The 25th Annual Beyond The Scope October 14th, 2017 Educational Symposium

Presented by:
The Connecticut Society of Gastroenterology Nurses and Associates
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CTSGNA gratefully acknowledges our Sponsors for their generous support of our educational endeavors!

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Colon and Rectal Surgeons of Greater Hartford
CTSGNA gratefully acknowledges our Exhibitors for their generous support. This is a great opportunity for attendees to obtain information on products used in GI practice.

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Please provide both addresses and check your preferred mailing address:

☐ Work

* Street Address ___________________________
* City ___________________________
* State/Province ___________________________  * ZIP ___________________________
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* Street Address ___________________________
* City ___________________________
* State/Province ___________________________  * ZIP ___________________________
* Country ___________________________
* Phone ___________________________
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REFERRED BY ___________________________

(Members who refer other members will be entered into an annual prize drawing.)

The following information will be used for demographic purposes only. Your response is optional but appreciated.

Gender:  ☐ Male  ☐ Female

Ethnicity:  ☐ African-American  ☐ Asian  ☐ Caucasian  ☐ Hispanic/Latino  ☐ Native American  ☐ Pacific Islander  ☐ Other ___________________________
☐ Do Not Care To Respond

Date of Birth ___________________________

PAYMENT INFORMATION • dues subject to change

A. Membership (SGNA membership runs on a calendar year from January 1 to December 31.) If you are applying mid-year please indicate the 18-month option below. Check the category of membership for which you are applying:

<table>
<thead>
<tr>
<th>Voting Status</th>
<th>Type</th>
<th>Definition</th>
<th>Annual Dues</th>
<th>Two-Year Dues</th>
<th>18-Month Dues (Available July 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Voting</td>
<td>Licensed Nurse</td>
<td>Limited to Registered Nurses and Licensed Vocational/Practical Nurses involved in or associated with gastroenterology and/or endoscopy nursing practice</td>
<td>$125</td>
<td>$235</td>
<td>$205</td>
</tr>
<tr>
<td>☐ Voting</td>
<td>Associate</td>
<td>Limited to Assisitive Personnel; such as technicians, technologists and assistants involved in or associated with gastroenterology and/or endoscopy nursing practice</td>
<td>$95</td>
<td>$180</td>
<td>$150</td>
</tr>
<tr>
<td>☐ Non-Voting</td>
<td>Affiliate</td>
<td>Includes, but is not limited to, physicians, consultants, industry representatives and educators involved in or associated with gastroenterology and/or endoscopy nursing practice</td>
<td>$110</td>
<td>$220</td>
<td>$175</td>
</tr>
<tr>
<td>☐ Non-Voting</td>
<td>Non-Practicing</td>
<td>Limited to those that have retired from the GI/endoscopy nursing field but want to continue to receive benefits and information regarding this profession</td>
<td>$60</td>
<td>$120</td>
<td>$90</td>
</tr>
</tbody>
</table>

SUBTOTAL A ___________________________

Continued on page 2
B. Regional Societies
All voting members residing in the U.S. are required to affiliate with an SGNA regional society.

Regional Society Preference:

Regional Society Dues:  
- **Voting Licensed Nurses and Associates**  
  - No additional payment needed  
  - Included in Annual Dues Amount

- **Non-Voting Affiliate and Non-Voting Non-Practicing**  
  - Optional payment; if interested, please indicate preferred region above and remit an additional $15

**SUBTOTAL B** (If applicable):

☐ C. E-SIGs (Electronic Special Interest Groups) — FREE!
Please **CHECK** box if you would like to join SGNA's e-SIGs and circle the group(s) of particular interest. These are online special interest groups only. For more information on SGNA e-SIGs visit www.sgna.org.

- Advanced Practice
- Legislative
- Ambulatory GI Practice
- Manometry
- Associates
- Nurse Endoscopist
- Capsule Endoscopy
- Pediatric
- Endoscopic Ultrasound
- Pulmonary
- ERCP
- Research
- Hepatology
- University
- Lab Management
- VA Nurses
- LPN/LVN

☐ Total Dues and Method of Payment

- **TOTAL A + B =** 
  
☐ Check enclosed for (amount)
☐ Credit card (please do not provide credit card information on this form. To pay by credit card, click "Join" in the upper right hand corner at www.sgna.org

Please mail your completed application and payment to:
SGNA Membership, 8287 Solutions Center, Chicago, IL 60677
If paying by check, please send in a sealed envelope.

SGNA membership dues are non-refundable and non-transferable. Contributions or gifts to SGNA are not tax deductible as charitable contributions for income tax purposes, but may be deductible as a business expense. Please consult your tax advisor. SGNA Federal I.D. #51-04-9057.
American Board of Certification for Gastroenterology Nurses

Each year ABCGN recognizes four award recipients at the Annual Gala during the SGNA Annual course. The awards are listed below.

**Excellence in Professionalism Award**: This award is given to the department with 50% or greater of their nurses that are certified. Closing date for application is February 15th, 2018.

**Outstanding Regional Society Award**: This recognizes the SGNA Regional Society most active in supporting ABCGN certification. Application due by November 15th.

**Certified GI Professional Of The Year Award** - Through awards this organization seeks to recognize those nurses who are dedicated in validating their qualifications through certification, and those who demonstrate commitment and leadership among colleagues and patients to enhance the practice of gastroenterology nursing. Deadline is November 15th.

**Recertification Scholarship Award** - The ABCGN Recertification Scholarship has been established to financially assist candidates for recertification by contact hours. Scholarships will be awarded each November; the number of scholarships awarded will depend on funds available. Application deadline is November 1st.

For more information on these wonderful opportunities please for to: http://www.abcgn.org/Resources/Awards-Scholarships
Medical Marijuana
&
GI Disorders

By:

John Gadea, Jr. R. Ph., Rotes LLC
CTSGNA
Connecticut Society of Gastroenterology Nurses and Associates

Director John Gadea, Jr., RPh., Retired
State of Connecticut,
Department of Consumer Protection,
Drug Control Division

Learning Objectives

At the completion of this presentation the participant will be able to:

• Have an understanding of the structure of the medical marijuana program in the state of Connecticut.
• Have an understanding of the claims of medical marijuana in the treatment of GI disorders.
THE CONNECTICUT MODEL

Medical Marijuana Program (MMP)
Understanding the Law

• Connecticut General Statute Chapter 420f, Section 21a-408, An Act Concerning the Palliative Use of Marijuana, signed into law on May 31, 2012.

• Designed to enable truly sick patients to engage in the palliative use of marijuana while preventing marijuana from being misused or diverted from its medical purpose.

• Provides immunity from state criminal and civil penalties for physicians, patients, caregivers, dispensaries and producers who act responsibly in accordance with the law.
Medical Marijuana Program (MMP)  
Understanding the Law  continued

• Medical Marijuana is a schedule:
  – Federally: a schedule 1
  – State of CT: Schedule 2
• Was given medical use by the CT legislature
• As a schedule 2 it is in the Prescription Monitoring Program.

Scope of Immunity

• Those who comply with the law are protected from negative consequences, including:
  • Arrest;
  • Prosecution;
  • Civil Penalties; or
  • Any other penalties, including disciplinary action by the Connecticut Medical Examining Board or other professional licensing board.
Understanding the Law

Immunity is Only for Those ActingResponsibly

- **Physicians:**
  - Have bona-fide physician-patient relationship;
  - Diagnose patient as having debilitating medical condition;
  - Explain potential risks and benefits of palliative use of marijuana to patient (or legal guardian);
  - Certification is based upon professional opinion after medically reasonable assessment; and
  - Physician does not have financial interest in a marijuana producer or dispensary.

- **Patients and Caregivers:**
  - Register with DCP;
  - Acquire, distribute, transfer, possess, use (patient only) or transport marijuana for a certified medical purpose;
  - Have no more than a one-month supply of marijuana; and
  - Do not use marijuana in an improper place or in a manner that puts others at risk.

Physicians are the Gatekeepers

- **Physicians Can Only Certify Patients for Marijuana Where there is a Bona-Fide Physician-Patient Relationship:**
  - Complete a medically reasonable assessment of the patient’s medical history and current medical condition;
  - Diagnose the patient as having a debilitating medical condition; and
  - Prescribe, or determine it is not in the patient’s best interest to prescribe, prescription drugs to address the symptoms or effects for which the certification is being issued.
Physicians are the Gatekeepers

• Patients and Caregivers Cannot Register with DCP Until their Physician Certifies that:
  • The patient has a qualifying, debilitating medical condition;
  • In the physician’s professional opinion, the potential benefits of the palliative use of marijuana would likely outweigh the health risks; and
  • The patient has a need for a caregiver, if applicable.

For Adults, Debilitating Medical Conditions Include:

• CANCER
• GLAUCOMA
• PARKINSON’S DISEASE
• MULTIPLE SCLEROSIS
• SPINAL CORD DAMAGE WITH INTRACTABLE SPASTICITY
• EPILEPSY
• POSITIVE STATUS FOR HIV OR AIDS
• CACHEXIA
• WASTING SYNDROME
• CROHN’S DISEASE
• POST-TRAUMATIC STRESS DISORDER
• SICKLE CELL DISEASE
• POST LAMINECTOMY SYNDROME WITH CHRONIC RADICULOPATHY
• SEVERE PSORIASIS AND PSORIATIC ARTHRITIS
• AMYOTROPHIC LATERAL SCLEROSIS
• ULCERATIVE COLITIS
• COMPLEX REGIONAL PAIN SYNDROME
• CEREBRAL PALSY
• CYSTIC FIBROSIS
• IRREVERSIBLE SPINAL CORD INJURY WITH OBJ INTRACTABLE SPASTICITY
• TERMINAL – END OF LIFE
• UNCONTROLLED INTRACTABLE SEIZURE DISORDER
For Patients Under 18 Years of Age
Debilitating Medical Conditions Include:

- CEREBRAL PALSY
- CYSTIC FIBROSIS
- SEVERE EPILEPSY
- IRREVERSIBLE SPINAL CORD INJURY WITH OBJ INTRACTABLE SPASTICITY
- TERMINAL – END OF LIFE
- UNCONTROLLED INTRACTABLE SEIZURE DISORDER

Medical Marijuana
Pharmacology

ADMINISTRATION AND INTOXICATION
- 420 chemicals (30 to 60 “cannabinoids”—most potent, delta-9-tetrahydrocannabinol, or THC)
- ingested orally, intoxication effects in 30 minutes
  - smoking inhalation, intoxication effects within minutes
  - 59% of smoked THC absorbed; 3% THC when orally ingested
- smoked THC effects 3 – 4 hours; longer if ingested orally
- 1960’s “joint” had 1-3% THC; wide range now (4-15%) 30%
  - one “joint” today equivalent to smoking 3-5 “joints” in the 1960s.
Medical Marijuana
Pharmacology

- marijuana is fat soluble
- effects may persist or reoccur for 12-24 hours
- the ability to drive a car or a plane, other motor performance tasks,
  alertness and the ability to concentrate may be affected for hours to days

GI Disorders

Currently the only two GI disorders are:

- ULCERATIVE COLITIS
- CROHN’S DISEASE
Medical Marijuana

Phytocannabinoids

Cannabis-derived cannabinoids

The classical cannabinoids are concentrated in a viscous resin produced in structures known as glandular trichomes. At least 113 different cannabinoids have been isolated from the Cannabis plant. Below are the main classes of cannabinoids from Cannabis are shown. The best studied cannabinoids include tetrahydrocannabinol (THC), cannabidiol (CBD) and cannabinol (CBN).

Types

All classes derive from cannabigerol-type compounds and differ mainly in the way this precursor is cyclized. The classical cannabinoids are derived from their respective 2-carboxylic acids (2-COOH) by decarboxylation (catalyzed by heat, light, or alkaline conditions):

- CBG (Cannabigerol)
- CBC (Cannabichromene)
- CBL (Cannabicyclol)
- CBV (Cannabivarin)
- THCV (Tetrahydrocannabivarin)
- CBDV (Cannabidiolvarin)
- CBGV (Cannabigerovarin)
- CBG (Cannabigerolvarin)
- CBGM (Cannabigerol Monomethyl Ether)
- THC (Tetrahydrocannabinol)
- THCA (Tetrahydrocannabinolic acid)
- CBD (Cannabidiol)
- CBDA (Cannabidiolic Acid)
- Cannabinoids
Medical Marijuana

Cannabinoid receptor type 1
Main article: Cannabinoid receptor type 1
• CB1 receptors are found primarily in the brain, more specifically in the basal ganglia and in the limbic system, including the hippocampus and the striatum. They are also found in the cerebellum and in both male and female reproductive systems. CB1 receptors are absent in the medulla oblongata, the part of the brain stem responsible for respiratory and cardiovascular functions. CB1 is also found in the human anterior eye and retina.

Cannabinoid receptor type 2
Main article: Cannabinoid receptor type 2
• CB2 receptors are predominantly found in the immune system, or immune-derived cells with the greatest density in the spleen. While found only in the peripheral nervous system, a report does indicate that CB2 is expressed by a subpopulation of microglia in the human cerebellum. CB2 receptors appear to be responsible for the anti-inflammatory and possibly other therapeutic effects of cannabis seen in animal models.

Possible Mechanism

• Chemicals bind to a receptor called TRPV1 (GI)
• These chemicals bind and the result is the cells make anandamide: an endocannabinoid.
• Anandamide causes the immune system to calm down.
• Same effect from feeding subjects these classes of chemicals:
  – Amandamine
  – Capsaicin
  – Marijuana
From:

- An article in UConn Today
  - *Chili Peppers and Marijuana Calm the Gut*
  - April 25, 2017
  - Lead investigator: Pramod Srivastava
  - Paper was published in:
  - *Proceedings of the National Academy of Sciences.*

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**Dosage Form**

- Dosage form and strength are tailored to the patient.
  - Have they used before?
  - Start at 1:1 CBD to THC or High CBD to THC.
  - With time increase THC ration until relief of symptoms, including pain.
    - Less sedative for the day (Sativa)
    - More sedative for the night (Indica)
  - Assess current medication.
  - Dosage form determination.
  - Pain medication-monitor for synergistic effect (PMP).
  - Patient reporting of effects.
  - Trial period and communication with patient’s physicians.
Patient Outcomes

• Calming of Symptoms
  – (Previously described pathway.)
• Increase appetite (with higher THC)
  – Patients find relief once able to eat.
    • Oral dosage forms
      – Onset: 45 minutes - 2 hours.
    • Breakthrough symptoms,
      – Inhalant (vaping delivery system)
      – Tincture

Use with Traditional Medication

• Breakdown (metabolism) of these products will be in competition for the same breakdown mechanism that is used with other drugs.
  – Potential for increase blood levels of drugs
    • Pain medication,
    • Anxiety or depression medications.
• Transparency with physician, especially if not the certifying physician.
Cost

• Cash only
• Rates will vary depending on amount of purchases.
• Inhaled dosage forms;
  – Dependent on the THC amount per product.
  – Can range on the low end: $50-$75 per week or $200-$300 per month
• Dosable dosage forms (tablets, tinctures, etc.);
  – Dependent on the THC-A amount per product.
  – Can range on the low end: $100 per week or $400 per month

Testing

• Active ingredients
• Pesticides
• Heavy metals
  – Arsenic, Cadmium, Lead, Mercury
• Mycotoxins
• Microbiologicals
Product Identification

• Packaging and Monogram:

Product

• Examples of Dosage Forms:
  — Wax
  — Tincture
  — Vapor cartridge (is there any controversy with these?)
  — Shatter
  — Concentrated Oil Blend
  — Plant material
  — Sublingual
  — Oral
Measurable Dosage Forms

Guidance

• Patient (MMP) is admitted into a:
  – Acute Care facility,
  – Long Tern Care facility,
  – Hospice,
    • The ‘Institution of Hospice’
      – Institution,
      – Home.
  – Guidance applies to all facilities
Factors to Consider

• Will your facility allow a marijuana product to be used in your facility?
  – Schedule 1 - Federal
  – Schedule 2 – CT

• Most facilities do not allow smoking on the premises.

• Many facilities do not allow personal medications to be used.

• No use of non formulary drugs.

Factors to Consider

In a medical marijuana break out session at a conference.

*Colorado does not allow MM in any certified facilities due to the federal regulations and the premise that all certified facilities accept federal money. CMS at same break out and affirmed prohibition.*

Minnnesota in some facilities doesn’t want to know.
Studies

• [https://www.projectcbd.org/gastrointestinal-disorder](https://www.projectcbd.org/gastrointestinal-disorder)

• [https://www.theroc.us/research-library](https://www.theroc.us/research-library)
  – PubMed.gov
    • US National Library of Medicine
    • National Institutes of Health, BUT they are not NIH studies
Connecticut

Ct.gov/dcp/dcd

Drug Control Division
Telephone: (860) 713-6065
E-Mail: DCP.DrugControl@ct.gov

Address:
Connecticut Department of Consumer Protection
Drug Control Division
165 Capitol Avenue, Room 145
Hartford, CT 06106

Ct.gov/dcp/mmp

Medical Marijuana Program
Telephone: (860) 713-6066
Fax: (860) 706-5361
E-Mail: dcp.mmp@ct.gov

Address:
Connecticut Department of Consumer Protection
Medical Marijuana Program
165 Capitol Avenue, Room 145
Hartford, CT 06106
Sterilization of Endoscopes: Why We Chose a Low Temperature Reprocessing Method

Study by:
Albert Csapo, BA
Vancouver Coastal Health

Presented By:
Carol K. Stevens, BSN, RN, CGRN, CFER
Clinical Specialist TSO3

This is a Study Summary that was presented at the World Congress 2017, in Bonn Germany. Sponsored by GETINGE
Saving Lives
Through Organ Donation

By

David C. Mulligan, MD, FACS, FAST, FAAASLD
Professor of Surgery, Yale University School of Medicine
Chief, Transplantation and Immunology
Yale New Haven Transplant Center
Saving Lives Through Organ Donation

David C. Mulligan, MD, FACS, FAST, FAAASLD
Professor of Surgery, Yale University School of Medicine
Chief, Transplantation and Immunology
Yale New Haven Transplant Center
At a glance

118,137 people need a lifesaving organ transplant (total waiting list candidates). Of those, 75,783 people are active waiting list candidates. Totals as of today 6:33pm EDT

5,367 transplants performed this year Total Transplants January - February 2017 as of 03/30/2017

2,554 donors Total Donors January - February 2017 as of 03/30/2017

Transplant trends

To learn more about transplant data, or to view a report, choose one of the following options:

Select an option: Waiting List Candidates by Organ Type
State of Transplant Center: All Patient States

Waiting List Candidates by Organ Type - All Patient States
Based on OPTN data as of March 30, 2017
That’s more people that can fill the Rose Bowl Stadium.
Patients in Need Growing Faster than Available Organs

Based on OPTN National Data as of December 24, 2010.
Kidney: 97,926
Liver: 14,405
Pancreas: 934
Heart: 3,988
Lung: 1,394
Kidney & Pancreas: 1,725
Heart & Lung: 45

Source: OPTN Data as of March 30, 2017. Totals may be less than the sums due to patients included in multiple categories.

118,137 TOTAL WAITING
# Waiting List Candidates by Organ Type - All Patient States

Based on OPTN data as of March 30, 2017

<table>
<thead>
<tr>
<th>Organ</th>
<th>Candidates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>97,926</td>
</tr>
<tr>
<td>Liver</td>
<td>14,405</td>
</tr>
<tr>
<td>Pancreas</td>
<td>934</td>
</tr>
<tr>
<td>Kidney / Pancreas</td>
<td>1,725</td>
</tr>
<tr>
<td>Heart</td>
<td>3,988</td>
</tr>
<tr>
<td>Lung</td>
<td>1,394</td>
</tr>
<tr>
<td>Heart / Lung</td>
<td>45</td>
</tr>
<tr>
<td>Intestine</td>
<td>280</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>118,055</strong></td>
</tr>
</tbody>
</table>

- Kidney
- Liver
- Pancreas
- Kidney / Pancreas
- Heart
- Lung
- Heart / Lung
- Intestine

Data subject to change based on future data submission or correction. Totals may be less than the sums due to patients included in multiple categories.
4,621 Patients Are Waiting For An Organ Transplant In New England

Many more people are in need of life saving and life enhancing tissue transplants.

Working together to
## Waiting List Candidates by Organ Type - Connecticut

Based on OPTN data as of March 30, 2017

<table>
<thead>
<tr>
<th>Organ</th>
<th>Candidates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>1,141</td>
</tr>
<tr>
<td>Liver</td>
<td>144</td>
</tr>
<tr>
<td>Pancreas</td>
<td>18</td>
</tr>
<tr>
<td>Kidney / Pancreas</td>
<td>15</td>
</tr>
<tr>
<td>Heart</td>
<td>55</td>
</tr>
<tr>
<td>Lung</td>
<td>10</td>
</tr>
<tr>
<td>Intestine</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1,364</strong></td>
</tr>
</tbody>
</table>

Data subject to change based on future data submission or correction. Totals may be less than the sums due to patients included in multiple categories.
The Problem

• 18 people die each day on average from the lack of available organs for transplant

• Every 13 minutes another name is added to the national transplant waiting list
18 People Will Die Today
Why is this so important?

When was the last time you made 1 phone call that saved 8 lives and enhanced the lives of over 50 people?
Benefits of Organ & Tissue Donation

• Donation helps families cope with their grief and loss

• Donation allows an individual’s final wish to be fulfilled, a legacy for the family

• Donation benefits transplant recipients
Organ Donation and Transplantation: How Does It Work?

organdonor.gov
History of Transplantation - Milestones

- **1954**—First successful kidney transplant performed. A living donor gave a kidney to his identical twin Joseph Murray, MD
- **1960**—First successful kidney transplant performed between siblings who were not twins.
- **1963**—First organ recovery from a brain dead donor.
- **1966**—First successful pancreas transplant performed. Richard Lellehei, MD
- **1967**—First successful liver transplant performed. Thomas Starzl, MD
- **1967**—First U.S. heart transplant performed. Norman Shumway, MD
- **1967**—First successful heart transplant performed in South Africa. Christiaan Barnard, MD
- **1968**—First definition of brain death based on neurological criteria developed by a Harvard Ad Hoc Committee.
Milestones in Transplantation (continued)

- **1968**—The first organ procurement organization (OPO) was established, New England Organ Bank based in Boston.
- **1968**—Uniform Anatomical Gift Act drafted by the National Conference of Commissioners on Uniform State Law
- **1976**—Discovery cyclosporine’s ability to suppress the immune system, helping to prevent the rejection of transplanted organs.
- **1981**—First combined heart/lung transplant performed.
- **1983**—First successful single lung transplant with significant recipient survival Dr. Bruce Reitz
- **1984**—The National Organ Transplant Act passed by Congress prohibits the selling of human organs, establishes the Organ Procurement and Transplantation Network to ensure fair and equitable allocation of donated organs, and the Scientific Registry of Transplant Recipients to conduct an ongoing evaluation of the scientific and clinical status of organ transplantation.
Milestones (continued)

• 1987—First successful intestine transplant performed.
• 1988—First split-liver transplant surgery performed. This procedure enables two recipients to each receive a portion of one donated liver. Henri Bismuth, MD
• 1989—First living donor liver transplant in U.S. Christolph Broelsch, MD
• 1995—First living donor kidney was removed through laparoscopic surgical methods
• 1999—First hand transplant performed in the U.S.
• 2001—Number of living donors exceeds number of deceased donors for the first time in the U.S.
• 2006—Donate Life America launched its Donor Designation Collaborative to increase the total number of registered donors in the U.S. to 100 million.
Organ Donation Can Occur in *Three Ways*

- **Living Donors:** Live patient donates a kidney, portion of liver, lung, intestine.

- **Donation after Brain Death:** Patient is declared dead based on *Brain Death Criteria*

- **Donation after Cardiac Death:** Patient is declared dead based on *Cardio-Pulmonary Criteria*
Methods to Increase Number of Donors

• Increase awareness about donation
  – Improve consent rates
• Expand criteria for donors
  – (segmental, increased risk, etc.)
• Live donation
• ? Pay prospective donors
• Financial incentives to defray costs of burial
• Presumed consent
• Organ donation after cardiac death
• Improve care of potential donors to allow for more organ donors and more organs/donation
Segmental Grafts
Segmental Grafts
Segmental Grafts
### Table 1. Donor Selection Criteria for Liver Splitting

<table>
<thead>
<tr>
<th>Donor</th>
<th>Intraoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;50 y</td>
<td>Macroscopic appearance: Soft liver with sharp edges</td>
</tr>
<tr>
<td></td>
<td>No or minimal yellow hue when fingerprint test is done</td>
</tr>
<tr>
<td>ICU stay &lt;3 days</td>
<td>Liver biopsy: macrovesicular steatosis &lt;10%</td>
</tr>
<tr>
<td>Last serum Na &lt;150 mEq/L</td>
<td>Bile production: yellow, viscous bile.</td>
</tr>
<tr>
<td>ALT: up to 2–3 times normal</td>
<td>Liver anatomy: Normal vascular and biliary anatomy.</td>
</tr>
<tr>
<td>Hemodynamic stability:</td>
<td></td>
</tr>
<tr>
<td>No vasopressor support or dopamine</td>
<td></td>
</tr>
<tr>
<td>≤10 μg/kg/min</td>
<td></td>
</tr>
</tbody>
</table>
Types of Grafts and Results

LDLT Donor Assessment

Pre-operative assessment by IQQA
LIVING DONATION SAVES LIVES!

YNHH performs CT's first eight-patient, paired kidney transplant exchange

With members of YNHH's transplantation teams at the press conference were kidney donors and recipients, front row (l-r): Patricia Menno-Coveney, David Rennie, Margaret Rennie, Raymond Murphy, Sylvie Murphy, Mario Garcia, Hilary Grant and Edward Brakoniecki.
Congratulations!!

Many more years of blessings await you!
Stuart Zeitlin ’77 and Robert Roth ’77 Forged Friendship As Freshmen in 1973

Robert Roth was on his back, staring up at fluorescent lights. His kidney transplant surgery was just moments away.

The HBO executive’s thoughts volleyed between his mom, who died three decades earlier from complications related to a kidney transplant, and his best friend, Stuart, who at the moment was across the hall having his left kidney harvested.

“It was almost one of those out-of-body experiences,” Roth, 58, said, “where you know what’s happening is real, but you can’t come to grips with the fact that momentarily, you will be cut open and your best friend’s organ will be placed inside of you.”

Roth met Stuart Zeitlin – the man who saved his life in December – during their first week as freshmen at Stony Brook University, back in 1973 when construction of the hospital and the Health Sciences Center was kicking off on the other side of Nicoll’s Road.

Zeitlin, then of Manhasset Hills, quickly struck up a friendship with Roth during his visits to see a high school pal a few doors down from Roth’s room in Irving College. Together with another freshman in the same residence hall – Kenny Cohen from Coney Island – Zeitlin and Roth formed a trio that remains intact today.

The three spent that fall sharing common interests, while pushing each other down the hall in shopping carts and rooting their hearts out for the New York Mets in the World Series. They then spent their lives cultivating their bond – graduating together from Stony Brook in 1977, serving as groomsmen in each other’s wedding parties, celebrating the births of each of their children, and making sure to routinely meet at Ben’s Kosher Deli in Greenvale for lunch or dinner.

Stony Brook University alums (L to R) Dr. Ken Cohen, Stuart Zeitlin and Robert Roth at Yale-New Haven Hospital after Zeitlin donated a kidney to Roth. The three met as freshmen in 1973 and graduated from Stony Brook in 1977.
Organ Donation After Cardiac Death

• Definition:
  – A procedure in which organs are surgically recovered following the pronouncement of death based on the “irreversible cessation of circulatory and respiratory functions.”
  
  – Organs recovered most often are kidneys and liver; sometimes pancreas/lung
Donation after Cardiac Death

- Driven by family of donor
- Not associated with as much hemodynamic instability
- Must be “neurologically devastated”
- Require significant hemodynamic support
- Different protocols for each hospital
Donation after Cardiac Death Procurement Technique

- Withdrawal of cardio-ventilatory support
- Monitoring of vitals and ECG tracing
- Spontaneous loss of BP, P, respiration, and ECG
- Declaration of death by physician not affiliated with procurement team
- Family, if present, leaves
- 5 minute waiting period
Donation after Cardiac Death

- Withdrawal of support in OR
- Management by hospital staff
  – NOT TRANSPLANT TEAM
- Monitoring of vitals
- No deliberate interventions to hasten death
- 1 hour max time for death to occur
Donation after Cardiac Death

- Organs
  - Kidneys
  - Liver
  - Pancreas
  - Lung
Principles of Ethics

- Autonomy (Respect for the person)
- Beneficence (Do Good)
- Non-malfeasance (Do No Harm)
- Justice
Ethical Issues in Organ & Tissue Transplantation

- Brain Death = Death?
- True informed consent for organ donors and registries
  - Vascularized Composite Allotransplantation issues
- Donation after Cardiac Death (DCD)
- Need far greater than number of organs
  - Scarce resource – value judgments and economic considerations – fairness
  - National or local resource
- Organ allocation schemes
  - Does one size fit all?
  - How to best stratify risk/attribute need
- Distribution of scarce resource
  - How to improve the access for all
  - Justice, Equity, Disparity
- Futility in transplantation – when is it enough?
Organ Allocation and Distribution
It’s Time to Compensate Kidney Donors

By TINA ROSENBERG  AUGUST 7, 2015 5:15 AM

A dialysis center in Paterson, N.J. Jennifer S. Altman for The New York Times

Second of two articles

Last week I wrote about Iran, the only country in the world that pays kidney donors.

Iran shows that a kidney market need not resemble organ trafficking. Indeed, its market is closely regulated and has preempted the exploitative and abusive illegal markets found in many other countries.

Iran’s program has flaws, such as lack of follow-up for donors and limited support for poor recipients, that are typical of an underdeveloped health system. But the program also has lessons for countries like the United States, where the wait for a kidney can be as long as a decade.
• Organ regeneration and resuscitation
  – Lungs
  – Kidneys
  – Livers
  – Intestines

• 3D Bioprinting of Organs using Stem Cells

• Uterine Transplantation
Probiotics 2017: Fulfilling the Promise

By:

Peter Buch, MD, AGAF, FACP
Associate Clinical Professor, University of Connecticut School of Medicine, University of New England College of Osteopathic Medicine, and Frank H Netter School of Medicine / Quinnipiac University
Probiotics 2017: Fulfilling the Promise

Peter Buch, MD, AGAF, FACP
Associate Clinical Professor
University of Connecticut School of Medicine
University of New England College of Osteopathic Medicine
Frank H Netter School of Medicine/Quinnipiac University
Disclosure:

• Speaker’s Bureau  AbbVie

Synergy Pharmaceuticals
Objectives

- To learn about the proven GI uses of Probiotics
- To understand the difficulty in comparing strains, studies, potency and results
- To understand how fecal transplants may be the ultimate Probiotic
- To review the potential future uses of Probiotics
“When you come to a fork in the road, take it”
• Crowd sourced from UC San Diego
• Sample kit and questionnaire about diet
• Developing a database
Microbiome Definitions

- Microbes

- Genetic Material
The Facts:

• 10 X more microbes than we have cells

• 100X more genes than we have

• We carry 2 kg of bacteria

• Over 500 species
Factors Affecting the Microbiome

• Antibiotic use
• Infections
• High fat/high sugar diet
• Exercise
• Vegetarian diet
Probiotic

- Live microorganisms that when administered in adequate amounts confer a health benefit to the host
Prebiotic

- Usually non digestible carbohydrate present in foods which provide health benefits indirectly by promoting the growth of beneficial microorganisms
  
  Jerusalem artichoke
  
  Garlic
  
  Leeks
Synbiotic

• A combination of Probiotic and Prebiotic

  Yogurt
  Whole grains
  Bananas
What in your judgment is the most important characteristic of a Probiotic?

1. Number of live organisms
2. Bacterial strains
3. Longevity of the product
Common Probiotics

• VSL #3 a combination of several bacteria
• Align B infantis
• Culturelle Lactobacillus GG
• Dan Active L casei
• Florastor Saccharomyces boulardi
Probiotic Regulation

• U.S. Food products with no specific health claim.
• None yet submitted to the FDA for specific health claim
• No viable cell counts required
• No shelf life/storage required
Probiotics in Europe

• Health claims must be substantiated
Most Common Adult Probiotic Use

1. Irritable Bowel Syndrome
2. Ulcerative Colitis Adjuvant Therapy
3. Treatment of Pediatric Viral Diarrhea

- Shortens diarrhea by 1 day

Allen SJ et al
Probiotics for treating acute infectious diarrhoea
Controversial Use
Antibiotic induced (Not Cl diff) diarrhea??

Hempel S et al
Probiotics for the prevention and treatment of antibiotic-associated diarrhea: a systematic review and meta analysis
JAMA 2012:307;1959
Cl difficile Prevention??

Goldenberg JZ et al
Cochrane Database Syst Rev 2013:5;CD006095
We need more data

• Traveler’s Diarrhea prevention
• Adjuvant treatment for H pylori infection
Doesn’t Work

- To treat Cl difficile
Are There Any Risks of Probiotic Use?

Brandt, LJ et al  Long term follow up of colonoscopic fecal microbiota transplant for recurrent Clostridium difficile infection  Am J Gastroenterology 2012: 107;1079
Risks

• Infections in immunocompromised patients??
What are the Research Difficulties in Studying Probiotics?

• Species and strain specific
• Dose
• Manufacturing standards
• Mechanism of action
Another Clinical Factor

- Probiotics are susceptible to die off during prolonged storage
Mechanisms??

- Antimicrobial
- Increase epithelial barrier
- Increased immunity
- Anti inflammatory
- Modulation of pain in IBS
- Prevent harmful bacteria from attaching to the gut
Is it the Bacterium or its Metabolite?

Butyrate

What is Butyrate???
Beneficial Properties of Butyrate

- Lowers pH
- Inhibits pathogens
- Improves gut immunity
- Improves Insulin sensitivity
- Signals the liver for less gluconeogenesis
- Is an energy source for colonic epithelial cells
High Fiber May Increase Butyrate Production
Probiotics are useful in all these conditions except:

1. Ulcerative colitis

2. Crohn’s disease

3. Rotavirus infection in children
Irritable Bowel Syndrome

• Probiotics improve the global symptoms of bloating and flatulence (limited effectiveness)
• Hard to compare studies
• Different species, strains, preparations and doses in different patient populations

• Ford, C et al American College of Gastroenterology Monograph on the Management of Irritable Bowel Syndrome and Chronic Idiopathic Constipation American Journal of Gastroenterology. 2014:109;suppl 1
Ulcerative Colitis

• VSL #3 is the only probiotic studied for the prevention and relapse of ulcerative colitis when added to a standard regimen controlling ulcerative colitis

• According to the Cochrane analysis; no evidence for usefulness alone in the maintenance of remission

Shen, R et al
Effect of probiotic on inducing and maintaining therapy in ulcerative colitis, crohn’s disease and pouchitis: meta analysis of randomized controlled trials
Inflammatory Bowel Disease
2014:20:21
Probiotics and Acute Infectious (Viral) Diarrhea

• Safe
• Reduces the duration of the diarrhea by 1 day
• 63 studies/8014 patients
• Includes infants and children
• NOT related to probiotic strain, number of organisms per capsule or type of infection

Allen SJ et al
Probiotics for treating acute infectious diarrhoea
Cochrane Database Syst Rev 2010 CD003048
What percentage of patients given antibiotics develop non specific diarrhea?

1. 10%
2. 30%
3. 50%
Question

• Do you recommend probiotics to your patients who have had antibiotic induced diarrhea (NON Cl difficile) previously related to the SAME antibiotic?
Probiotics may reduces this number

Hempal S et al
Probiotics for the prevention and treatment of antibiotic associated diarrhea: A systematic review and meta-analysis
JAMA 2012:309;1959
Questions

• Are Probiotics useful to prevent Cl difficile?

• What is the standard of care?
What’s the Data on Probiotic Prevention of Cl difficile?

• 3818 patients in 20 trials
• Probiotics reduced Cl difficile by 66%
• (Lactobacillus and Saccharomyces boulardii)

Johnston BC et al
Probiotics for the prevention of Cl difficile-associated diarrhea. A systematic review and meta analysis
Ann Int Med 2012:157;878
Cl difficile Prevention??

- 23 RCTs  N 4213
- Cl diff infection 2%  Probiotic cohort 5.5%
- Probiotics MAY prevent Cl diff

Goldenberg JZ et al  
Cochrane Database Syst Rev  2013;5;CD006095
We need more data

- Specific antibiotics matched to specific Probiotics
- Use in different populations; in and out patient; very sick; mildly ill
- Which probiotics are most efficacious?
- Studies don’t start Probiotics at the same time

Rao K and Young V
Probiotics for the prevention of Clostridium difficile infection in hospitalized patients: is the jury still out?
Gastroenterology 2017:152;1817
Ernie

- Is a 78 y.o recently diagnosed with a urinary tract infection
- He was given Septra DS for 10 days
- Unfortunately developed Cl difficile
- The treated with Metronidazole 250 mg qid for 10 days
- Diarrhea recurred 2 weeks later
- Then given Vancomycin 125 mg qid
- Diarrhea returned 2 weeks later
What should we do now?

1. Fidaxomicin (Dificid)

2. Vancomycin AND Metronidazole

3. Repeat stool for Cl difficile

4. Fecal transplant
All of the following are true regarding Fidaxomicin

1. Reduces recurrence rates for Cl difficile

2. More effective than Vancomycin

3. No adjustment is needed for renal compromise
Why is Cl difficile Important?

• Three times more prevalent than in 2000*

• Increasingly causing deaths in the elderly, estimated to be 29,300 in 2011 *

• Sporadic outbreaks in healthcare facilities

• Virulent strain (NAP1/027)
  • *Peery AF et al  Burden of gastrointestinal disease in the United States:2012 update  Gastroenterology 2012:143;1179
  • Fernanda, C et al  The Burden of Cl diff Infection in the US. NEJM.2015: ;372;825
Celeste

• Is a 50 y.o who had Cl diff 3 weeks ago treated with Vancomycin 125 mg qid for 10 days

• Now diarrhea again

• Would you:
  1. Treat again for Cl diff?
  2. Do another stool test?
Martha C

- Is a 76 y.o female who had an unknown antibiotic exposure 2 weeks ago and now has Cl diff with:
  - T 101F
  - Diffuse abd pain
  - WBC 20,000 and shift to left

What is the ABX of choice?
How do you treat if she develops an ileus?
How Long After Antibiotic Use Can We Expect to See Cl diff?
What percentage of hospitalized asymptomatic patients are carriers of Cl difficile?

1. 5%
2. 10%
3. 20%
4. 50%
What percentage of asymptomatic extended care facility patients are carriers of Clostridium difficile?
Risk factors for recurrent Cl difficile

- PPI use
- Renal insufficiency
- Malnourished
- Elderly
- Long length of stay
- Serious illness/immunocompromised
Why stool transplants?

• 20-30% of patients treated for Cl difficile have a recurrence
• Many patients have multiple recurrences
• Fecal transplants break the cycle
Routes of Delivery

- Fecal Enemas
- Endoscopy
- Colonoscopy
- NG tube
- Freeze dried capsules
Success Rates for Fecal Transplants

• 90% by colonoscopy

• Patients can feel better within hours of their transplant!!!
Tests for Stool Donor

• Hepatitis A,B,C

• HIV

• Stool O&P, C&S, Cl difficile

• MAY NOT BE COVERED BY HEALTH INSURANCE
Should there be a standard donor pool?

Brown Cross
Choose Stool Wisely

• Case reports of fecal transplants from obese relatives causing significant wt gain in recipients
• No other causal factors

• Boggs, W
• Fecal transplants may up risk of obesity onset
• May 13, 2015
• Scientific American
Synthetic Stool

• “RePOOPulate”

• Has only 30 strains of bacteria

  • Petrof, EO
  • Stool substitute transplant therapy for the eradication of Clostridium difficile infection: “RePooPulating the gut
  • Microbiome 2013
All of the following are risk factors for recurrent Cl difficile EXCEPT:

1. Age

2. PPI use

3. Hospitalization

4. Diphenoxylate use
Which of the following are complications of Cl difficile

1. Renal failure
2. Toxic megacolon
3. Death
4. All of the above
What is the Future of Probiotics?

Obesity

Non Alcoholic Fatty Liver Disease (NAFLD)

Diabetes

Antimicrobial resistance

Autoimmune diseases

Allergies

Neurological probiotics for well being
Summary

• Probiotics have been shown to be helpful in treating:  Irritable Bowel Syndrome
  Ulcerative Colitis
  Acute Infectious Diarrhea in peds, especially Rotavirus
• The role of Probiotics in treating many other diseases remains controversial
• Fecal transplants prevent recurrence of Cl difficile
Understanding GERD:

The 3 diagnostic testing options used in the motility lab

By

Janet R. King, BSN, RN, CGRN
Massachusetts General Hospital
Boston, Massachusetts
Understanding GERD and the 3 diagnostic testing options used in the motility lab

Janet R. King
BSN. RN. CGRN
Objectives

- Define Gastro-Esophageal Reflux Disease

- Compare and Contrast the 3 pH testing methods
  - Catheter pH
  - Bravo
  - pH Impedance
Universal Accepted Definition Developed

by the Montreal Consensus Group

- A condition that develops when the reflux of gastric content causes troublesome symptoms or complications

- Symptoms are troublesome if they adversely affect an individual’s well being.

(AGA position statement advocates using this definition)

(Gastroenterology 2008:135:1392-1413)
Gastroesophageal Reflux Disease:

- Is the most common Ambulatory Care DX in the United States
- Affects 20-30% of the US population

(Digestive Disease Science 2017)
GERD occurs when the LES barrier is not able to prevent backflow

- Hypotensive LES
- Due to transient relaxation in the lower esophageal sphincter (LES)
- Hiatal Hernia
- Weakened sphincter

Factors that can increase your risk of GERD:

- Obesity
- Hiatus Hernia
- Pregnancy
- Smoking
- Dry mouth
- Asthma
- Diabetes
- Delayed Stomach Emptying
- Connective tissue disorders (Scleroderma)
Symptoms of GERD

- Heartburn
- Regurgitation
- Epigastric pain
- Nausea/Vomiting
- Odynophagia
- Trouble swallowing liquids or solids
- Cough
- Asthma
- Hoarseness
- Laryngeal irritation
- Globus
- Sore or burning throat
- Aspiration Pneumoniae

1st Line Treatment: Empiric Therapy
Uncomplicated Gerd Symptoms

- Lifestyle Modifications
- Medication Therapy - (PPI Trial)
Lifestyle Modifications:

- **Avoidance of foods that may precipitate reflux**
  - Coffee
  - Chocolate
  - Alcohol
  - Fatty foods

- **Avoidance of acidic foods that precipitate heartburn**
  - Carbonated drinks
  - Spicy foods
  - Citrus

- **Adoption of behaviors that reduce risk of acid exposure**
  - Weight loss
  - Raising the head of the bed for sleep
  - Smoking cessation
  - Avoid lying down for 2-3 hours after meals

(Gastroenterology 2008)

Medical Therapies:

- **Proton Pump Inhibitor (PPI)**
  - Prilosec: Omeprazole
  - Nexium: Esomeprazole magnesium
  - Prevacid: Lansoprazole
  - Protonix: Pantoprazole
  - Aciphex: Rabeprazole sodium

- Initial trial single daily dose

- Two week Reassessment
  - Measure of success if 80% symptom improvement
  - May increase PPI to twice daily dosing
    (If only some improvement + still displeased)
Ambulatory pH Monitoring Techniques

- Allows for Direct Quantification of Reflux
- Provides correlation between symptoms and episodes of reflux
- Is considered the Gold Standard for DX GERD

**Indications for pH Testing?**

- Patients on PPI’s still having reflux symptoms
- Evaluate acid exposure prior to anti reflux surgery
- Following anti reflux surgery in a patient still having ongoing reflux
- Evaluate GERD patients with laryngitis or chronic cough while on PPI for at least 4 weeks
- Patients with gastro esophageal reflux-induced asthma
3 Types of Testing Methods

• pH monitoring with catheter

• pH monitoring without catheter (Bravo)

• pH Impedance monitoring

pH Monitoring Studies:

Measures the reflux of acid into the esophagus during a 24 or 48 hour period

• Provides information regarding:
  › Duration of reflux
  › Frequency
  › Timing
  › Correlation
Advantages of pH Studies

- Detects reflux events under normal physiologic conditions and activity
  (Before 1974 – Stationary Technology Barium Swallow and Video Fluoroscopy)

- Longer monitoring period

- Symptoms can be correlated with episodes of Reflux

- Allows determination of efficacy of therapy

pH Study Contraindications

- Recent gastric surgery

- Esophageal tumors or ulcers

- Esophageal varices

- Uncontrolled coagulopathy

- Severe maxillofacial trauma

- Poor patient cooperation
Catheter pH Monitoring

- **Single Channel pH study**
  - One sensor placed 5cm above the Lower esophageal sphincter (LES)

- **Double Channel pH study**
  - 2 Channel Pulmonary
  - 2 Channel Gastric
  - 2 Channel ENT

2 Channel Pulmonary pH Study

Frequently used for Patients with:
- Non Allergic Asthma
- Pulmonary symptoms
Pull back 5 cm from the Proximal LES border.

PULMONARY PACEMENT.
PULL OUT 5 CM

Advance (push in) 10 cm from the proximal LES border.

GASTRIC STUDY
PUSH IN 10 CM

Pull out 5 cm from the proximal LES border.

1 CHANNEL Ph STUDY/IMPE DANCE
PULL OUT 5 CM

Digitrapper
pH-Z
2 channel - 24 hr pH Study Analysis

(Cough symptoms correlates with acid reflux episodes)

2 channel - 24 hr pH Study Analysis

(Chest pain symptoms correlates with acid reflux episodes)
2 Channel Study
Poor Symptom Correlation

Tips for pH Testing

- Accurate positioning of the pH probe is critical to obtain useful data

- Intubation into the Stomach
  - confirm there is acid in the stomach
  - look for a change from acid to alkaline if off meds

- Patient Instructions
  - Verbal Teaching
  - Written Instructions
Patient Pulled Catheter
Limitations of 24 hr Catheter study

- Patient Intolerance to the catheter
  - Nasal pharyngeal irritation or pain
  - Epitaxis
  - Dysphagia
  - Runny Nose

- Change in patient activity level
  - Decrease in diet intake and physical activity

- Technical Limitations of the ph probe
  - catheter drifting, poor positioning,

- Short recording period (24 hrs)

- Requires Manometry procedure first
Catheter less pH Monitoring
Bravo
Advantages of Bravo pH Study

- No nasal pharyngeal irritation
- Patient freedom to maintain normal daily activities
- Eliminates catheter movement or drifting
- Longer recording periods (48 - 96 hours)

Contraindications

- Patients with:
  - Bleeding diathesis
  - Strictures
  - Severe esophagitis
  - Esophageal varices
  - Obstructions
- It is also contraindicated in patients with pacemakers or implantable cardiac defibrillators
BRAVO 48-96 hr pH Study

**pH Capsule**

- Size of a gel cap
- Dimensions: 6 x 6.3 x 26 mm
- Measures esophageal pH
- Radio-Telemetry sends the data to the Receiver box
- Contains: suction chamber, locking pin, transmitter and pH sensor+ref

FDA cleared the use of BRAVO Procedure for patients 4 years and older in 1/2011

---

**Bravo pH Capsule with Delivery System**

- For trans-oral placement
- Single-Use item
- One-handed operation
- 100 cm long with working length of 80 cm
- Distance marks every 5 cm up to 60 cm
Transoral pH Bravo Capsule placement Endoscopically

Squamous Epithelium

Columnar Epithelium

6 CM
Transoral pH Bravo Capsule placement without Endoscopy

(A) TN manometry for placement of a Bravo capsule 5 cm above the LES
(B) TO placement of a Bravo capsule using the 4 cm TN to TO conversion factor

Bravo capsule and delivery system

American Journal of Gastroenterology 2007
Capsule Attachment and Release

Step 1: Position Bravo Capsule
Step 2: Apply Suction
Step 3: Advance Pin
Step 4: Release Capsule
Step 5: Begin pH Recording

Bravo 48 hr pH Study

pH Capsule
Limitation of Bravo pH Study

- Requires EGD or manometry to determine placement of capsule

- Early capsule detachment

- Some patients experience vague chest discomfort or foreign body sensation

  (Study Dr. John Pandolfino: < 4% of patients developed severe chest pain requiring endoscopic removal of capsule - 7/300 patients capsules placed)

Bravo Capsule Early Detachment
Patient Teaching

Capturing events and symptoms are required for accurate analysis of patient data

Press to report Meal event start and end time.

Press to report Supine event start and end time.

Press to report Chest Pain

Press to report Heartburn

Press to report Cough

Case Study
Patient S.

- Sent to Dr. Kuo for consultation re: evaluation of possible reflux
- February 14: EGD
  - Noted small erosions were seen at the GE junction
  - Z Line irregular
  - Stomach normal
  - Biopsies were taken
- Placement of a Bravo capsule
- Returned 48 hours later with patient log and Bravo recorder box
Case Study: Patient S.

Follow up:

- Patient notified of Test results:
  - EGD procedure
  - Bravo Study

- Appointment scheduled
  - Patient treated with high dose acid suppression medications
  - Omeprazole 20 mg Bid

pH Impedance Testing

(Approved by the FDA in 2002)

- Two separate sensing technologies:
  - Multi-Channel Impedance – the use of conducting electrode rings along the catheter to sense movement of stomach contents into the esophagus
  - pH monitoring – identifies acid events
MII pH Catheter

Clinical Gastro Hepatology 2007

Pediatric Catheter
has 7 Impedance conducting rings
(-1,1,3,5,9,11 cm markings)
and a pH sensor at 0
Impedance Range

Low Conductivity = High Impedance

High Conductivity = Low Impedance

2009 Gastrointestinal Endoscopy
Impedance pH study

- Detection of all reflux episodes
- Assists in determining the reflux makeup
  - ex liquid or gas or mixed
- Distance the reflux travels up the esophagus
- Acid Reflux Composition
  - Acidic
  - Weakly acidic
  - Weakly alkaline

Gastrointestinal Endoscopy 2009
Indications for Impedance Testing

- Refractory GERD failure of PPI Treatment
- Chronic Cough
- Evaluation for Nissen Fundoplication

Contraindications

- Nasopharyngeal or upper esophageal obstruction
- Uncontrolled coagulopathy
- Severe maxillofacial trauma
- Cardiac instability
- Recent gastric surgery
- Esophageal tumors or ulcers
- Esophageal varices
- Uncooperative Patient
CASE STUDY
Patient G

- 61 year old female

- PMH
  - Hypercholesterolemia
  - GERD since 1998
  - Cholesystectomy in 2000
  - EGD short segment of Barrett’s esophagus
  - Sigmoid diverticulosis

CASE STUDY
Patient G

- Medications
  - Prilosec 40 mg BID
  - Multivitamin

- Social History
  - Does not smoke or drink
CASE STUDY
Patient G

 Symptoms
  ◦ Severe burning in chest and mouth
  ◦ Coughing
  ◦ Sleeps on patio chair due to chest burning
  ◦ Eats a bland diet and is a vegetarian

Past Studies:
  ◦ Barium swallow
    ◦ Showed esophagitis
  ◦ Repeat EGD normal
CASE STUDY
Patient G

- **Patient assessment sheet and diary:**
  - Daily chest pain, heartburn, and cough
  - Records multiple episodes of coughing
  - “Have been sitting up (propped with pillows on bed since 8PM, sat up a couple of times, sat on chair for awhile. My throat hurts, chest hurts, mouth hurts, All burning almost all day. Pain is less if I pull my arms up or behind my back.”
CASE STUDY
Patient G

**Impedance Report:**

Reflux Episodic Activity:

<table>
<thead>
<tr>
<th>Channel 1</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acidic reflux</td>
<td>1 (55)</td>
</tr>
<tr>
<td>Weakly Acidic reflux</td>
<td>191 (26)</td>
</tr>
<tr>
<td>Non–acid reflux</td>
<td>35 (1)</td>
</tr>
</tbody>
</table>

Reflux Symptom Association Probability:
Non–acid reflux 94.9%

**CASE STUDY**
Patient G

- **Impedance test**
  - Increased weakly acidic reflux and non–acid reflux
  - Non–acid reflux with good correlation of symptoms

- **Diagnosis**
  - Non–acid reflux

- **Esophageal motility study**
  - Low LES pressure
  - Contraction of esophageal body are peristaltic with low amplitude
CASE STUDY
Patient G

Treatment and Recommendations:

- Reglan 10 mg before meals and at bedtime
- Zantac 300 mg at hs
- Prilosec 40 mg bid
- Lozenges or chewing gum
- Amitriptyline 25 mg at hs

In Summary:

- GERD is a common clinical problem
  - Diagnosis of uncomplicated GERD
    - Diet, Lifestyle Modifications and PPI Trial
  - Motility Lab Testing options:
    - pH catheter/ catheterless testing:
      - measures esophageal reflux acid exposures and correlation of symptoms with reflux episodes
    - pH Impedance:
      - Detects bolus movement within the esophagus lumen
      - Detects reflux events independent of pH with higher sensitivity
Resources

PPI’s;
What’s the Hype all About?

By:
Miechelle O’Brien MD, PhD
WCHN Danbury Hospital
Risks associated with PPI use: What’s real and what’s hype?

Miechelle O’Brien, MD, PhD

Roadmap

• How do PPIs work?
• When do we use them?
• Side Effects
• Risk in Pregnancy
• Idiosyncratic Reactions
• In the News: What’s Real (Signal) and What’s Noise???
PPI Mechanism of Action
Benefits of PPI use
AGA Best Practice Advice

1) Patients with GERD and acid-related complications should take a PPI for short-term healing and long-term symptom control
2) Patients with uncomplicated GERD who respond to short-term PPIs should subsequently attempt to stop or reduce them
   *If not possible, employ reflux testing to sort out functional symptoms
3) Patients with Barrett’s esophagus with symptomatic GERD should take a long-term PPI
4) Asymptomatic patients with Barrett’s should consider a long-term PPI
5) Patients at high risk for ulcer-related bleeding from NSAIDs should take a PPI if they continue NSAIDs
6) The dose of long-term PPIs should be periodically re-evaluated so that the lowest effective dose is used.


Side Effects of PPIs

• Headache (7%)
• Dizziness (2%)
• Rash (2%)
• Abdominal pain (5%)
• Diarrhea (4%)
• Vomiting (3%)
• Constipation (2%)
Safety during Pregnancy and Lactation

- Omeprazole known to cross placenta: Category C
- Other PPIs: Category B

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Controlled studies show no risk.</td>
</tr>
<tr>
<td>B</td>
<td>No evidence of risk in humans; the chance of fetal harm is remote.</td>
</tr>
<tr>
<td>X</td>
<td>Contraindicated.</td>
</tr>
</tbody>
</table>

The Safety of Proton Pump Inhibitors (PPIs) in Pregnancy: A Meta-Analysis

Smershak KG, Gil P, Lisa O’Brien, Thomas B. Hinton, and Gillesk Yen, MD, BCPC

1530 in utero exposures and 133,410 controls

The Safety of Proton Pump Inhibitors (PPIs) in Pregnancy: A Meta-Analysis


Reported Adverse Effects of PPIs

Reported Adverse Effects of PPIs

- Kidney Disease
- Dementia
- Bone Fracture
- MI
- SIBO
- *Campylobacter* or *Salmonella*
- SBP
- Pneumonia
- *C difficile*
- Micronutrient Deficiencies
- GI malignancies

*RED=RCT*
PPIs and MI

HR=0.34
p<0.110

HR=0.99
p=0.96

PPIs and Pneumonia

Prevention of peptic ulcers with esomeprazole in patients at risk of ulcer development treated with low-dose acetylsalicylic acid: a randomised, controlled trial (OBERON)

James M Scheiman,1 P J Devereaux,2 Johan Hortlitz,3 Peter H Koteles,4 Angel Lanas,5 Sander Veldhuyzen van Zanten,6 Emma Naucke,7 Lars-Erik Svedberg7

Table 2 Number (%) of patients with adverse events judging

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>OBERON Long arm 100 mg/day</th>
<th>OBERON Long arm 20 mg/day</th>
<th>OBERON 20 mg/day</th>
<th>PPIs 20 mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>7.0%</td>
<td>17.2%</td>
<td>11.1%</td>
<td>13.5%</td>
</tr>
<tr>
<td>Headache</td>
<td>13.8%</td>
<td>12.0%</td>
<td>9.9%</td>
<td>11.3%</td>
</tr>
<tr>
<td>Nausea</td>
<td>19.7%</td>
<td>15.2%</td>
<td>15.0%</td>
<td>16.4%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>31.6%</td>
<td>31.0%</td>
<td>23.9%</td>
<td>29.3%</td>
</tr>
<tr>
<td>Flatulence</td>
<td>39.3%</td>
<td>39.1%</td>
<td>31.8%</td>
<td>37.1%</td>
</tr>
</tbody>
</table>

Scheiman J et al. Heart 2011;97:797
PPI use and GI malignancies

- Plausibility:
  - Pan-gastric colonization by *H pylori*
  - Hypergastrinemia
- NO association in humans with gastric cancer or NETs
- SOPRAN and LOTUS trials:
  - 812 patients
  - Anti-reflux Surgery vs. PPI
  - 12 years follow-up
  - No difference: Pre-malignant changes or NETs

Reported Adverse Effects of PPIs

- Kidney Disease
- Dementia
- Bone Fracture
- MI- No association in RCTs
- SIBO
- SBP
- *C difficile*
  - Pneumonia- No association in RCTs
  - Micronutrient Deficiencies
  - GI malignancies- No association in RCTs

Relative Risk vs Absolute Risk

• Two ways of saying the same thing
• Absolute Risk - an absolute difference
• Relative Risk - Ratio of the two risks
  makes effect size seem larger

Think Lottery Ticket....... 

• One Ticket:
  • Odds of winning 1 in 292,200,000
• Two Tickets:
  • Odds of winning are 2 in 292,200,000
  • Odds Ratio increased 2-fold!
WHY THE NUMBERS MATTER

“New wonder drug reduces heart attack risk 50%”

“New Wonder drug reduced heart attacks from 2 per 10,000 to 1 per 10,000”

The absolute risk is more useful at conveying the true impact of an intervention, yet is under-reported in the research and the media.

Limitations of Observational Epidemiology

- Residual confounding from unknown, unmeasured, or poorly measured confounders

Howden CW. Am J Gastroenterol 2010:105:2438-2439
PPI and Bone Fracture

Proton Pump Inhibitors and Risk of Fracture: A Systematic Review and Meta-Analysis of Observational Studies


Risk Hip Fracture Risk Vertebral Fracture

Risk of Hip Fracture sub-group analysis


- BMD testing femoral neck, total hip and lumbar spine of 8,370 subjects
- Baseline, 5 years and 10 years
- PPI users had lower BMD at baseline (femoral neck and total hip)
- PPI users over 10 years did not have accelerated BMD loss

Targownik, et al., Am J Gastroenterol 2012; 107:1361
Long-term PPI users (>5 years)
• aBMD using DXA, volumetric BMD using 3D-QCT
• 104 subjects
• No association with BMD or bone strength
• Further evidence that association between PPI use and fracture is not causal.

Targownik, et al., Am J Gastroenterol 2017; 112:95
No difference in aBMD on DXA

<table>
<thead>
<tr>
<th>T-score</th>
<th>PPI users (n=82)</th>
<th>PPI non-users (n=82)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total hip</td>
<td>-0.33±1.01</td>
<td>-0.29±1.16</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>0.13±0.89</td>
<td>0.12±0.07</td>
</tr>
<tr>
<td>Trabecular</td>
<td>-0.20±0.17</td>
<td>-0.18±0.15</td>
</tr>
<tr>
<td>L3-L4</td>
<td>-0.73±1.50</td>
<td>-0.56±1.87</td>
</tr>
</tbody>
</table>

Percentage with T-score -1≤T≤2.5

<table>
<thead>
<tr>
<th></th>
<th>Total hip</th>
<th>Femoral neck</th>
<th>Trabecular</th>
<th>L3-L4</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPI users (n=82)</td>
<td>30.0</td>
<td>67.0</td>
<td>31.0</td>
<td>94.7</td>
</tr>
<tr>
<td>PPI non-users (n=82)</td>
<td>29.0</td>
<td>63.0</td>
<td>25.0</td>
<td>91.1</td>
</tr>
</tbody>
</table>

No difference in vBMD

<table>
<thead>
<tr>
<th></th>
<th>Total bone vBMD (mg/cm²)</th>
<th>Cortical BMM (g)</th>
<th>Trabecular vBMD (mg/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPI users (n=82)</td>
<td>No PPI users (n=82)</td>
<td>PPI users (n=82)</td>
<td>No PPI users (n=82)</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>296±53</td>
<td>278±52</td>
<td>2.49±0.10</td>
</tr>
<tr>
<td>Trabecular</td>
<td>476±27</td>
<td>396±20</td>
<td>21.3±10.3</td>
</tr>
<tr>
<td>Total hip</td>
<td>341±59</td>
<td>333±59</td>
<td>36.0±12.0</td>
</tr>
</tbody>
</table>

3D-QCT, three-dimensional quantitative computed tomography; BMM, bone mineral mass; PPI, proton pump inhibitor; vBMD, volumetric bone mineral density.
No difference in measurements between PPI users and PPI non-users were statistically significant.
No difference in structural or mechanical characteristics

Table 4. Comparison of structural and mechanical characteristics of femoral neck between PPI users and non-users

<table>
<thead>
<tr>
<th></th>
<th>PPI users (n=50)</th>
<th>PPI non-users (n=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean cortical thickness</td>
<td>2.66±0.65</td>
<td>2.59±0.66</td>
</tr>
<tr>
<td>Mean section modulus</td>
<td>2.52±1.01</td>
<td>2.34±0.68</td>
</tr>
<tr>
<td>Mean buckling ratio</td>
<td>7.6±1.8</td>
<td>7.4±2.0</td>
</tr>
<tr>
<td>Buckling ratio &gt;10%</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

PPI, proton pump inhibitors. No differences in measurements between PPI users and PPI non-users were statistically significant.

Comparison of metabolic markers in long-term PPI vs non-PPI

Table 5. Comparisons of metabolic markers between PPI users and non-users

<table>
<thead>
<tr>
<th></th>
<th>PPI users (n=52)</th>
<th>PPI non-users (n=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (mmol/L)</td>
<td>2.35±0.07</td>
<td>2.32±0.03</td>
</tr>
<tr>
<td>Magnesium (mmol/L)</td>
<td>0.85±0.06</td>
<td>0.88±0.06</td>
</tr>
<tr>
<td>Phosphorus (mmol/L)</td>
<td>1.02±0.20</td>
<td>1.02±0.16</td>
</tr>
<tr>
<td>25-OH vitamin D (nmol/L)</td>
<td>76.8±22.0</td>
<td>74.5±25.3</td>
</tr>
<tr>
<td>Bone-specific alkaline phosphatase (μg/L)</td>
<td>14.3±5.5</td>
<td>13.4±3.5</td>
</tr>
<tr>
<td>Osteocalcin (μg/L)</td>
<td>22.6±8.8</td>
<td>23.1±8.0</td>
</tr>
<tr>
<td>C-reactive protein (mg/dL)</td>
<td>3.3±1.48</td>
<td>3.87±1.54</td>
</tr>
<tr>
<td>PTI</td>
<td>44.4±14.4</td>
<td>47.0±14.8</td>
</tr>
<tr>
<td>Zn (μg/L)*</td>
<td>105±70.4</td>
<td>97±59.6</td>
</tr>
</tbody>
</table>

PPI, proton pump inhibitors. *P<0.001, all others, no differences in measurements between PPI users and PPI non-users were statistically significant.
Systematic review: Proton pump inhibitor-associated acute interstitial nephritis.
Serra L*, Suárez M, Rey M, Vela ME

Abstract

BACKGROUND: A number of recent case reports and case series suggest that proton pump inhibitors may cause acute interstitial nephritis.

AIM: To establish the nature of the relationship (cause or association) between proton pump inhibitor use and development of interstitial nephritis.

METHODS: DATA COLLECTION: Two researchers independently searched electronic databases (MEDLINE, EMBASE, COCHRANE) for articles from 1970 to 2006, including all study designs, populations and languages. Two independent reviewers studied quality and collected the data.

SELECTION CRITERIA: Absence of baseline renal failure, development of interstitial nephritis after proton pump inhibitor exposure, confirmed by creatinine plus either renal biopsy or recurrence upon reinstituting proton pump inhibitor.

RESULTS: Sixty-four cases (60% females, mean age 78 years) of proton pump inhibitor-associated interstitial nephritis were included in this review (56 confirmed by renal biopsy, one by recurrence upon reinstituting proton pump inhibitor). The most common symptoms were non-specific. The mean proton pump inhibitor treatment duration before diagnosing nephritis was 13 weeks, average range 3.5–5.5 weeks. One patient required permanent dialysis, there were no deaths.

CONCLUSION: Proton pump inhibitor-related interstitial nephritis is rare, idiosyncratic and difficult to predict. It requires a high degree of suspicion. While there is not sufficient evidence to establish a causal relationship with certainty, there does appear to be a low level association.
PPIs and acute interstitial nephritis (AIN)

- 64 case reports
- Conclusion: PPI associated AIN is rare, idiosyncratic and difficult to predict
- Insufficient evidence to establish causal relationship

Relative Risk: 50% increased risk for CKD
17% increased risk for CKD

Absolute Risk CKD: 0.1%-0.3% per patient/year
### Association of Proton Pump Inhibitors With Risk of Dementia: A Pharmacoepidemiological Claims Data Analysis

**Authors:** Gomm W, et al

**Journal:** JAMA Neurol 2016; 73:410-416

---

#### Table: Risk of Incident Dementia

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Both Sexes</th>
<th>Male Sex</th>
<th>Female Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient admission</td>
<td>1.44 (1.36-1.53)</td>
<td>&lt;.001</td>
<td>1.42 (1.33-1.51)</td>
</tr>
<tr>
<td>Inpatient potential confounding factors</td>
<td>1.76 (1.66-1.87)</td>
<td>&lt;.001</td>
<td>1.78 (1.66-1.90)</td>
</tr>
<tr>
<td>Without potential confounding factors</td>
<td>1.80 (1.69-1.92)</td>
<td>&lt;.001</td>
<td>1.82 (1.68-1.95)</td>
</tr>
<tr>
<td>Agea</td>
<td>1.00 (1.00-1.00)</td>
<td>&lt;.001</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>Sexb</td>
<td>1.45 (1.31-1.60)</td>
<td>&lt;.001</td>
<td>1.43 (1.30-1.57)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.28 (1.24-1.32)</td>
<td>&lt;.001</td>
<td>1.24 (1.20-1.29)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.05 (1.02-1.08)</td>
<td>&lt;.001</td>
<td>1.04 (1.01-1.07)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.17 (1.29-1.44)</td>
<td>&lt;.001</td>
<td>1.15 (1.13-1.18)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>0.93 (0.91-0.95)</td>
<td>&lt;.001</td>
<td>0.94 (0.91-0.96)</td>
</tr>
<tr>
<td>Polypathologyc</td>
<td>1.16 (1.11-1.20)</td>
<td>&lt;.001</td>
<td>1.16 (1.10-1.22)</td>
</tr>
</tbody>
</table>

---

**Footnotes:**

- Use of PPI before the diagnosis of dementia.
- In the beginning of the study in 2004.
- End of administration of 5 or more drugs.

---

**Source:** Gomm W, et al. JAMA Neurol 2016; 73:410-416
Proton Pump Inhibitors and Risk of Mild Cognitive Impairment and Dementia

Goldstein F, et al; 2017 (June): JAGS

No Difference in Risk

Association Between Proton Pump Inhibitor Use and Cognitive Function in Women

Lochhead P, et al; 2017 (June): JAGS

No Difference in Cognition
<table>
<thead>
<tr>
<th></th>
<th>PPI</th>
<th>1st Gen Ceph</th>
<th>3rd Gen Ceph</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>1.6</td>
<td>5.6</td>
<td>9.2</td>
</tr>
</tbody>
</table>

Systematic Review of the Risk of Enteric Infection in Patients Taking Acid Suppression

Ch.B., Ph.D., M.P.H., F.R.C.P.(London), F.R.C.P.C.

Department of Medicine, Division of Gastroenterology, McMaster University, Hamilton, Ontario, Canada

11 papers n= 126,999 patients.

OR= 2.05 (95% CI 1.47–2.85)

Absolute Risk Cdiff: 0.0%-0.09% per patient/year


A total of four papers n= 10,430 patients.

The OR was 3.33 (95% CI 1.84–6.02)

Absolute Risk Campylobacter or Salmonella: 0.03%-0.2% per patient/year

Proton pump inhibitor therapy does not increase the incidence of spontaneous bacterial peritonitis in cirrhosis: A multicenter prospective study

- Multicenter, Prospective Study
- n=519 patients
- SBP in 95 out of 394 patients with ascites (24.7%).
- No association of PPI use and SBP
**Bacterial infections in cirrhosis: role of proton pump inhibitors and intestinal permeability**

Lotta G. van Vlerken1,2, Ellen J. Hulman1,2, Bart van Haast1, Wismen Renooij1, Felix W. M. de Rooij1,3, Peter D. Siemensa4 and Karol J. van Erpecum5

1Department of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, 2Department of Gastroenterology and Hepatology, Gelders University Medical Center, Laren, 3Department of Surgery, University Medical Center Utrecht, Utrecht, 4Department of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands

- Prospective study
- Median duration of PPI use = 16 months
- No association between PPI and SBP

**Micronutrient Deficiencies**

- Calcium
- Iron
- Magnesium
- Vitamin B12
Micronutrient Deficiencies

**Calcium (Ca$^{2+}$)**

- Profound acid suppression may interfere with absorption
- **NOT** relevant for water soluble calcium salts
- **NOT** relevant for calcium in milk or cheese
- Can be completely reversed when calcium is taken with slightly acidic meal


**Iron (Fe$^{3+}$)**

- Few studies to evaluate link between iron and PPIs
- Zollinger Ellison:
  - PPI use 6 yrs had no association with decreased total body iron stores or Fe deficiency
- Hereditary hemochromatosis:
  - decreased absorption of dietary iron following meal
  - decrease in annual phlebotomy requirements in the long-term.

Micronutrient Deficiencies

**Magnesium (Mg^{2+})**

- Cases of profound hypomagnesemia associated with chronic PPI use since 2006
- Rare, Idiosyncratic
- ? Congenital mutation in transmembrane channel
- Pooled Relative Risk 1.43 (CI 1.08-1.88)


Micronutrient Deficiencies

**Vitamin B_{12}**

- Increased risk of B12 deficiency with >2 year exposure of PPI
- Relative Risk= 1.63-1.95 (1.77-2.15)
- Absolute Risk= 0.3%-0.4% per patient/year
Take Home Message: We must be careful when interpreting observational studies

ABSOLUTE RISK more important than Relative Risk


Benefits of PPI use
AGA Best Practice Advice

1) Patients with GERD and acid-related complications should take a PPI for short-term healing and long-term symptom control
2) Patients with uncomplicated GERD who respond to short-term PPIs should subsequently attempt to stop or reduce them
   *If not possible, employ reflux testing to sort out functional symptoms
3) Patients with Barrett’s esophagus with symptomatic GERD should take a long-term PPI
4) Asymptomatic patients with Barrett’s should consider a long-term PPI
5) Patients at high risk for ulcer-related bleeding from NSAIDs should take a PPI if they continue NSAIDs
6) The dose of long-term PPIs should be periodically re-evaluated so that the lowest effective dose is used.

Benefits of PPI use
AGA Best Practice Advice

7) Long-term PPI users should not routinely use probiotics to prevent infection
8) Long-term PPI users should not routinely raise their intake of Ca²⁺, vit B12 or Mg²⁺ beyond RDA
9) Long-term PPI users should not routinely screen or monitor bone mineral density, serum creatinine, Mg²⁺ or vit B12
10) Specific PPI formulations should not be selected based on potential risks

Thank-you for attending CTSGNA’s 25\textsuperscript{th} Beyond The Scope Program