THE PATIENT WHO DIED RECEIVED AN EXPERIMENTAL FECAL MICROBIOME TRANSPLANT, OR FMT

• “WE THEREFORE WANT TO ALERT ALL HEALTH CARE PROFESSIONALS WHO ADMINISTER FMT ABOUT THIS POTENTIAL SERIOUS RISK SO THEY CAN INFORM THEIR PATIENTS,” HE SAID
<table>
<thead>
<tr>
<th>Potential Clinical Indications</th>
<th>Current Research Status</th>
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<tbody>
<tr>
<td><em>Clostridium difficile</em> infection</td>
<td>1 randomized controlled trial and multiple meta-analyses showing efficacy; <strong>currently in clinical use</strong></td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>Limited to case reports and case series; not in clinical use</td>
</tr>
<tr>
<td>Irritable bowel syndrome</td>
<td>Limited to case reports; not in clinical use</td>
</tr>
<tr>
<td>Obesity and diabetes mellitus</td>
<td>Limited to animal and human study; further research needed</td>
</tr>
<tr>
<td>Multiple sclerosis and Parkinson disease</td>
<td>Limited to animal and human study; further research needed</td>
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<tr>
<td>Atopy and rheumatoid arthritis</td>
<td>Limited to animal and human study; further research needed</td>
</tr>
<tr>
<td>Autism</td>
<td>1 open-label trial showing possible efficacy; further research needed</td>
</tr>
<tr>
<td>Depression</td>
<td>Limited to animal study; further research needed</td>
</tr>
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THANK YOU, AND WAR EAGLE!!!!

CLEPANE@HOTMAIL.COM
RESOURCES

1. KEY STATISTICS FOR COLORECTAL CANCER. AMERICAN CANCER SOCIETY WEBSITE. HTTPS://WWW.CANCER.ORG/CANCER/COLON-RECTAL-CANCER/ABOUT/KEY-STATISTICS.HTML. ACCESSED JANUARY 10, 2018


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