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**GASTROENTEROLOGY**

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**ACCEPTED  
ABSTRACTS**

## HEPATITIS C ERADICATION: A PROMISE UNFULFILLED

**David H Van Thiel**

Rush University Medical Centre, USA

**H**epatitis non-A and non-B hepatitis was recognized as a unique form of viral hepatitis distinct from hepatitis A, hepatitis B, and other unusual types of a chronic hepatitis such as CMV, EBV as well other more uncommon types of viral hepatitis in the late 1970s. His clinical characteristics, biochemical manifestations as well as its chronicity from its initial presentation followed by increasing stages of chronic hepatitis and hepatic fibrosis ultimately resulting in cirrhosis and occasionally progressing to hepatic cancer and required an additional 15-30 years. A host of potentially antiviral agents were utilized initially to treat the disease process with minimal or no success. With the introduction of interferons (alfa 2a or alfa 2b) with or without additional ribavirin, a modicum of success defined as a reduction in transaminase levels was achieved with little or no retrospectively determined viral clearance. With the isolation and characterization of the hepatitis C virus genome and the various polypeptides it codes for, a new era of treatment directed at inhibiting viral replication as opposed to enhancing the immune response against the virus began. The initial direct acting antiviral agents increased viral clearance rates to 40%. Agents more recently developed have increased the rates of viral clearance to 95 to 100%. This initiated reports (a promise) that hepatitis C would be eliminated as a disease process by 2020 with a progressive decline in the rates of cirrhosis and hepatocellular carcinoma thereafter through at least 2030. Unfortunately, this does not appear to be the case as multiple obstacles prevent these favourable outcomes. The issues and remaining and prohibit the promises full film and include the following: Lack of knowledge of primary care physician's that the disease is a serious hepatic disease that slowly and quietly progresses to cirrhosis and potentially hepatic cancer and is treatable. As a result, large numbers estimated to be three quarters of the infected population failed to be identified. Secondly the cost of the drugs is prohibitive to those individuals with no insurance and contributes to the effort by third party peers and cover mental agencies to limit treatment to selected groups with advanced liver disease. As a result, only, a minor fraction of the infected population is identified for treatment and receives treatment. In addition, individuals with non-hepatic manifestations of hepatitis C are not recognized this having the disease process and are excluded from treatment even though this population represents the largest group of individuals perpetuating the disease in the community as they do not know they have the disease. In order with a promise of the elimination of hepatitis C and a reduction in long-term consequences of the infection universal defecation of infected patients to include all forms of hepatic dysfunction as well as nonhaptic manifestations of the disease need to be recognized in treated. To accomplish this the cost of treatment will have to be dramatically reduced and includes not only the cost of the therapeutic agent but also through numerous tests required to justify treatment. Some progress is being made by governmental agencies that are looking at the concept of micro-elimination as a potential means of reducing the prevalence of the disease in high prevalence groups such as men having sex with men, individuals enrolled in drug treatment programs, who said receive multiple transfusions as result of clotting disorders and/or haemolytic anaemias. This is clearly a started but only if start.

[dvanthiel@dr.com](mailto:dvanthiel@dr.com)

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## **EFFECTS OF PROSPECTIVE METFORMIN ADMINISTRATION ON ANTICANCER THERAPY AND CANCER STEM CELLS IN PATIENTS WITH GI AND OTHER MALIGNANCIES**

**Wasif M Saif and Robert E Martell**

Tufts University School of Medicine, USA

**Background:** Observational studies have demonstrated association of Metformin with reduced cancer incidence and mortality in multiple cancer types. The anti-neoplastic effects of metformin are believed through many mechanisms including activation of AMP-activated protein kinase, which controls the mammalian target of rapamycin (mTOR) growth regulatory pathway.

**Patients & Methods:** We conducted delayed start randomized trial of non-diabetic patients in two stages: patients were randomized to two arms during stage I - concurrent arm (metformin + chemo) vs. delayed arm (chemo alone) and in stage two, patients in delayed arm were crossed over to receive metformin. Patients received metformin 500 mg twice daily + chemotherapy to define DLTs in both stages. Translational correlates included effects of metformin on expression and phosphorylation of AMPK by western blot in PBMCs. In another pilot study, we evaluated the safety and impact of pretreatment with metformin on colorectal cancer stem cells (CCSC) in patients undergoing resection and evaluate the effects of metformin on the expression of CCSC markers by measuring relative mRNA levels of CD133, OCT4 and NANOG using RT-PCR and immunohistochemistry.

**Results:** In the randomized study, DLTs seen only included those associated with established chemo AEs. No lactic acidosis or hypoglycemia occurred. Restaging showed stable disease in 46% and 28% of patients had decline in tumor markers. Analysis of phospho-AMPK $\alpha$  showed that phosphorylation of AMPK $\alpha$  was increased after metformin (mean=1.114 $\pm$ 0.512) and analysis of total levels of AMPK $\alpha$  showed similar results (mean=1.04 $\pm$ 0.28). In the pilot study on patients undergoing surgery, no grade three or four AEs related to metformin including hypoglycemia and lactic acidosis were observed. No unexpected post-operative complications were witnessed. CCSC markers showed decrease in expression of CD133, OCT4 and NANOG following metformin.

**Conclusions:** Our studies include the largest prospective study in cancer patients who received metformin in combination of chemotherapy and the first one that prospectively demonstrates the impact of metformin on AMPK phosphorylation and impact on CCSC. These preliminary data warrant further investigation to explore the benefits of metformin both as a chemotherapeutic and chemopreventive agent in adequately powered prospective studies.

[WSaif@tuftsmedicalcenter.org](mailto:WSaif@tuftsmedicalcenter.org)

## **BCL-G IS A NOVEL PROTEIN OF BAX**

### **Faris Qalenzi**

Prince Sattam bin Abdulaziz University, Saudi Arabia

**Background & Objective:** BCL-G is a novel protein of Bax (BCL-G associated protein X) inducing caspase-mediated apoptosis. These proteins are involved in regulating apoptosis both in normal, and in neoplastic cells although their cellular and tissue distribution is currently unknown. Accordingly, the objective of the current study was to ascertain and define the pattern of distribution and expression of BCL-G in normal and malignant gastrointestinal human tissues.

**Methods:** Using a rabbit monoclonal antibody against BCL-G, the distribution and expression of BCL-G was assessed by immunohistochemistry in formalin-fixed, paraffin-embedded, benign and malignant human tissues

**Results:** We found a variable pattern of positive expression of BCL-G within all the tissues we studied. BCL-G expression was typically localized in the cytoplasmic paranuclear granules in the epithelial cells in most organs we examined. The intensity of BCL-G staining related to the maturation state in benign tissue.

**Conclusion:** We have demonstrated that BCL-G exhibits a specific distribution pattern that appears to correlate with cellular differentiation. However, while these distribution patterns are complex they do give a tantalizing insight into function, and consequently need further investigation to determine their physiological/pathological significance.

[fqalenzi@ksu.edu.sa](mailto:fqalenzi@ksu.edu.sa)

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## HEPATITIS E VIRUS INFECTION: AN UNDERESTIMATED EVOLVING PROBLEM

**Fatma Amer and Ergenekon Karagoz**

Zagazig University School of Medicine, Egypt

**H**epatitis E virus (HEV) is one of the human hepatitis viruses (family Hepeviridae). This family includes: Orthohepevirus (A-D species), which infects terrestrial vertebrates, and Piscihepevirus, which infects fish. Orthohepevirus A contains the HEV variants infecting humans. Eight genotypes are recognized within Orthohepevirus A; 1- 7. It is estimated that 71% of the world population, are infected with HEV, and the infection results in approximately 3 million symptomatic acute cases and 70000 deaths annually. The disease predominantly affects young adults. The incubation period ranges from 15-60 days. The course of infection has 2 phases, the prodromal phase which is usually of short duration and the icteric-phase which lasts days to several weeks. In nonendemic (autochthonous) type of acute HEV infection, most patients have subclinical manifestations and mild symptoms, especially in women and young persons. Autochthonous hepatitis E has a striking spectrum of serious complications. For unknown reasons, is predominantly severe and can progress to hepatic failure in pregnant women. Individuals could be infected with HEV genotypes 1 and 2 from drinking contaminated water. Specifically, HEV genotype three is zoonotic in developed countries. HEV genotype four infections could be detected in both human and swine in Eastern Asia and Europe. In developed countries, some cases of vertical transmissions of HEV have been reported as well as in homosexual men. The laboratory diagnosis of HEV infection depends on the detection of HEV antigen, HEV RNA, and serum antibodies against HEV (immunoglobulin [Ig]A, IgM, and IgG). Besides improved personal hygiene, sanitation and health education, vaccination might play a crucial role in the future prevention and control of HEV infection. Chinese vaccine HEV 239 vaccine, which contains truncated HEV capsid protein was approved in China by the State Food and Drug Administration in January 2012.

[egyamer@yahoo.com](mailto:egyamer@yahoo.com)



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## **FUNCTIONAL ASSESSMENT OF THE DIGESTIVE SYSTEM - THERAPEUTIC ASSESSMENT OF SUB-CLINICAL SYMPTOMS AND DIGESTIVE HEALTH**

**Keri Brown**

Wide Awake Wellness, USA

**F**unctional Assessment of the Digestive System is a clinical diagnosis presentation based on physical observations that identify the root causes, help target priorities, and insures a measurable evaluation of the patient. This presentation focuses on actionable information and take-home strategies that provide an effective, efficient, and recordable pattern of the patient for digestive health. Through lecture, example, and demonstration this information provides knowledge on pre and post-evaluations, creating a recordable and visual benchmark of the patient for deficiency patterns for the digestive system. Learning how to assess the digestive system can help one determine nutritional deficiency patterns and health needs prior to disease occurring. This information is imperative in today's health care and in the clinical and "sub-clinical" patient. Traditional doctors use functional assessments and physical observations of our body to confirm our health issues. It enables one to take the guess work out of nutritional deficiencies and digestive health patterns. This class insures a measurement of patient evaluation as a critical tool in the medical toolbox. If pre-and post-nutritional evaluations and sound patient observations are added, the practitioner can confirm the findings while creating a recordable and even visual benchmark for patients to see the change and progress. This approach heightens the practitioner's ability to identify root causes, target priorities, and integrate patient interaction, while improving understanding, retention and compliance. Using functional assessments of the digestive system, the health and direction of care becomes more obvious to see, treat, and monitor. While correlating specific observations and testing procedures, one can determine organ health, utilization of nutritional factors, and what direction is best for the client. We will look at the tongue, face, nails, reflex points, simple office testing procedures and holistic care to determine how to help our patients through functional assessment of the digestive system.

[keri@drkeribrown.com](mailto:keri@drkeribrown.com)

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## TREATMENT OF SEVERE ACUTE PANCREATITIS AND ITS COMPLICATIONS

**Enver Zerem**

University of Tuzla, Bosnia and Herzegovina

The management of severe form of acute pancreatitis varies with the severity and depends on the type of complication that requires treatment. Severe acute pancreatitis is associated with high morbidity and mortality due to the development of pancreatic and extra-pancreatic necrosis, their subsequent infection and multisystem organ failure. Despite overall reduced mortality in the last decade, SAP is a devastating disease that is associated with mortality ranging from less than 10% to as high as 85%, according to various studies. The management of SAP is complicated because of the limited understanding of the pathogenesis and multi-causality of the disease, uncertainties in outcome prediction and few effective treatment modalities. Generally, sterile necrosis can be managed conservatively in the majority of cases with a low mortality rate (12%). However, infection of pancreatic necrosis can be observed in 25%–70% of patients with necrotizing disease; it is generally accepted that the infected non-vital tissue should be removed to control the sepsis. Laparotomy and immediate debridement of the infected necrotic tissue have been the gold standard treatment for decades. However, several reports have shown that early surgical intervention for pancreatic necrosis could result in a worse prognosis compared to cases where surgery is delayed or avoided. Therefore, several groups worldwide have developed new, minimally invasive approaches for managing infected necrotizing pancreatitis. The applicability of these techniques depends on the availability of specialized expertise and a multidisciplinary team dedicated to the management of SAP and its complications. Although no universally accepted treatment algorithm exists, the step-up approach using close monitoring, percutaneous or endoscopic drainage, followed by minimally invasive video-assisted retroperitoneal debridement has demonstrated to produce superior outcomes to traditional open necrosectomy and may be considered as the reference standard intervention for this disorder.

[zerem@live.com](mailto:zerem@live.com)



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## **OVERLAP SYNDROME AS A CAUSE OF SEVERE HEPATITIS IN A FEMALE PATIENT WITH SYSTEMIC LUPUS ERYTHROMATOSIS- CASE STUDY**

**Marwa Ibrahim, El Shazley M, Abouismail A, Nageeb A, Sami M, Ismail M, Gabbour R, Wahib E J, Khalid M, Hanno R and Hamed B**

Alexandria University, Egypt

**Case study:** A 30 years old female patient known to have systemic lupus was admitted to tropical medicine department because of jaundice and hepatic encephalopathy associated with low grade fever, vomiting and right hypochondrial pain. Upon examination patient had grade I to II hepatic encephalopathy, yellow sclera, tender hepatomegaly. Laboratory tests showed: a white cell count of 13,000 cells/ $\mu$ l, a platelet count 90,000 cells/ $\mu$ l, serum albumin 1.5g/dl, CRP 20 ng/ml, Alanine aminotransferase 1400 ul, Aspartate aminotransferase 1100 ul, a total bilirubin of 15 mg/dl, direct bilirubin of 11 mg/dl and prothrombin activity of 25%. Viral hepatitis markers were negative except for IgG for hepatitis A, Autoimmune markers were as follow; ANA (antinuclear antibody) 1/220, ASMA (anti-smooth muscle antibody) negative, LKMA (liver kidney microsomal antibody) negative, SLA (soluble liver antigen) negative, AMA (antimitochondrial antibody) negative, but a positive gamma globulin IgG and a negative IgM. Imaging by computerized tomography with intravenous contrast revealed acute hepatitis with patches of necrosis. Our patient scored six according to simplified diagnostic criteria of the International Autoimmune Hepatitis Group table, two provisional supportive treatment were initiated upon admission in the form of fresh frozen plasma infusions with broad spectrum antibiotics together with anti-encephalopathy measures and lactulose enemas. Also, steroid therapy in the form of oral prednisolone in a dose of 60 mg/day was administered. Fortunately, gradual improvement of laboratory analysis occurred till prothrombin activity reached 85% where we performed a liver biopsy that showed the following histologic features with acute hepatitis pattern of injury, with portal and periportal lymphoplasmacytic infiltrate and interface hepatitis. Plasma cells were prominent, the severity of necro-inflammatory activity ranged from bridging necrosis to massive hepatic necrosis. Hepatocyte regeneration was prominent, with regenerating rosette-like structures with florid bile duct destruction.

[marwaibrahim90@yahoo.com](mailto:marwaibrahim90@yahoo.com)



## **PATHOGENESIS OF CHRONIC DIARRHEA, IBS**

**Huseyin Sancar Bozkurt**

Medical Park Private Tarsus Hospital, Turkey

**P**athogenesis of chronic diarrhea, IBS are thought to be through different factors and there is a relationship between the gut flora and the risk of its development. Probiotics can manipulate the microflora in chronic inflammation and may be effective in treating inflammation. *Bifidobacterium strains* are saccharolytic and their growth in the gut can be promoted by non-absorbable carbohydrates and its increase in the colon appears to be of benefit. Intracolonic probiotic application may resolve chronic diarrhea, IBS which are unresponded conventional medical treatment.

[sancarb79@gmail.com](mailto:sancarb79@gmail.com)



## **TRANS ABDOMINAL SONOGRAPHY OF THE STOMACH AND DUODENUM**

**Vikas Leelavati Balasaheb Jadhav**

D Y Patil University, India

**T**rans abdominal sonography of the stomach and duodenum can reveal following diseases: gastritis and duodenitis, acid gastritis or an ulcer, whether it is superficial, deep with risk of impending perforation, perforated, sealed perforation, chronic ulcer and post-healing fibrosis and stricture. polyps and diverticulum. benign intra-mural tumours, intra-mural haematoma. duodenal outlet obstruction due to annular pancreas. gastro-duodenal ascariasis, pancreatic or biliary stents. foreign body, necrotizing gastro-duodenitis, tuberculosis, lesions of ampulla of vater like prolapsed, benign and infiltrating mass lesions. Neoplastic lesion is usually a segment involvement and shows irregularly thickened, hypoechoic and aperistaltic wall with loss of normal layering pattern. It is usually a solitary stricture and has eccentric irregular luminal narrowing. It shows loss of normal gut signature enlargement of the involved segment seen. Shouldering effect at the ends of stricture is most common feature and enlarged lymphnodes around may be seen. Primarily arising from the walls, itself and secondary are invasion from peri-ampullary malignancy or distant metastasis. All these cases are compared and proved with gold standards like surgery and endoscopy. Some extra efforts taken during all routine or emergent ultrasonography examinations can be an effective non-invasive method to diagnose primarily hitherto unsuspected benign and malignant Gastro-Intestinal Tract lesions, so should be the investigation of choice.

[drvikasjadhav@gmail.com](mailto:drvikasjadhav@gmail.com)

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## PANCREATIC INNERVATIONS IN HUMAN FETUS: AN OBSERVATIONAL STUDY

**Aritra Banerjee**

AIIMS, India

In the developing human pancreas, the cholinergic neurons are distributed singly or in the form of ganglia in the inter lobular connective tissue from 14WG and in the intra lobular connective tissue from 16WG onward. From 25–27 WG onward the typical adult type islets were observed. The aim of the study was to document the morphological changes of neurons and ganglia of human foetal pancreas at various gestational ages. The present study was performed on human foetuses (n=13) of different gestational ages. The sample collection was started after getting ethical permission from the Human Ethical Clearance Committee of AIIMS, New Delhi. Pancreatic tissue samples (Head, body and tail) from aborted foetuses aged 13– 40 weeks of gestation(WG) were processed. The neurons were studied by using NADPH-d and ChAT for enzyme histochemistry and immunohistochemistry. With increasing gestational age, the number of neurons in human foetal pancreas was appeared to be reduced in the head, body and tail of the pancreas and the ganglions were skewed towards the tail. The neurons were mainly surrounding the islets. Numerical density of cholinergic neural tissue is more in tail than body than head whereas, the nitrergic neuronal tissue is more in head than body than tail in human foetal pancreas. The knowledge from this study may help in understanding the pathophysiology of various congenital disorders, relationship between the growth of neurons and islets cells in development of type 1 DM and pain due to pancreatitis.

[aritra.aiims@gmail.com](mailto:aritra.aiims@gmail.com)



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## HBV AND HEPATOCARCINOGENESIS IN TRANSLATIONAL MEDICINE

**Xiaodong Zhang**

Nankai University, China

**H**CC is the fifth-most common cancer and the third leading cause of cancer death worldwide. HBV infection is one of the major causes of HCC. HBx plays critical roles in the development of liver cancer. Our group has reported that HBx modulates oncogene YAP via CREB to promote growth of hepatoma cells. HBx promotes the development of liver fibrosis and hepatoma through down-regulation of miR-30e targeting *P4HA2* mRNA up-regulates Lin28A/Lin28B through Sp1/c-Myc to enhance the proliferation of hepatoma cells. Up-regulated long non-coding RNA HULC by HBx enhances growth of hepatoma cells via down-regulating p18. HULC modulates abnormal lipid metabolism in hepatoma cells through a miR-9-mediated RXRA signaling pathway. *MicroRNA-520e* suppresses growth of hepatoma cells by targeting the NF-κB-inducing kinase (NIK). Therapeutically, anti-HBV drugs suppress the growth of HBV-related hepatoma cells via down-regulation of hepatitis B virus X protein. Our findings provide new insights into the mechanism by which HBV promotes the development of HCC. Our findings develop novel targets for anti-HCC therapy. Current antiviral therapies inhibit cytoplasmic HBV genomic replication, but rarely achieve a cure because they do not directly target nuclear HBV covalently closed circular DNA (cccDNA), the genomic form that serves as a HBV replication intermediate and viral persistence reservoir. We report that HBx-elevated MSL2 modulates HBV cccDNA through inducing degradation of APOBEC3B to enhance hepatocarcinogenesis.

[zhangxd@nankai.edu.cn](mailto:zhangxd@nankai.edu.cn)

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## THE HALLMARKS OF INFLAMMATORY BOWEL DISEASE -IBD

**Susan A Joyce, Alvaro Lopez Gallardo, Julia Eickenberger, Adam Clooney, Cormac G Gahan, Carthage Moran, Marcus Claesson and Fergus Shanahan**

University College Cork, Ireland

Irritable bowel disease (IBD) includes Crohn's disease (CD) and Ulcerative colitis (UC), both characterized by chronic relapsing intestinal inflammation that leads to diminished quality of life, and during flare-up to severe disability. IBD is not a classic autoimmune disease, IBD etiology is believed to be complex and multifactorial with genetics, the exposome (environment, diet, lifestyle) the microbiome and the immune system interacting to manifest disease. Life style choices, the diet and metabolism can influence disease status, we have applied a multivariate approach to analyze the same IBD disease cohort across the BMI spectra, to include the microbiota, and microbially altered metabolites including precursors for bile acid synthesis, bile acids and fatty acid signatures as well as some gut hormone and inflammation levels. Hallmarks of IBD that differentiate CD and UC have been identified.

[s.joyce@ucc.ie](mailto:s.joyce@ucc.ie)



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## THE USE OF TRANSVERSE LUMBOSACRAL FLAP FOR RECURRENT PILONIDAL SINUS: A NEW CONCEPT FOR A NEW FLAP

**Ahmed Farag and Sahar Ezzat Nasr**

Cairo University, Egypt

**Background:** Despite the facts that flattening the natal cleft and shifting of the scar from the midline were the basis of many modern surgical procedures for pilonidal sinus disease (PSD), yet recurrences still take place. The aim of the present work is to study the histologic difference between the skin of the sacral area of patients with PSD and normal skin as well as the topography of the pilonidal area a basis of a new flap for the treatment of patients with recurrent PSD.

**Patients & Methods:** Comparing the topography of the sacral area in De-Novo pilonidal sinus, recurrent pilonidal Sinus and normal controls in relation to primary and secondary pits, and comparison of the histology between the edge of the normal skin at the margins of excision of the patients with recurrent PSD, normal controls and the skin of the proposed flap. Using the new flap for closure of the defect after excision of the recurrent pilonidal sinus in 28 male patients.

**Results:** A pilonidal valley was described and should be flattened; the skin of the PSD patients shows abnormal hyperplasia and deep hair follicles into the dermis in contrast to the skin of the controls and the flap which look like normal thick skin. The new flap repair was done in 28 patients with recurrent PSD. Age range 18–39 years (average=26.428). They totally underwent 66 procedures before presentation (1–6 procedure Average=2.357 procedures). 26 cases completed Follow up from 14–60 months in 26 patients (Average 41.846 months). Only one case of recurrence 3.8%. and few cases of minor to moderate complications managed conservatively.

**Conclusion:** Providing a normal quality of thick skin cover of the pilonidal area after excision is based on histologic findings and may help to minimize recurrences. The presence of abnormal skin in the PN and surrounding buttocks may give a new insight into the congenital predisposition to PNSD.

[farag2a@gmail.com](mailto:farag2a@gmail.com)

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## **CHARACTERIZATION OF *ESCHERICHIA COLI* ISOLATED FROM STOOLS OF PATIENTS SUFFERING FROM DIARRHOEA IN BENIN CITY NIGERIA**

**Francis Enifo Oronsaye**

University of Benin, Nigeria

**Background:** Diarrhoea disease is very common in the tropical regions of the world where high temperatures favour bacterial growth and food are served cold; Moreover, excrement contaminate the environment because low standard of hygiene, *E. coli*, abnormal biotype in the gut of humans and animals, but some strains have been incriminated in both bloody and non-bloody diarrhoea and many of them are toxigenic strains. Thus, the determination of these toxigenic strains cannot be over emphasized.

**Methods:** Three hundred stool samples were collected from patients attending various hospitals in Benin City, Nigeria and were cultured using routine methods of culture and sensitivity in the Medical microbiology department of University of Benin Teaching Hospital, Benin city, Nigeria.

**Results:** The enter virulent isolated were identified to species level using the protocol of Cowan and steel. Antibiotics susceptibility pattern of the strains were determined using the agar diffusion and dilution methods of Stokes. None of the strain exhibited high MIC to many antibacterial agents including the fluoroquinolones and were thus subjected to investigation for R-plasmid. R-plasmid analysis using a horizontal appearance plasmid Tus showed three plasmid bands greater than the reference plasmid marker.

**Conclusion:** This study presents, the isolation of enter virulent *Escherichia coli* that harbour transferable R-plasmid mediated resistance to the fluoroquinone antibacterial agents and other antibiotics in Benin city, Nigeria.

[sayfrankon@yahoo.com](mailto:sayfrankon@yahoo.com)



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## ROBOTIC RECTAL RESECTION: PRELIMINARY RUSSIAN EXPERIENCE

**Atroshchenko Andrey Olegovich**

Moscow Clinical Scientific and Practical Center, Russia

**Introduction:** Even though laparoscopic rectal resection is clearly feasible, with comparative oncological results when compared with open surgery, the laparoscopic approach remains technically challenging. Some of these challenges reflect the ergonomic limitations of the current instrumentation where there is a restricted tactile feedback. Moreover, the constraint of 2-dimensional visualization significantly reduces depth perception and hand-eye coordination. The introduction of the robot for proctectomy provides a 3-dimensional view and a fixed retraction by the assisting robotic arm with flexible instrumentation which with the Da Vinci® robotic system (intuitive surgical, Sunnyvale CA) enhances maneuverability. In rectal resection, the robot can partially overcome the negative impact of a narrow field of vision, most notably in a small pelvis, magnifying both the autonomic nerves and the correct plane of mesorectal fascial excision.

**Purpose:** To outline the first initial experience of the da Vinci robotic system as used in a Moscow tertiary colorectal referral center for an unselected range of benign and malignant rectal diseases.

**Methods:** Prospective non-randomized single-center study which analyzed results of 26 robotic rectal resections performed between January 2014 and December 2016.

**Results:** The initial group included 10 females and 16 males (mean age 61.6 years). Three patients were operated on for benign rectal villous adenomas. Two-thirds of patients had significant comorbidities with a median ASA score 4.5-5.5. Of the surgeries, there were 19 total mesorectal excisions (TME) with 6 patients undergoing a multivisceral resection. The mean operating time was 358 minutes with a mean blood loss of 203 mL. All mesorectal excision specimens were adjudged as safe grades specifically with a mean of 18.5 lymph nodes identified. Of these there were 10 patients (38.5%) with lymph node metastases. The mean pain score was 2.1/10 on the visual analogue scale and 1.5/10 on the Brief Pain Inventory (BPI). There were 3 patients with postoperative urinary difficulty. The median preoperative wexner continence score was 2.7 with a 10-day postoperative -3.1 and a six month postoperative -1.6. One patient underwent early repeat surgery for an adhesive small bowel obstruction. The median length of hospital stay was 11 days.

**Conclusion:** Our initial experience with a totally robotic rectal resection has shown it to be safe and feasible, particularly in patients where conventional laparoscopic rectal resection would be anticipated to be challenging.

[dr.atroshchenko@gmail.com](mailto:dr.atroshchenko@gmail.com)



## EVALUATION OF *MIR-32* AND *PTEN* GENES IN COLORECTAL CANCER PATIENTS

**Bitá Sepehri, Milad asadi, Ahmad Shokohi and Behzad Baradran**

Tabriz University of Medical Sciences, Iran

**Background:** Genes involved in various cellular processes, such as cell cycle, apoptosis and cell migration, play an important role in the process of colon cancer. *miR-32* and *PTEN* gene are two important genes that previous studies have confirmed their role in cancer development. In the present study, the change in the relative expression level of these genes was analyzed through the carcinogenesis phenomenon and the relative expression of these genes in response to common treatments in the laboratory was evaluated on two LS180 and SW480 cell lines in colorectal cancer as a third most common cancer in the world.

**Methods:** Through the surgical procedure of colorectal cancer patients, a total of 50 tumor tissues and normal marginal tissue was collected. After extraction of RNA, Real-time PCR was used to measure changes in gene expression. The differences in expression level of mRNAs of these genes as well as changes in the expression of these genes in response to common treatments were investigated by appropriate statistical tests. In statistical tests, P value <0.05 was considered significant level.

**Results:** The level of expression of *miR-32* in tumor tissues increased compared to healthy peripheral tissues but this change was not significant (P= 0.078). On the other hand, the level of *PTEN* gene expression in tumor tissues significantly decreased compared to healthy tissue (P= 0.032), and this downregulation was related to cancer stage. The changes in expression of both genes in both cell lines after treatment with oxaloplatin showed significant changes in expression level.

**Conclusion:** Our findings demonstrated that the expression of *miR-32* and *PTEN* can be used as a diagnostic or predictive biomarker for CRC. And both of genes play a role in the therapeutic pathways of the oxaloplatin, but more studies are needed to validate this claim.

[Sepehribrr@yahoo.com](mailto:Sepehribrr@yahoo.com)

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## VON WILLEBRAND FACTOR AND PORTAL HYPERTENSION IN CIRRHOTIC PATIENTS

**Ehab Mostafa**

Zagazig University, Egypt

Portal hypertension is associated with various hemodynamic changes not only in the portal circulation but in the systemic circulation as well. These changes are related to several mediators secreted from endothelial cells. Von Willebrand factor (vWF) is an endothelial derived coagulation factor and is believed to be involved in the pathogenesis of cirrhosis. This study aims to clarify the relation between the vWF and the severity of liver disease and portal hypertension. 60 patients were included in this study divided into three groups. Group I: 30 patients with decompensated cirrhosis. Group II: 20 patients with compensated cirrhosis, group III: 10 healthy control subjects, the VWF level was highest in group I followed by group II then group III with significant difference between all groups ( $114.2 \pm 27.5$  in group I,  $88.9 \pm 9.1$  in group II, and  $65 \pm 3.9$  in group III). The level of VWF was correlated to ascites, encephalopathy, child's grade and esophageal varices grade in group I. von Willebrand factor level rises significantly with deterioration of liver disease and directly correlated to the grade of esophageal varices.

[hobanoh@yahoo.com](mailto:hobanoh@yahoo.com)



## MINIMALLY INVASIVE AND ENDOSCOPIC METHODS OF TREATMENT OF POST-NECROTIC PSEUDOCYSTS OF PANCREAS

**Nazar Omelchuk**

Ivano-Frankivsk National Medical University, Ukraine

**Statement of the Problem:** Acute necrotic pancreatitis (ANP) remains complicated problem of urgent surgery because of high frequency of systemic, purulent and septic complications, mortality rate, which is in patients with infected pancreonecrosis 14,7 – 26,4 %.

**The Purpose:** The purpose of this study is to evaluate efficiency and establish indications for minimally invasive methods of treatment of post-necrotic pseudocysts of pancreas.

**Methodology & Theoretical Orientation:** For diagnostics we used ultrasonography, diagnostic laparoscopy, helical CT with contrast strengthening. Endoscopic interventions were applied by duodenoscopes Olympus under control of x-ray machine siemens BV 300. Cystodigestive fistulas were created by prickly papilotoms. For providing of long passability of cystodigestive fistula we used two endoprosthesis pig tail sized 10 Fr with length 5–6 sm. For transpapillary drainage we used pancreatic endoprosthesis like pig tail, sized 5–7 Fr with length 5 sm.

**Findings:** In 62 (68,2%) patients were applied minimally invasive methods of treatment. Percutaneous external drainage in 33 (53,2 %) patients, endoscopic transmural drainage of post-necrotic pseudocysts in 11 (17,7%) patients. Combined endoscopic interventions were applied in 18 (29,1%) patients. Endoscopic transmural drainage with temporary stenting of pancreatic duct in 11 (61,1%) patients, endobiliary stenting with temporary stenting of pancreatic duct in 3 (16,67%) patients, temporary stenting of pancreatic duct in 3 (16,67%) patients, endoscopic transmural drainage with percutaneous external drainage in 1 (5,56%) patient.

**Conclusion & Significance:** Usage of combined minimally invasive methods of treatment of acute necrotic pancreatitis complicated by postnecrotic pseudocysts help to improve results of treatment, reduction of complications amount, contraction of stationary treatment terms and improving of life quality.

[dr.nazaromelchuk@gmail.com](mailto:dr.nazaromelchuk@gmail.com)

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## CLINICAL FEATURES OF GASTRIC OUTLET OBSTRUCTION IN KIGALI, RWANDA

**P Kamali and E Kabuyaya S Benson**

Centre Hospitalier University, Rwanda

**Background:** In developed countries, the main cause of Gastric Outlet Obstruction (GOO) is malignancy. However, the benign causes continue to be the major cause of GOO in the developing world, but there is growing evidence proving the contrary. There is no data of GOO from Rwanda.

**Aims:** A retrospective analysis of the endoscopic findings of patients presenting with features of GOO to determine the demographic and etiological patterns.

**Materials & Methods:** A retrospective study of the endoscopic findings of patients with GOO from January 2013 to January 2015 was done. The diagnosis of GOO was based on clinical presentation, and an inability during the upper endoscopy to enter the second portion of the duodenum as documented in the endoscopy registers. Patients who have already been diagnosed with malignancy prior to the endoscopy were excluded from the study; so were the patients with gastroparesis.

**Results:** A total of 250 patients with GOO underwent the endoscopy during the study period. 180 were had benign GOO, while malignancy was present in 30 patients, others were with different findings. The causes for benign obstruction were predominantly peptic ulcer disease. The major cause for malignant obstruction was carcinoma of stomach involving the distal stomach. The male to female ratio was 3.2:1. The patients with malignancy were older than patients with benign disorders. Most of the patients were in the fifth and sixth decade. The risk of malignancy was higher with increasing age, especially in women. A third of all carcinoma stomach presented with GOO.

**Conclusion:** The study demonstrates that the cause for GOO in Kigali, Rwanda is predominantly benign.

[pakamali@yahoo.fr](mailto:pakamali@yahoo.fr)



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## THE IMPACT OF CARNITINE ON DIETARY FIBER AND GUT BACTERIA METABOLISM AND THEIR MUTUAL INTERACTION IN MONOGASTRICS

**Abdallah Ghonimy<sup>1</sup>, Dong Ming Zhang<sup>1,2</sup>  
Mohammed Hamdy Farouk<sup>1,3</sup> and Qiuju Wang<sup>1</sup>**

<sup>1</sup>Jilin Agricultural University, China

<sup>2</sup>Tonghua Normal University, China

<sup>3</sup>Al-Azhar University, Egypt

Carnitine has vital roles in the endogenous metabolism of short chain fatty acids. It can protect and support gut microbial species, and some dietary fibers can reduce the available iron involved in the bioactivity of carnitine. There is also an antagonistic relationship between high microbial populations and carnitine bioavailability. This review shows the interactions between carnitine and gut microbial composition. It also elucidates the role of carnitine bacterial metabolism, mitochondrial function, fiber fermentability, and short chain fatty acids (SCFAs).

[abdomscphd@yahoo.com](mailto:abdomscphd@yahoo.com)

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## **GASTROILEOSTOMY FOR WEIGHT REDUCTION AND LIPID PROFILE CONTROL: AN EXPERIMENTAL RAT MODEL**

**Erfan Sheikh**

Isfahan university of medical sciences, Iran

**Objective:** Although the exact mechanism of obesity remains a matter of debate, there is a direct correlation between development of obesity and elevated lipid profile. Malabsorptive procedures decrease the effectiveness of nutrient absorption by shortening the length of the functional small intestine. Profound weight loss can be achieved by a malabsorptive operation. Investigational procedures such as gastroileostomy also work by malabsorption. In this study we aim to investigate the early effects of gastroileostomy on weight reduction and lipid profiles.

**Materials & Methods:** Gastroileostomies were performed in 15 male New Zealand rats. Blood samples were obtained at base line and one week after gastroileostomy. Blood samples were analyzed for lipid profiles including TC, LDL, HDL, and TG. The body weight of each rat was evaluated before and after surgery.

**Results:** The data show that gastroileostomy surgery leads to a significant decrease of weight ( $330\pm 15$ gr vs.  $240\pm 25$  gr before and after surgery, respectively) in operated rats ( $P<0.05$ ). The levels of TG decreased in plasma ( $99.21\pm 29.012$  mg/dl vs.  $95.64\pm 48.668$  mg/dl respectively;  $P=0.807$ ). TC ( $71.14\pm 13.416$  mg/dl vs.  $72.64\pm 22.455$  mg/dl;  $P=0.813$ ), and LDL ( $12.96\pm 4.853$  mg/dl vs.  $15.36\pm 5.665$  mg/dl  $P=0.121$ ) had no significant changes after the operation.

**Conclusion:** Based on the results of this study, gastroileostomy could be effective in weight reduction but has no statistically significant change on lipid profiles in a short time. Therefore, this surgery could be a promising surgery for weight reduction.

[erfan.shikhbahaei@gmail.com](mailto:erfan.shikhbahaei@gmail.com)



## GASTROESOPHAGEAL REFLUX IN PRETERM INFANTS

**Daouda Diamane Ndour**

Cheikh Anta Diop University, Senegal

**G**astroesophageal reflux disease (GERD) is a common problem in neonatology. GERD is often incriminated in various clinical manifestations occurring in premature infants. However there is no consensus about the clinical and para clinical diagnosis. Further explorations and treatment offered to premature infants with symptoms are discussed. From a literature review we discuss at length the different aspects of the problem.

[daoudandour@hotmail.com](mailto:daoudandour@hotmail.com)



## NON-ALCOHOLIC FATTY LIVER DISEASE

### Maisam Akroush

Prince Hamzeh Hospital, Jordan

**N**on-alcoholic fatty liver disease (NAFLD), is the most commonly diagnosed form of liver disease in Hepatology clinics and often associated with type II Diabetes Mellitus and Metabolic Syndrome. Whilst it is known that chronic liver disease (Cirrhosis) is associated with Hepatocellular Carcinoma in most of liver diseases, in NAFLD however, the incidence and prevalence of Hepatocellular Carcinoma is rising and hence, it is imperative that health care professionals endeavour to raise awareness on preventative measures of the disease and the importance of early detection. This would ensure that NAFLD finds its place in public discourse, to minimise the burden that such diseases have on the health system, in addition to the person affected by the disease. Causative factors are plentiful, starting from a genetic predisposition (proven by the recurrence of the disease after liver transplant) to environmental factors, not limited to obesity and lack of exercise, concluding with other pathologies, which are notably the primary cause of NAFLD; namely Diabetes, Hyperlipidaemia, Insulin Resistance and Metabolic Syndrome, amongst others. Diagnostic tools are available, accessible, affordable and non-invasive (such as blood markers and imaging). Previously, treatment was limited to life style changes (exercise and diet), coupled with treating the associated diseases (Diabetes, Insulin resistant and Hyperlipidaemia). This is no longer the case, with the introduction of specific medication recently, that is aimed at reversing the histopathological as well as the biochemical abnormalities associated with the disease to prevent progression to chronic liver disease (Cirrhosis with or without complications).

[yg@mail.nankai.edu.cn](mailto:yg@mail.nankai.edu.cn)





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## **DIVIDED LAPAROSCOPIC CHOLECYSTECTOMY FOR UNUSUAL GALL STONES COMPLICATION OF MIRIZZI'S SYNDROME**

**Ahmed E. Lasheen,<sup>1</sup> Mostafa Baioumy,<sup>1</sup> Mansour Morsy,<sup>1</sup> Wael Mahmoud,<sup>1</sup> Wael Mansy,<sup>1</sup> Ashraf Ismail,<sup>1</sup> and Yasser Hussein**

<sup>1</sup>General and laparoscopic Surgery Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt

**Background:** Chronic complications of symptomatic gallstone disease such as Mirizzi's syndrome are rare. The importance and implications of these conditions are related to their associated surgical complications which are potentially serious such as bile duct injury and to the modern management when encountered during laparoscopic cholecystectomy.

**Objectives:** This research offers a technique to avoid surgical complications in Mirizzi's syndrome cases during laparoscopic cholecystectomy.

**Patients and Methods:** Between November 2012 and February 2015, 17 patients (12 females and 5 males) with mean age of 51 years (between 29 and 57 years) suffering from Mirizzi's syndrome underwent the divided cholecystectomy. In this technique the gall bladder was divided into two parts above the gall bladder infundibulum. The distal part was dissected for short distance and used to push liver up. The proximal part of gall bladder was cleared from all its contents and reevaluated from inside. Management was achieved according to the stage of disease.

**Results:** The mean operative time was 70 minutes (between 60 and 90 minutes). No biliary tract obstruction or leakage or stenosis was recorded in this patient group during the period of follow up (18 months).

**Conclusions:** Divided laparoscopic cholecystectomy is a safe and effective technique to face the unusual gallstones complications (Mirizzi's syndrome).

[lasheenahmed@yahoo.com](mailto:lasheenahmed@yahoo.com)



## GASTROESOPHAGEAL REFLUX DISEASE(GERD)

**Rakesh Kalpala**

Asian Institute of Gastroenterology, India

**G**astro-esophageal reflux disease (GERD), affects one third of the population worldwide and prevalence in India ranges between 8 to 19%. (Gut consensus) Majority of the patients have impaired quality of life (QOL) due to symptoms such as heartburn, regurgitation or dysphagia and long-term complications associated with it. The pathogenesis of GERD is multifactorial, involving transient lower oesophageal sphincter relaxations and other lower oesophageal sphincter pressure abnormalities. As a result, reflux of acid, bile, pepsin and pancreatic enzymes occurs, leading to oesophageal mucosal injury. Other factors contributing to the pathophysiology of GERD include hiatus hernia, impaired oesophageal clearance, delayed gastric emptying and impaired mucosal defensive factors Current treatments include lifestyle modifications, long term pharmacological therapies, surgical fundoplication, and more recently, endoscopic procedures<sup>5</sup>. About 10% of patients with endoscopically proven reflux esophagitis are resistant to proton pump inhibitors (PPIs). Further, almost 20% of patients have inadequate symptom control resulting in heartburn and regurgitation that cause detrimental effects on the quality of life. Also, potential side effects of long-term PPIs use (B12 deficiency; iron deficiency; hypomagnesaemia; increased susceptibility to pneumonia; enteric infections; fractures; hypergastrinemia), results in many patients discontinuing treatment. Surgical options for GERD have their limitations with respect to increased costs, hospitalization, complication rate and recovery. Data from 5-year LOTUS study suggests that 15–20% of patients who have undergone fundoplication may have GERD symptoms. Uncontrolled GERD results in a significant decrease in quality of life, productivity at work and economic burden on the patients from hospital admissions due to acid-induced non-cardiac chest pain. In addition, it is associated with worrisome complications such as strictures, Barrett's esophagus and oesophageal adenocarcinoma. The rising concern of long term side effects of the popular proton-pump inhibitors and the more recent evidence raising doubts about the durability of fundoplication have spurred re-interest in endoscopic procedures such as Stretta and GERD-X to treat reflux disorder. Several clinical studies including a systematic review showed that the Stretta and GERD-X procedure improves GERD symptoms, quality of life, oesophageal acid exposure, and eliminates the need for anti-secretory drugs in majority of patients.

[drkalpala@yahoo.com](mailto:drkalpala@yahoo.com)



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## HAT1 ENHANCES HEPATOCARCINOGENESIS THROUGH MODULATION OF EPIGENETIC MODIFICATION

**Guang Yang**

Nankai University, China

**H**CC is the fifth-most common cancer and the third leading cause of cancer death worldwide. Epigenetic modification plays key roles in the development of liver cancer. Here, we found that a histone acetylase HAT1 was up-regulated in liver tissues of HCC samples. Clinical data showed that high-levels expression of HAT1 revealed a low rate of survival for HCC patients. And the expression levels of HAT1 were positive related to pathologic stage of HCC patients. Interestingly, MTT assays and Edu assays showed that HAT1 could promote the proliferation of hepatoma cells in vitro. Next, we explored the global impact of HAT1 on host gene expression profiling. Gene expression microarray analysis showed that 1360 mRNAs were up-regulated and 096 mRNAs were down-regulated in HepG2 cells transfected with siHAT1 relative to HepG2 cells transfected with sicontrol. GO and KEGG analysis showed that HAT1 displayed crucial roles in many important processes, such as DNA replication, chromatin remodeling, chromatin binding, cell cycle, p53 pathway, TNF signaling pathway and Hippo signaling pathway. Our findings provide new insights into the mechanism by which epigenetic modification factor regulates the development of liver cancer. Therapeutically, HAT1 may serve as a novel target for anti-HCC therapy.

[mayoos\\_moh@yahoo.com](mailto:mayoos_moh@yahoo.com)



## **PREDICTORS OF SPONTANEOUS BACTERIAL PERITONITIS IN EGYPTIAN PATIENTS WITH CIRRHOTIC ASCITES**

**Khaled Metwally, Tamer Fouad, Medhat Assem, Eman Abdelsameea and Mohamed Yousery**

National Liver Institute - Menoufiya University

**Background:** Spontaneous bacterial peritonitis (SBP) is a serious complication of liver cirrhosis and finding a prognostic model to predict it is needed. **Objective:** to test the ability of different laboratory tests and the new Wehmeyer's SBP scoring system to predict it.

**Methods:** Three hundred patients admitted at the National Liver Institute, University of Menoufiya, Egypt (2015-2016) with liver cirrhosis and ascites were included in our study. SBP was diagnosed if ascetic neutrophils count  $\geq 250/\mu\text{L}$  with no sign of secondary peritonitis.

**Results:** Median age 56 (29 –81 years), 60% men and primary cause of liver disease was hepatitis C, 91.7%. By univariate analysis: age, total bilirubin, AST, creatinine, international normalized ratio, MELD score, total leucocytic count, platelet count and C-reactive protein (CRP) were significant. By multivariate analysis independent predictors were age, platelet count and CRP ( $p = 0.004$ ,  $0.013$  and  $< 0.001$ , respectively). CRP at a cutoff point  $\geq 13.5$  mg/L could predict SBP (sensitivity 86.4% and specificity 66.0%). Wehmeyer's SBP scoring system was able to predict it ( $p < 0.001$ ), only 4% of patients with 0 score developed SBP (CRP cutoff is 30 mg/L), while 92.8% with score of 3 or 4 developed it. By using our CRP cutoff value of 13.5 mg/L, no patient with 0 score developed SBP.

**Conclusion:** Age, CRP and platelet count are independent predictors for SBP and a scoring system including them could easily predict it. SBP diagnosis could be excluded in patients with zero score, using CRP cutoff value of 13.5 mg/L.

[Kh\\_m55555@yahoo.com](mailto:Kh_m55555@yahoo.com)



## THE USE OF ENDOSCOPY IN BARIATRIC SURGERY

**Jean Francois Rey**

Institut Arnault Tzanck, France

**D**igestive endoscopy plays multiple role in bariatric surgery: assessment of patient, endoscopic treatment of surgical complications and more recently development of bariatric endoscopy. Assessment of patient is important as bariatric surgery request evaluation of GI tract and eradication if needed of Helicobacter pylori infection. Bariatric surgical patents are part of multidisciplinary protocol. Endoscopic treatment of surgery has been important for many years with routine endoscopy for ulceration or bleeding as in any surgery. But more specific are endoscopic treatment of stenosis with dilation and stenting. Leakage and fistulas require particular skill are closing digestive tract with specific clips and stents are often demanding but very important for patient. Last 10 years digestive endoscopy has introduced multiple devices and procedures for bariatric treatment: intragastric balloon and sleeve procedure are the more popular and achieved. Duodenal bypass and resurfacing are even more promising as part of bariatric or diabetes treatment. In any case, all new procedures have to be assess with clinical trial. All patient involve in bariatric treatment should be included in a multidisciplinary protocol.

[jean-francois.rey@wanadoo.fr](mailto:jean-francois.rey@wanadoo.fr)



## IODINE DEFICIENCY A PERSISTING WORLDWIDE PROBLEM- THE POPULATION CONSEQUENCES

**José Eduardo C. Santos**<sup>1,2,3</sup>, **Carla P. Fonseca**<sup>1,2</sup>, **Miguel Castelo Branco**<sup>1,2,3</sup>

<sup>1</sup> Faculty of Health Sciences, University of Beira Interior, Portugal <sup>2</sup> CICS-UBI Health Sciences Research Centre, Faculty of Health Sciences, University of Beira Interior, Covilhã, Portugal <sup>3</sup> Centro Hospitalar Cova da Beira, Covilhã

**Introduction:** Iodine deficiency (ID) still affects more than two billion people worldwide, (266 million school-aged children). The adverse effects of ID include an increase in the prevalence of thyroid cancer, higher percentages of the more aggressive follicular and anaplastic subtypes of thyroid cancer. An inversion of the frequency ratio of papillary to follicular thyroid cancer ratio, variable degrees of intellectual impairment and impairment of reproductive potential. Iodine is only acquired through the diet and absorbed in the digestive tract as iodide. China successfully eliminated ID through implementing legislation, in 1978, making iodized salt available to the population of the entire country. Portugal has no national general population data on iodine nutrition (IN). The evaluation of combined data on the IN of the general population through urinary iodine concentration (UIC) and thyroid histology profile from the inland region of Beira Interior (BI), Portugal is reported. A comparative evaluation of the thyroid histology pattern of the population of BI and of Johannesburg (JHB), South Africa was made. These populations although geographically distant and heterogeneous had in common being iodine deficient at the time of data gathering. Mandatory salt iodization introduced in SA in 1995 has recently been shown to have resulted in the correction of ID.

**Methods:** Evaluation of thyroid histology reports over a 6 year period in BI and a 5 year period in the JHB area. Median urinary iodine concentration (UIC) was obtained from a population sample of 214 volunteers from BI, (131 females and 83 males), ages ranging from 8 to 97 years (mean 51.5 years).

**Results:** Region of BI: 279 histology reports evaluated- 60 malignancies (21.2%): 31 papillary carcinomas, 22 follicular cancers (18 follicular carcinomas and 4 Hürthle cell tumours) 3 medullary carcinomas and 4 anaplastic carcinomas. Region of JHB: 136 histology reports- 33 malignancies (24.3%): 13 papillary carcinomas, 15 follicular cancers (10 follicular carcinomas and 5 Hürthle cell tumours), 1 medullary carcinoma, 3 anaplastic carcinomas and 1 metastatic carcinoma into the thyroid. There was an overlap in the frequencies of all histology types including the relatively high anaplastic carcinoma incidences and in the papillary to follicular carcinoma ratios being close to 1 in both areas- BI area ratio: 1.4 and JHB area ratio 0.87, with overlapping 95% CI's, confirmed by chi-square calculations. Median UIC of the population sample tested was 62.6µg/L, 92% of samples having a UIC<100µg/L.

**Conclusions:** Iodine supplementation consistently decreases the incidence of endemic goitre and eradicates ID. During the study periods both regions evaluated displayed patterns and results characteristic of ID evidenced particularly by the papillary to follicular carcinoma ratios (close to 1 in both areas) and the relatively high number of anaplastic carcinomas. The persistent problem of ID could be eliminated by the combination of eliciting a proactive behaviour from an informed population as to the serious consequences of ID, the availability of adequately iodised salt and promoting sea- based nutrition. These measures could be applicable to other populations in different parts of the world still experiencing ID.

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endosantos@hotmail.com