AN EVIDENCE-BASED APPROACH TO CURRENT CONCEPTS IN GASTROENTEROLOGY

CHARLENE A LEPANE DO MSPH FACOI FACG FASGE
ADVENTHEALTH GASTROENTEROLOGY FELLOWSHIP
ADVENTHEALTH MEDICAL GROUP
***NO DISCLOSURES***
COLORECTAL CANCER

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

• AMONG PATIENTS PERFORMING FECAL IMMUNOCHEMICAL TESTING (FIT) EVERY TWO YEARS, THE RATE OF DETECTION OF CLINICALLY IMPORTANT CRC STEADILY DECLINED IN THE LEFT COLON OVER 12 YEARS, BUT REMAINED RELATIVELY UNCHANGED IN THE RIGHT COLON AFTER THE SECOND SCREENING ROUND
COLORECTAL CANCER

- These results are consistent with a lower sensitivity of FIT for proximal colon lesions, although the result could also 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.
FIT (Fecal Globin by Immunohemistry or Fecal Immunohemistry Test)

- Colorectal cancer (CRC) is the third most common cancer, and second leading cause of cancer death in the United States. The American Cancer Society estimated there was approximately 140,000 new cases of CRC in 2018, and about 50,000 deaths.

- 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.

- The American Cancer Society recommends screening starting at age 45.

- For individuals with above-average risk (e.g., African Americans, individuals with strong family or personal history), screening should begin at an earlier age (2).

- Unfortunately, only two-thirds of adults who are eligible receive appropriate screening.
FIT (Fecal Globin by Immunochemistry or Fecal Immunochemistry Test): CRC Facts

- Screening for CRC effectively reduces incidence and mortality by ≥50% (3).
- Early detection is crucial, as survival rates decrease dramatically with increasing cancer stage.
- The 5-year survival rate for persons with disease confined to the primary site is approximately 90%.
- 5-year survival for those with distant metastasis is approximately 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.
IMMUNOCHEMISTRY

– MONOCLONAL, MOUSE ANTI-HUMAN HEMOGLOBIN-COATED CHROMATOGRAPHY TEST STRIP

– COLORIMETRIC DETECTION

ANALYTICAL SENSITIVITY: 50 MG HB/G FECES

POSITIVE RESULTS INDICATE OCCULT BLOOD IN THE FECES AND SHOULD BE FOLLOWED UP WITH DIRECT VISUALIZATION

NEGATIVE RESULTS INDICATE THE ABSENCE OF FECAL BLOOD; HOWEVER, FALSE-NEGATIVE RESULTS CAN OCCUR BECAUSE OF UNEVEN DISTRIBUTION OF BLOOD IN THE FECES OR INTERMITTENT BLEEDING
FOBT VS FIT (Fecal Globin by Immunochemistry or Fecal Immunochemistry Test)

- FOBTs fall into 2 main categories: guaiac-based (GFOBT) and immunochemical.
- A drawback to GFOBTs is that they 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-positive results.
  - Vitamin C (excess of 250 mg/day) from supplements or citrus fruits and juices may cause a false-negative guaiac test result (5).
- A special diet is frequently recommended for several days before the test.
FOBT VS FIT (FECAL GLOBIN BY IMMUNOCHEMISTRY OR FECAL IMMUNOCHEMISTRY TEST)

- In contrast, immunochemical FOBTs (fecal immunochemical tests) do not react with non-human hemoglobin or peroxidase, eliminating the need for food restrictions.
- The lack of dietary restrictions, along with relatively simple "brush" sample collection of the stool specimen, may result in increased participation in FOBT screening.
- Immunochemical FOBTs are also 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 FECAL IMMUNOCHEMICAL TEST SCREENING 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 THAN DISTAL COLORECTAL NEOPLASIA

• OBJECTIVE:
  • TO ASSESS THE LONG-TERM DETECTION RATES FOR ADVANCED ADENOMA AND COLORECTAL CANCER (CRC), ACCORDING TO ANATOMICAL LOCATION

• DESIGN:
  • RETROSPECTIVE STUDY. SETTING: POPULATION-BASED, ORGANIZED 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 ADVANCED ADENOMA AND 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 FECAL IMMUNOCHEMICAL TEST SCREENING PROGRAMS: A RETROSPECTIVE COHORT STUDY

• RESULTS:
  • BETWEEN 2002 AND 2014, A TOTAL OF 123 347 PARTICIPANTS HAD 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, AND 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

• LIMITATIONS:
  • PARTICIPANTS WITH IRREGULAR ATTENDANCE WERE CENSORED
  • THOSE WHO HAD A FALSE-POSITIVE RESULT ON A PREVIOUS FIT BUT NEGATIVE COLONOSCOPY RESULTS WERE INCLUDED IN SUBSEQUENT ROUNDS

• CONCLUSION:
  • THIS FIT-BASED, MULTIPLE-ROUND, LONG-TERM SCREENING PROGRAM HAD A NEGLIGIBLE REDUCTION IN DETECTION RATES FOR NEOPLASTIC LESIONS IN THE PROXIMAL VERSUS THE DISTAL COLON AFTER THE FIRST ROUND
  • THIS WAS RELATED TO A HIGHER PICR IN THE PROXIMAL COLON AND SUBOPTIMAL EFFICACY IN PREVENTING THE AGE-RELATED PROXIMAL SHIFTING OF CRC
THE IMPACT OF COLORECTAL SCREENING PROGRAM ON THE DETECTION OF RIGHT-SIDED COLORECTAL CANCER. A 5-YEAR COHORT STUDY IN THE MANTUA DISTRICT (7)


- **BACKGROUND:**
  - High rates of advanced colorectal cancer (CRC) are still diagnosed in the right side of the colon. This study aimed to investigate whether screening programs increase CRC detection and whether 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. Other than patient-, disease-, and treatment-related factors, detection mode and tumor location were recorded. Overall (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. A 5-YEAR COHORT STUDY IN THE MANTUA DISTRICT

• RESULTS:
  • MEAN AGE OF 386 PATIENTS INCLUDED WAS 62.0 YEARS, 59 % WERE MALES
  • CRC WAS DETECTED BY SCREENING IN 17 % OF CASES, AND DIAGNOSIS WAS MADE FROM SYMPTOMS IN 67 % AND EMERGENCY SURGERY FOR 16 %
  • SCREEN-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 PTNM STAGE (P = 0.001), ADEQUATE HARVEST COUNT NODES (P = 0.0001), METASTATIC NODES (P = 0.02), AND POOR DIFFERENTIATION GRADING (P = 0.0001)
  • WITH MULTIVARIATE ANALYSIS, POOR DIFFERENTIATION GRADE WAS INDEPENDENTLY ASSOCIATED WITH BOTH WORSE OS (HR 3.6, P = 0.05) AND WORSE DFS (HR 8.1, P = 0.0001), WHILE DISTANT RECURRENCE WAS ASSOCIATED WITH WORSE OS (HR 20.1, P = 0.0001)
THE IMPACT OF COLORECTAL SCREENING PROGRAM ON THE DETECTION OF RIGHT-SIDED COLORECTAL CANCER. A 5-YEAR COHORT STUDY IN THE MANTUA DISTRICT

• 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 (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, AND 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

• HOWEVER, THESE CELLS BECOME SO ABNORMAL, BECAUSE OF THIS FEATURE, THAT THE IMMUNE SYSTEM, WHICH IS USED TO PROTECTING THE BODY AGAINST BACTERIA AND VIRUSES AND OTHER FOREIGN INVADERS, CAN ACTUALLY LOOK AT THE CANCER AND RECOGNIZE THAT SOMETHING IS VERY WRONG

• THIS CAN CALL THE BODY’S NORMAL DEFENSES AGAINST INVADERS TO TRY TO ATTACK THE CANCER
CAUSE OF MSI-H

• Most commonly it is caused by genetic lack of certain proteins which, when working normally, help repair DNA in cells when it breaks

• When these proteins aren’t present, 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?

• COLORECTAL CANCER (CRC) IS THE DISEASE MOST COMMONLY ASSOCIATED HERE, BUT ESSENTIALLY ANY CANCER CAN BE IMPlicated, JUST AT VARIABLE AND RELATIVELY LOW PERCENTAGES

• WE HAVE KNOWN FOR SOME TIME THAT THE BEHAVIOR OF MSI-H CRC IS DIFFERENT FROM SO-CALLED MICROSATellite STABLE (MSS, OR NON-MSI-H) CRC

• GENERALLY, THEY ARE ASSOCIATED WITH A BETTER PROGNOSIS, ALTHOUGH THIS IS NOT UNIVERSAL. MOST IMPORTANTLY, THEY ARE NOW ASSOCIATED WITH A CHANGE IN THE WAY WE TREAT THEM

• WHILE TRADITIONAL CHEMOTHERAPY DRUGS ARE STILL USED FREQUENTLY IN MSI-H CRC, IMMUNOTHERAPY DRUGS AFFECTING THE INTERACTION OF SOMETHING CALLED PD-1, OR 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 WHETHER IT COMES FROM THE COLON, LUNG, BREAST, OR ANY OTHER ORGAN

• THIS IS TRULY A BIG STEP FORWARD, EVEN THOUGH IT AFFECTS SUCH A SMALL PERCENTAGE OF TUMORS
WHY IS IT IMPORTANT TO TEST FOR MSI-H STATUS FOLLOWING A PATIENT’S DIAGNOSIS?

• SINCE THIS IS FREQUENTLY ASSOCIATED WITH GENETIC DEFICIENCIES THAT CAN BE HEREDITARY, IT IS IMPORTANT TO UNDERSTAND THE IMPLICATIONS FOR FAMILY MEMBERS

• MSI-H FINDINGS ON A CANCER CAN BE SPORADIC THOUGH, MEANING THAT THEY DON’T ALWAYS CHANGE A FAMILY MEMBER’S RISK OF DEVELOPING THE SAME TYPES OF CANCER

• IT IS IMPORTANT TO UNDERSTAND THE MSI STATUS AS IT MAY CHANGE THE DRUGS WE USE. THAT BEING SAID, UNIVERSAL TESTING FOR ALL CANCER IS NOT AN ACCEPTED PRACTICE, AS THERE ARE OFTEN IMPLICATIONS OF TRYING TO GET THAT INFORMATION (IN OTHER WORDS, EXPOSING PATIENTS TO THE RISK OF ANOTHER BIOPSY AND THE COST OF TESTING) RELATIVE TO ITS INFREQUENCY IN MANY TYPES OF CANCERS
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, AND AT A YOUNGER AGE (BEFORE 50), INCLUDING 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, AMONG MANY OTHERS
LYNCH SYNDROME, ALSO KNOWN AS HEREDITARY NON-POLYPOYSIS COLORECTAL CANCER (HNPCC)

• THESE GENES (MLHL, MSH2, MSH6, PMS2, AND EPCAM) NORMALLY PROTECT YOU FROM GETTING CERTAIN CANCERS, HOWEVER SOME MUTATIONS IN THESE GENES PREVENT THEM FROM WORKING PROPERLY

• EVERYONE HAS TWO COPIES OF EACH OF THE GENES INVOLVED IN LYNCH SYNDROME→ ONE FROM THEIR MOTHER AND ONE FROM THEIR FATHER

• EVEN IF A PERSON INHERITS A MUTATION IN A LYNCH SYNDROME GENE, THEY STILL HAVE THE NORMAL COPY OF THE GENE FROM THE OTHER PARENT
  • CANCER OCCURS WHEN A SECOND MUTATION AFFECTS THE NORMAL WORKING COPY OF THE GENE, SO THAT THE PERSON NO LONGER HAS A COPY OF THE GENE THAT WORKS PROPERLY
  • UNLIKE THE INHERITED LYNCH SYNDROME MUTATION, THE SECOND MUTATION WOULD NOT BE PRESENT THROUGHOUT THE PERSON'S BODY, BUT WOULD ONLY BE PRESENT IN THE CANCER TISSUE

• INTERESTINGLY, NOT EVERYONE WITH LYNCH SYNDROME WILL GET CANCER

• COLORECTAL CANCER ALSO CAN BE CAUSED BY MUTATIONS IN GENES OTHER THAN THOSE RELATED TO LYNCH SYNDROME THEREFORE SOME FAMILIES WITH A HISTORY OF COLORECTAL CANCER WILL NOT HAVE MUTATIONS IN A LYNCH SYNDROME GENE (MLHL, MSH2, MSH6, PMS2, AND EPCAM)
WHO GETS TESTED FOR LYNCH?

• TUMOR SCREENING RESULTS (IHC OR MSI) ARE ABNORMAL
• INDIVIDUAL WITH COLORECTAL CANCER
• INDIVIDUAL WITH UTERINE (ENDOMETRIAL CANCER) BEFORE AGE 50
• INDIVIDUAL WITH MULTIPLE PRIMARY CANCER DIAGNOSES
• INDIVIDUAL WITH SEVERAL FAMILY MEMBERS WHO HAVE DOCUMENTED CANCERS RELATED TO LYNCH SYNDROME
• INDIVIDUALS WITH A FAMILY MEMBER WITH LYNCH SYNDROME
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, SO IT IS IMPORTANT NOT TO ASSUME THAT THERE ARE UNIVERSAL “RULES” ABOUT HOW WE TREAT THESE CANCERS

• THE SITUATION (STAGE, TYPE OF CANCER, EXTENT OF DISEASE, AND PATIENT’S OTHER MEDICAL PROBLEMS) MAY GREATLY CHANGE THE APPROPRIATE APPROACH

• 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
• Adding simethicone intraprocedural may result in endoscopic contamination.

• Adding simethicone with bowel prep reduces need to flush simethicone through the scope.

• Trial of 268 patients undergoing colonoscopy with bowel prep containing simethicone were less likely to need TTS simethicone to improve visualization compared to bowel prep alone (2 vs 49%).
CLIP CLOSURE TO PREVENT POST POLYPECTOMY BLEED
GASTROENTEROLOGY JUNE 2019

• BLEEDING CAN BE SERIOUS COMPLICATION FOLLOWING EMR

• TRIAL INCLUDING >900 PATIENTS WITH NON-PEDUNCULATED POLYPS> CM, COMPARED WITH NO CLIPS, CLIP CLOSURE REDUCTED THE POSTPOLYPECTOMY BLEEDING RATE FOR PROXIMAL COLON POLYPS (3 VS 10%) BUT NOT FOR DISTAL POLYPS
• Topical glucocorticoids are a first-line treatment for eosinophilic esophagitis

• First randomized trial compared the efficacy of oral viscous budesonide vs swallowed fluticasone for 8 weeks

• Equally effective in treatment of EOE
EOSINOPHILIC ESOPHAGITIS (EOE) BACKGROUND

• IMMUNOLOGIC REACTION TO INGESTED OR INHALED ALLERGENS CHARACTERIZED BY ESOPHAGEAL EOSINOPHILIA AND GASTROINTESTINAL SYMPTOMS

• MORE COMMON IN MEN THAN WOMEN, 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 PER 100,000 INDIVIDUALS (10)

• THE MAJORITY OF PATIENTS WITH EOE ARE ATOPIC; SOMEONE WHO HAS A FAMILY HISTORY OF ALLERGIES OR ASTHMA AND SYMPTOMS OF ONE 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 (> 15 EOS/HPF), ALLERGY BLOOD TEST, PRICK SKIN TEST AND FOOD PATCH TEST (FINN CHAMBER) (ALL CAN HAVE FALSE POSITIVES)

• TREATMENT OPTIONS
  • ELIMINATION AND ELEMENTAL DIETS TO DECREASE ALLERGEN EXPOSURE
  • ACID SUPPRESSION
  • TOPICAL GLUCOCORTICOID TO DECREASE ESOPHAGEAL INFLAMMATION
  • FLUTICASONE 220 UG 2 PUFFS (SWALLOWED) BID X 8 WEEKS
  • VISCOUS 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)
• LIFESTYLE MODIFICATION CONFIRMS BENEFIT, LITTLE DATA ON MEDICATIONS

• 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

• COHORT STUDY>360 PATIENTS WITH NAFLD DAILY ASPIRIN USE
  • ASSOCIATED WITH A LOWER BASELINE RISK OF 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

- The NAFLD fibrosis score is a validated, noninvasive tool for identifying patients whose NAFLD has advanced to liver fibrosis (12) 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/](http://NAFLDScore.com/)
• FOR PREGNANT WOMEN WITH HEPATITIS B VIRUS (HBV) INFECTION AND HIGH VIRAL LOADS, 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)

  • POSTEXPOSURE 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 MONOINFECTION, 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 ALAFENAMIDE DURING PREGNANCY GIVEN THE LACK OF SUFFICIENT SAFETY DATA
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:**

- 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, CONSIDERED AUTOIMMUNE, IN WHICH THE BILE DUCTS IN YOUR LIVER ARE SLOWLY DESTROYED

• WOMEN, 30-60, AMERICAS AND NORTHERN EUROPE

• MORE THAN HALF THE PEOPLE WITH PRIMARY BILIARY CHOLANGITIS DO NOT HAVE ANY NOTICEABLE SYMPTOMS WHEN DIAGNOSED, BUT RATHER DEVELOP OVER 5-20 YRS

• 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, ASCITES, XANTHOMAS ON THE SKIN AROUND THE EYES, EYELIDS OR IN THE CREASES OF THE PALMS, SOLES, ELBOWS OR KNEES, JAUNDICE, 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, DYSPEPSIA, 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. TREATMENT DISCONTINUATION SHOULD BE CONSIDERED IF THE ABOVE PARAMETERS INCREASE TO A LEVEL CONSIDERED CLINICALLY SIGNIFICANT IN PATIENTS WITH STABLE HISTORICAL LIVER FUNCTION TEST LEVELS.

• 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, OCP, AND CLOFIBRATE INCREASE HEPATIC CHOLESTEROL SECRETION → CHOLESTEROL GALLSTONE FORMATION → MAY COUNTERACT THE EFFECTIVENESS OF URSO
OBETICHOLIC ACID

- OBETICHOLIC ACID IS A 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
- OBETICHOLIC ACID IMPROVES ENZYMES IN NONALCOHOLIC STEATOHEPATITIS (NASH) AND PBC
- OBETICHOLIC ACID WAS GIVEN PROVISIONAL APPROVAL FOR USE IN THE UNITED STATES FOR PRIMARY BILIARY CHOLANGITIS IN 2016 AND IS CURRENTLY UNDER EVALUATION IN OTHER LIVER DISEASES INCLUDING PRIMARY SCLEROSING CHOLANGITIS (PSC) AND NONALCOHOLIC STEATOHEPATITIS (NASH)
- OBETICHOLIC ACID IS 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 GRADUALLY
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, RATHER THAN THE 5 MG DAILY DOSING USED FOR OTHER PBC PATIENTS, AND IF NEEDED, 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
  - IF LIVER INJURY IS SUSPECTED, DISCONTINUE OCALIVA. AFTER THE PATIENT HAS STABILIZED, WEIGH THE BENEFITS AGAINST THE RISKS WHEN DECIDING WHETHER TO RE-INITIATE TREATMENT
EVALUATION OF GENETIC SUSCEPTIBILITY TO PANCREATIC CANCER
J CLINICAL ONCOLOGY

- 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 UPTODATE 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 GENETIC 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

• While only about 10% of pancreatic cancers are considered familial or hereditary, researchers are interested in specific inherited genes

• The following are disorders that are being studied for connections to pancreatic cancer
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
   - A MUTATION IN THIS GENE CAN BE FOUND IN APPROXIMATELY 1% OF INDIVIDUALS OF ASHKENAZI JEWISH DESCENT
   - 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 noncancerous 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, many skin moles and multiple primary melanomas.
   - 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.
   - Patients with HNPCC have approximately a 9 fold increased risk of developing pancreatic cancer.
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 HEREDITARY PANCREATITIS WHO ALSO SMOKE MAY DEVELOP EARLIER ONSET PANCREATIC CANCER
   • 80% D/T MUTATION OF PRSS1 (CFTR, CTRC, PRSS1, SPINK1) THEREFORE ORDER SEQUENCING

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 PIGMENTED SPOTS ON THE LIPS AND NOSE
   • PATIENTS WITH THIS SYNDROME HAVE A 11-36% RISK OF DEVELOPING PANCREATIC CANCER
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

- The TTG-IGA test is an enzyme-linked immunosorbent assay (ELISA) test.
- Is the preferred screening method and has a sensitivity of 93%, yielding few false negative results and has a specificity 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.
- In addition to screening, the 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 IMMUNOFLOUORESCENT 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 WHEN 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
• 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

• HOWEVER, 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-G I ALLELE IN ADDITION TO HLA-DQ2
FECAL MICROBIOTA TRANSPLANTATION (FMT) MAY BE AN EFFECTIVE AND SAFE TREATMENT FOR ULCERATIVE COLITIS, BUT THE OPTIMAL DOSING SCHEDULE, STOOL PROCESSING REGIMEN, AND DELIVERY METHOD ARE UNCLEAR.

IN A TRIAL COMPARING MULTI-DONOR ANAEROBICALLY PREPARED FMT WITH STANDARD AUTOLOGOUS FMT IN OVER 70 PATIENTS WITH ULCERATIVE COLITIS, ANAEROBICALLY PREPARED DONOR FMT RESULTED IN HIGHER RATES OF GLUCOCORTICOID-FREE REMISSION AT EIGHT WEEKS [19].

FURTHER STUDIES ON STOOL PROCESSING METHODS AND LONG-TERM EFFICACY ARE NEEDED BEFORE FMT CAN BE ROUTINELY USED FOR TREATING ULCERATIVE COLITIS.
• 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.
THE FOOD AND DRUG ADMINISTRATION ON THURSDAY 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 FECAL TRANSPLANT.

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.
THANK YOU
CLEPANE@HOTMAIL.COM

December 8, 2019
California International Marathon
Sacramento, CA
RESOURCES

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