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* We now present a fully interactive menu. It works best with Adobe reader application (on computers, mobile phones and tablets)





MESSAGE FROM THE EDITORIAL TEAM

Dear All!

*“Ring out the old, ring in the new,
Ring, happy bells, across the snow:
The year is going, let him go;
Ring out the false, ring in the true.”*

—Lord Alfred Tennyson

The What’s Up team wishes all of you a Merry Christmas and a Happy 2020. We are pleased to release the thirty eighth issue of “What’s Up? @ St John’s Hospital” magazine today.

The magazine which began in August 2018 has come a long way with many talented editorial team members. We acknowledge that the magazine is growing bulkier with many new sections having been added as we went along this satisfying journey. As the editorial team works constantly to provide the best reading experience, some changes have been made in the magazine frequency and format to improve readership. Some of these are: a reduction in the frequency of the magazine to monthly as opposed to fortnightly and splitting the original 20 sections to 10 in each issue on a rotating basis. We will also try to bring you more updates from the Academy, for quick reading.

Please feel free to communicate with us to publish your achievements. Feedback on any section of the magazine is welcome. We are happy to evolve to meet the needs to our beloved readers. Happy Reading!!

Editorial Team

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UPDATES THIS MONTH

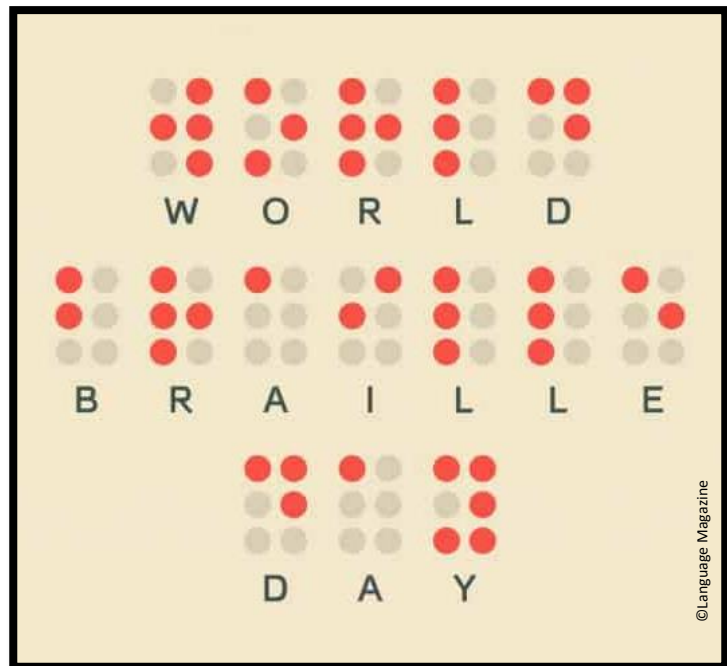
WORLD BRAILLE DAY

4th January 2020

World Braille Day is observed on 4th of January to raise awareness of the importance of Braille as a means of communication in the full realization of the human rights for blind and partially sighted people.

What is Braille?

Braille is a code that uses bumps and indentation on a surface to represent letters, which can be recognized by touch.



Braille (named after its inventor in 19th century France, Louis Braille) is used by blind and partially sighted people to read the same books and periodicals as those printed in a visual font.

Before Braille invented this form of communication, visually impaired people read and wrote using the Haüy system which embossed Latin letters on thick paper or leather. This was a complicated system that required much training and only allowed people to read, not write. Discouraged by this, Braille at the age of 15 invented the Braille code.

While there are now several different versions of Braille, Louis Braille's code was arranged in small rectangular blocks called cells with raised dots in a 3 x 2 pattern. Each cell represented a letter, number or punctuation.

Since Braille is a code, all languages and even certain subjects like mathematics, music and computer programming can be read and written in braille.

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World Disability Day Celebration

4th December 2019 – The Department of Community health celebrated World Disability Day in the community health training centre, Mugalur. The program was well attended by around 150 Persons with Disability, Taluk level officials from Dept of Education, Staff from Primary Health Centre, Anganwadis, Panchayat representative community members. The event was marked by the formation of A formal Trust of Persons with disability representing different villages. Its a day to commemorate the Empowerment of Persons with disability celebrated every year on 3rd December.



Training For Rehabilitation Workers, Chattisgarh

11th to 13th December 2019 – Team from Unit of Hope, St. John's conducted training for rehabilitation workers in CF Shore, Rajnandgaon, Chattisgarh. The objective was to train them on early detection, assessment and referral of various disability. Dr. Annie spoke on Locomotor Disability and accessibility, Mrs. Nagapournima on speech & hearing impairment, Dr. Shilpa on developmental delays and Dr. Deepti Shanbhag on community based rehabilitation and visual impairment.

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Hospital Day 2019

11th December 2019

HospitalDay 2019 celebrated in St. John's Medical college Hospital Campus on 11th December 2019. Faculty & Staff attended the Event. Silver Jubilarians, Retirees and Outstanding Performers were felicitated during the event. Executive members of St. John's National Academy of health Sciences presided over the Event. 20 Employees (non-doctors) were rewarded as best employees of the year. Following are the winners in the wards.

1. INTENSIVE CARE UNITS:

- a) Best Intensive Care Unit – Neonatal Intensive Care Unit (NICU)
- b) Second Best Intensive Care Unit – Surgical Intensive Care Unit (SICU)

2. PRIVATE WARDS:

- a) Best Private Ward – AC Block
- b) Second Best Private Ward – 5th Rear Private Ward

3. COMMON WARDS:

- a) Best Common Ward – Pediatric Medicine Ward
- b) Second Best Common Ward – Male Chest Medicine Ward



Congratulation to the Winners!

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Memorial Service for Mr. Chenna Reddy Ganji

18th December 2019

Mr. Chenna Reddy Ganji was working as a tutor in the department of Anatomy in St. John's Medical College since 13th February 2017. He passed away due to cardiac failure on 18th December 2019. We express our sincere condolences to his family and friends. The memorial service was organised on 18th December 2019.



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Department of Radiation Oncology

Accelerated Partial Breast Irradiation

20th December 2019, Department of Radiation Oncology successfully completed the first case treated with Accelerated Partial Breast Irradiation (APBI). APBI is a technique where radiation is delivered with high dose per fraction to a portion of breast within a short span of time. Unlike the conventional Radiotherapy which takes nearly 4-5 weeks, APBI gets completed within 5 days. The technique is ideal for elderly women with early breast cancer, whose tumor is hormone receptor positive. This patient who was treated was a 81 year old women with early breast cancer.



ARTTICON 2019

15th December 2019, Mrs. Shibina Noorjahan (Senior Radiotherapy Technologist, Department of Radiation Oncology) was awarded cash prize (Best paper award) for her paper presentation in Annual Radiotherapy Technologist of India Conference 2019 in New Delhi. Her study was on the 'Impact of bladder and rectal protocol on uterine position during external beam radiotherapy of carcinoma of uterine cervix.'



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St. John's College of Nursing

World AIDS Day

1st December 2019 – St. John's College of Nursing, observed World AIDS Day on 1st December 2019. The theme for this year was "Ending HIV AIDS epidemic: Community by Community". There was a health education program at St John's Medical College Hospital OPD Foyer to spread awareness. Prof GD Ravindran, Dept of Family Medicine was the Chief Guest & emphasized on the Topic.



RGUHS Annual Sports Meet 2019



11th to 14th November 2019– RGUHS (Rajiv Gandhi University of Health Sciences) Annual SportMeet 2019-20 was held at Alva Foundation, Moodbidri. 6 students from St. John's College of Nursing participated & won 5 medals including 1Gold, 3Silver & 1 Bronze. Jasmine James & Aleena J were selected to represent RGUHS at 80th All India Inter-university competition in January 2020.

Lamp Lighting 2019

December 20th, 2019 was marked by the Lamp Lighting ceremony of the 31st Batch of B.Sc. nursing and the 40th batch of GNM. This auspicious day began by invoking God's blessings through a Holy Eucharistic celebration with Rev. Fr. Pradeep Kumar Samad, ADH, as the main celebrant. Rev. Sr. Ria Emmanuel, CNS, administered the Florence Nightingale oath to 160 budding nurses formally recognizing the student's entry into nursing profession.

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St. John's College of Nursing

The lighting of the lamp is a symbolic tradition among the nursing sorority at the brink of their profession, that depicts the concept of light that shines within their hearts; a light that the nurse becomes to her patients, a symbol of hope and comfort to those who are suffering. Rev. Dr. Paul Parathazham, Director, SJNAHS, the chief guest of the day spoke about the characteristics of light and the need for the students to embody the very nature of light and disseminate the light they carry to all cadres of the society irrespective of caste, color, religion and social class.



International Conference on Integrating Psychology

SJCON, organized an International conference on the theme “Integrating Psychology towards optimal nursing education” on 12th December 2019. A total of 102 delegates attended the conference. The key note speaker was Dr. Paula Baisden, Mental Health nursing Course co-ordinator, University of North Carolina, Wilmington. In her key note address she emphasized on the need to emphasize on quality of nurses rather than the quantity. Mrs. Jenifer Tavares, Counsellor and special educator Pledge Academy, Bangalore discussed various learning styles. Insights on “emotional quotient and intelligent quotient in learning today was given by Mr. Vithoba Mhalkar, Asst. Prof. Institute of Psychiatry and human behavior, Bambolin, Goa. Prof. Reena Menon, Principal, SJCON elaborated on student - teacher relationship, its importance and core competencies that the teacher should possess. A very lively and thought-provoking session by Dr. Balamurugan, registrar and HOD, Dept of Mental Health Nursing, M.S. Ramaiah CON, Bangalore on “Evaluation its true purpose”. The conference was successful and a learning experience for the students and delegates.

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FRIDAY CLINICAL MEETING

29th November 2019

“Kilimanjaro: A photographic journey to the roof of the world”

Dr. Chittaranjan Andrade, Dean NIMHANS, Bangalore

This Friday conference was truly a “Far from the madding academics experience”. A team of five doctors (All Geriatric Age!) climbed Mount Kilimanjaro.



The TEAM of doctors who made it to the top (20000ft in 5days and 6hrs is inspiring!:

Davis MJ (Batch 1972)

Peter D'Sa (Batch 1974)

Dr Zia Ahmed (Batch 1975)

Dr George D'Souza (Batch 1975)

Dr. Chittaranjan A (Batch1977)

Mount Kilimanjaro is Located in Tanzania and it is tallest mountain in Africa. It is one of the Seven Summits and highest free-standing mountain in the world. One of the largest volcanoes in the world. One of the tallest mountains from base to summit. The height is 5895 m (19,341 feet).



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RESEARCH SNIPPETS

OBSERVATION

Observation is a technique for collecting all the data or acquiring information through occurrences that can be observed through senses with or without mechanical devices. The main purpose of observation is to understand an ongoing situation, to gather data on individual behaviors and to learn about a physical setting.

There are 4 types of observation:

- Structured observation
- Unstructured observation
- Participant observation
- Non-participant observation.

Planning for observation:

- Determine the focus
- Design a system for data collection
- Select the sites
- Select the observers
- Train the observers
- Time your observations



Instruments such as checklists, rating scales, video recording, field notes, anecdotes and field diaries can be also used for observation.



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Department of Palliative Medicine

Dr. Mary Olapally our former Dean was instrumental in starting the services of pain management in year 2000. At that time it was called 'Pain and Palliative Care Unit' and was a unit of the Department of Anesthesia. The Initial Staff consisted of Dr. Mary Olapally, Dr. Vasudev Upadhyaya and Dr. Bharathi.

In year 2008, the unit was given a status of an Independent Department and was rechristened as Department of Palliative Medicine and its association with Department of Anesthesia was concluded. The Department provides multidisciplinary care for all the departments of Oncology services as well as other departments of the institution. In year 2016, additional services for interventional management of chronic pain were introduced.

LOCATION AND TIMING:

Palliative Medicine OPD: Room No. 44, 1st Floor Oncology block.

The department is located on the first floor of the oncology block and offers consultation on all working days from 9.00AM to 1.00 PM. The registration closes at 12.30 PM as per hospital policy.

Chronic Pain Clinic: Silver Jubilee Block

Wednesday and Friday Room no. 26, Silver Jubilee Block from 9.00 am to 1.00 pm for all chronic non cancer pain. Patients are referred from various departments.

Inpatient services.

Patients requiring palliative care are admitted in Oncology Block. The Department provides dedicated multidisciplinary care for patients with cancer and non cancer diseases with heavy symptom burden. In addition to that the department also offers counseling services.

Day care services:

The department has daycare beds in its OPD area where it provides treatment facilities needing short stay. Administrations of drugs like Ketamine, Zolendronic acid and Morphine trials are done in OPD. Procedures like acupuncture, dry needling, ascitic tap and pleural tap are also done here.



THE SCOPE OF SERVICES:

The department provides multidisciplinary care across specialties in the hospital.

1. Palliative care for advanced metastatic cancer.
2. Palliative care for Pediatric and Geriatric patients.
3. End of life care for patients with terminal illness.
4. Management of Pain; Cancer and Non-cancer pain.
5. Breaking bad news to patients admitted to various oncology services
6. Counseling for patients transitioning from curative treatments to best supportive care
7. Bereavement counselling
8. Organization of care at home.
9. Interventional pain procedures for chronic pain like nerve and ganglion blocks, epidural injections, radiofrequency ablations, neurolysis, spinal cord stimulation and insertion of spinal pumps are done in #rd floor Cath Lab under C-arm guidance. Some of these procedures may need Operation Theatre facilities.
10. Acupuncture and dry needling.
11. Respite care is provided to caregivers whenever there is a significant stress or fatigue in caregivers.

SUPPORT FROM NGOS.

The institution has entered an MOU with Indian Cancer Society for support. They have a group of trained volunteers which form the Emotional Support Group. Members of this group visit the department once a week to provide emotional support and counseling to patients. This service has been extended to other Oncology Services as well.

ACADEMIC ACTIVITIES AND RESEARCH:

1. The department has a vibrant academic program where all members of the department participate. Activities are planned twice a week which include seminars, journal clubs and case presentations.



2. The Department conducts “Certificate Course in Essentials of Palliative Care” in association with Indian Association of Palliative Care twice a year in the month of June and November.
3. The department provides hands on training for 10 days for doctors who complete the above mentioned course.
4. The Department conducts a workshop called “Essential Pain management (EPM)” for interns of every batch. Dr. Sangeeta Das is a trained instructor for this program which has been developed by Faculty of Pain Medicine, Australian and New Zealand College of Anesthetists and participants get a certificate after attending the workshop.
5. The Faculty of the Department is often invited to give talks on various aspects of Palliative care and Interventional Pain Management at Local, State and National level.
6. The Executive Committee of St. John’s National Academy of Health Sciences has approved a one year distance learning “Fellowship in Palliative Medicine” in September 2019. This includes two hands on training session in a year. We are hoping that alumni serving in rural areas will benefit from this course and be able to integrate Palliative Care in their area of practice.
7. The Department encourages students to work on short research projects. The residents in the Department have been able to present papers and posters in Annual Conferences of the IAPC. At present Dr. Renuka Pai has two research projects approved by the EC. There have been seven publications from the Departments in last five years.

Current Research projects

- A. Perception of Pain specialists about integration of Palliative care in their Practice.
- B. International Collaborative on Dying ; a multicentre project on streamlining care of dying patients to provide Good Death.
- C. Patient perceptions about sleep disturbances in Patients with advanced Metastatic cancer.





Patient Counselling Services in the Department of Palliative Medicine



THE TEAM: *Back Row* (Left to Right) - Dr. Tamilselvam Prabhakaran (Physician's Assistant) Dr. Geraldine Monteiro (Registrar), Dr. Sangeeta Das (Assistant Professor), Dr. Subhash D Tarey (Professor and Head), Dr. Renuka Pai (Junior Consultant), Dr. Deepak Peter (Physician's Assistant)
Front Row (Left to Right) - Ms. Shefali D'souza, (Staff Nurse), Ms. Elda Mary K,(LDC),Ms. Bhagya (Nursing Aide) Ms. Jhansi (Nursing Aide)



IG NOBEL

1996 – CHEMISTRY

George Goble

George Goble of Purdue University, for his blistering world record time for igniting a barbeque grill in **three seconds**, using charcoal and liquid oxygen.



Lighting a coal barbeque grill takes atleast 10 to 15 mins. After lighting the coal, flames will subside, and one will see the edges of the coal turn grey. Eventually the ash will spread to each briquet. The coals are now ready to spread out and use. However George Goble used liquid oxygen to hasten this process to just 3 seconds! Click the youtube icon to watch the video.



SURVIVOR's CORNER

A 29 year old unmarried male, an IT professional working in Gurgaon was admitted to our ICU in the last week of August'19 after getting discharged from a nearby corporate hospital where he was admitted and evaluated for almost 3 weeks. He was a known asthmatic and hypertensive. He was extensively worked up there for pyrexia of unknown origin (PUO), which started off as pain abdomen, progressing to fever, bicytopenia and respiratory distress. While in that hospital a bone marrow aspiration and biopsy revealed a ZN positive sample and he was strongly suspected to have tuberculosis (TB) and was started on antitubercular drugs. Shortly after starting the antitubercular medications he developed a drug induced liver injury and bicytopenia which was attributed to a secondary hemophagocytic lymphohistiocytosis (HLH), and was started on steroids. They brought him to St. John's once he developed respiratory distress for further workup and treatment.

He was quite fearful and anxious, and always wanted his brother by his side. We couldn't utter words like intubation or bone marrow biopsy around him. He had lost both his parents, one in 2011 and the other in 2015 and memories of their death in a ICU plagued him. His family was terrified that every 4 years a family member was succumbing to an illness, but they were positive he would make it to celebrate Durga Puja this year. After 9 days of being on Non invasive ventilation, he became severely distressed and hypoxic. It took us half a day to convince him for intubation but all he said before intubation was "Please help me. I want to live". Post intubation, we sedated him well and performed another bone marrow biopsy and much to our dismay, this test reported negative for TB. All other blood/ body fluid samples sent also were negative for TB as well as for other possible causes of PUO. We put all our best minds together and decided to continue the second line antitubercular drugs and steroids. The persisting high fever and pancytopenia was worrisome. We took inputs from the Hematology team in the Department of Medicine who suggested chemotherapy drugs as a last ditch resort for what we believed to be secondary HLH. He battled through several hospital acquired infections, septic shock, a sacral bed sore, and a catabolic state where he lost almost 40% of his body weight. He also suffered a severe nephrogenic diabetes insipidus, which reversed slowly with time. After a month, we finally got around to extubating him. His blood counts improved gradually. After 2 more weeks of recuperation in the ICU, we shifted him to the ITU. He ended up being in the hospital for Durga Puja but did manage to get discharged on Nov 14th 2019. His will to live, strong family support and fabulous care by the ICU team, nurses, the Department of Medicine and other allied teams went a long way in his 2 and a half month battle in the ICU.

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New Section!!!

**“ST. JOHN’S
FOUNTAINHEAD”**

We will publish Abstracts of your
published research.....

Based on criteria laid down by the
Editorial Board.....

Email your Full Articles at the earliest to
Dr. Santu Ghosh

santu.g@stjohns.in

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APPLICATION OF KARYOTYPING AND FLOURESCENT IN SITU HYBRIDISATION IN DETECTION OF KLINEFELTER SYNDROME

Anjali Shastry, Preetha Tilak, Amudha Subramaniam

Department of Anatomy, St Johns Medical College, Bangalore, Karnataka, India

Abstract

Introduction:

Klinefelter Syndrome is one of most common sex chromosomal abnormality in males with incidence of 1 in 600 live births. Fluorescence in situ hybridization (FISH) is a powerful molecular cytogenetic technique which allows rapid detection of aneuploidies on interphase cells and metaphase spreads along with conventional GTG banding technique.

Aims and objectives:

To evaluate application of karyotyping and FISH as important diagnostic tool in diagnosis Klinefelter Syndrome.

Materials and Methods:

A retrospective study was conducted on 44 patients who were referred for karyotyping and counselling with suspected Klinefelter Syndrome and hypogonadism to Division of Human Genetics, Department of Anatomy, St. John's Medical College, Bangalore from January 2014 to October 2017. Chromosomal preparations were done using the peripheral lymphocyte culture method followed by GTG banding technique, automated photography and karyotyping. FISH was performed with dual colour X/Y probes once abnormality was detected using GTG banding technique.

Results:

Out of 44 patients, 9 had typical karyotype of Klinefelter syndrome (47,XXY) and Four had variants of Klinefelter syndrome

Conclusion:

We can conclude that cytogenetic analysis forms important investigation in diagnosis , treatment and fertility status in patients with Klinefelter syndrome

Int J Anat Res 2018, Vol 6(3.3):5682-85. ISSN 2321-4287 DOI: <https://dx.doi.org/10.16965/ijar.2018.310>



INDICATIONS FOR SPLENECTOMY IN A TERTIARY CARE HOSPITAL IN SOUTH INDIA

Sridar Govindaraj and AP Roshini

Department of General Surgery, St. John's Medical College and Hospital, Bengaluru,
Karnataka, India**Abstract****Background:**

Splenectomy is a surgical treatment for a wide range of diseases including symptomatic splenomegaly, autoimmune, malignant, hereditary and congenital disorders, splenic injury/rupture secondary to blunt trauma to abdomen. By far the two most common atraumatic indications for splenectomy are malignancy and haematological autoimmune disorders, such as Idiopathic Thrombocytopenic Purpura (ITP) and Autoimmune Hemolytic Anemia (AIHA).

Methods:

We did a retrospective study in a tertiary care hospital, of all patients undergoing splenectomy over a 5-year period to describe the indications for splenectomy.

Results:

186 patients underwent splenectomy, both emergency and elective (Open or Laparoscopic – conventional and hand-assisted). Most common indication was hematological in 153 patients, of which ITP-70 (37.6%) was the highest. Non-hematological indications were secondary to splenic cyst or abscess, neuroendocrine tumour of the pancreas, hydatid cyst of spleen. Emergency splenectomy was done for blunt trauma to abdomen, and grade 5 injury was commonly encountered. Among all, 16 (8.6%) patients had spleniculi.

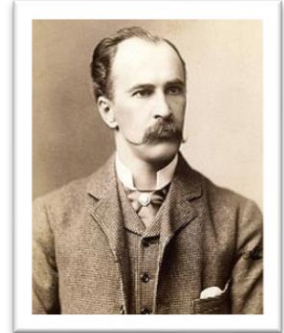
Conclusion:

In patients with hematological disorders, splenectomy must be undertaken only after anticipating both, short- and long-term risks and potential benefits to the patient.

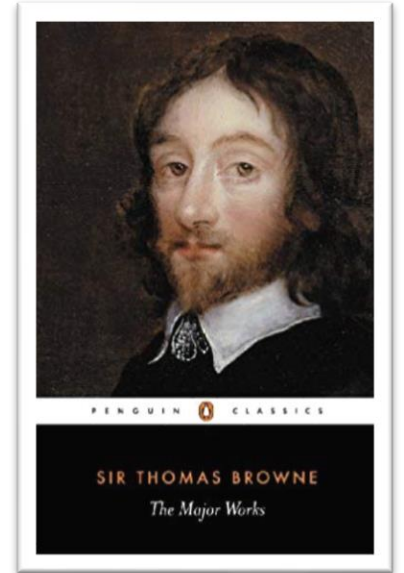
International Journal of Surgery Science, Vol. 3, Issue 1, Part A pp 4-6, (2019)



THE QUOTABLE OSLER



SIR WILLIAM OSLER



© Amazon.com

Three lessons are to be learned from Thomas Browne.

There are three lessons to be gathered from the life of Sir Thomas Browne [(1605-1682), physician who attempted to reconcile scientific scepticism and faith in his 1643 book *Religio Medici*], all of them of value to-day. First, we see in him a man who had an ideal education... The second important lesson we may gain is that he represents a remarkable example in the medical profession of a man who mingled the waters of science with the oil of faith... The third lesson to be drawn is that the perfect life may be led in a very simple, quiet way.

REF: The Quotable OSLER: Edited by Mark E Silverman, T. Jock Murray, Charles. S Bryan



MEDICINE DIS MONTH

A Bird's Eye View.....

Lenalidomide for high-risk smoldering multiple myeloma.

Observation is the current standard of care for smoldering multiple myeloma. Systemic treatment deferred until progression to symptomatic disease. In a multicentric randomised control trial of 182 patients assessed the efficacy of single-agent lenalidomide compared with observation in patients with intermediate- or high-risk smoldering multiple myeloma. One-, 2-, and 3-year progression-free survival was 98%, 93%, and 91% for the lenalidomide arm versus 89%, 76%, and 66% for the observation arm, respectively. Hence, Early intervention with lenalidomide in smoldering multiple myeloma significantly delays progression to symptomatic multiple myeloma and the development of end-organ damage.

- Lonial S et al J Clin Oncol. 2019.

Risk of congenital anomalies following preconception bariatric surgery.

Bariatric surgery prior to pregnancy is associated with a reduced frequency of some obesity-related pregnancy complications, such as gestational diabetes, but concerns remain about possible risks to offspring. In a study of data from the Swedish Medical Birth Register comparing the risk of birth defects in offspring of nearly 3000 women who underwent Roux-en-Y gastric bypass (RYGB) with that in matched controls managed medically, RYGB was associated with an approximately 30 percent reduction in congenital anomalies in subsequent pregnancies. While this finding is reassuring, the generalizability to women who undergo other types of bariatric surgeries is not known.

- Neovius M et al JAMA. 2019;322(15):1515. Uptodate



Randomized Trial of Lenalidomide Versus Observation in Smoldering Multiple Myeloma

Sagar Lonial, MD¹; Susanna Jacobus, MSc²; Rafael Fonseca, MD³; Matthias Weiss, MD⁴; Shaji Kumar, MD⁵; Robert Z. Orlowski, MD, PhD⁶; Jonathan L. Kaufman, MD¹; Abdulraheem M. Yacoub, MD⁷; Francis K. Buadi, MD⁵; Timothy O'Brien, MD⁸; Jeffrey V. Matous, MD⁹; Daniel M. Anderson, MD¹⁰; Robert V. Emmons, MD¹¹; Anuj Mahindra, MD¹²; Lynne I. Wagner, PhD¹³; Madhav V. Dhodapkar, MBBS¹; and S. Vincent Rajkumar, MD⁵

PURPOSE Observation is the current standard of care for smoldering multiple myeloma. We hypothesized that early intervention with lenalidomide could delay progression to symptomatic multiple myeloma.

METHODS We conducted a randomized trial that assessed the efficacy of single-agent lenalidomide compared with observation in patients with intermediate- or high-risk smoldering multiple myeloma. Lenalidomide was administered orally at a dose of 25 mg on days 1 to 21 of a 28-day cycle. The primary end point was progression-free survival, with disease progression requiring the development of end-organ damage attributable to multiple myeloma and biochemical progression.

RESULTS One hundred eighty-two patients were randomly assigned—92 patients to the lenalidomide arm and 90 to the observation arm. Median follow-up is 35 months. Response to therapy was observed in 50% (95% CI, 39% to 61%) of patients in the lenalidomide arm, with no responses in the observation arm. Progression-free survival was significantly longer with lenalidomide compared with observation (hazard ratio, 0.28; 95% CI, 0.12 to 0.62; $P = .002$). One-, 2-, and 3-year progression-free survival was 98%, 93%, and 91% for the lenalidomide arm versus 89%, 76%, and 66% for the observation arm, respectively. Only six deaths have been reported, two in the lenalidomide arm versus four in the observation arm (hazard ratio for death, 0.46; 95% CI, 0.08 to 2.53). Grade 3 or 4 nonhematologic adverse events occurred in 25 patients (28%) on lenalidomide.

CONCLUSION Early intervention with lenalidomide in smoldering multiple myeloma significantly delays progression to symptomatic multiple myeloma and the development of end-organ damage.

J Clin Oncol 37. © 2019 by American Society of Clinical Oncology

INTRODUCTION

Smoldering multiple myeloma (SMM) is an asymptomatic precursor stage of multiple myeloma (MM).^{1,2} It is associated with a risk of progression to symptomatic MM of 10% per year,³ although patients with certain adverse prognostic factors may have a higher risk of progression of approximately 25% per year.⁴⁻⁶

Observation has been the current standard of care for SMM until the emergence of end-organ dysfunction meeting the criteria for clinical MM.^{7,8} Data from randomized trials that show the efficacy of therapy to prevent such end-organ dysfunction or improve outcome are limited. Types of early therapy can take two different approaches. First, one can take a prevention approach with low-intensity therapy directed at clonal control or, second, one can take a more intensive treatment approach for which the goal is the

eradication of the malignant clone. The Spanish myeloma group assessed the combination of lenalidomide plus dexamethasone versus observation in patients with high-risk SMM.⁷ Although the study demonstrated improved progression-free survival (PFS) and overall survival with early intervention, it was not adopted as the standard of care for three main reasons. First, a combination regimen was used and the specific added value of lenalidomide could not be clearly isolated. Second, the study did not use modern imaging at randomization as the trial was designed before the use of magnetic resonance imaging or positron emission tomography scans were introduced as standard, more sensitive measures,^{9,10} leading to concerns about the possible enrollment of patients with symptomatic myeloma in this trial. Third, multiparametric flow cytometry criteria that were used to define high-risk SMM for this trial was



ASSOCIATED CONTENT

Appendix
Data Supplement
Protocol

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on September 4, 2019 and published at jco.org on October 25, 2019; DOI <https://doi.org/10.1200/JCO.19.01740>

RESEARCH LETTER

Association of Maternal Gastric Bypass Surgery With Offspring Birth Defects

Maternal body mass index (BMI) and glucose control are associated with offspring birth defects.^{1,2} Bariatric surgery results in weight loss and glucose normalization but is also associated with nutritional deficiencies and substance abuse,³ which could cause birth defects as hypothesized based on case series.⁴

It could be unethical to randomize pregnant women to bariatric surgery, and it is impossible to perform a randomized trial requiring pregnancy after alternative interventions. We conducted a nationwide matched cohort study to investigate major birth defect risk in infants born to women after gastric bypass surgery vs infants born to comparable women without bariatric surgery.

Methods | We identified live-born singleton infants in the Swedish Medical Birth Register born in 2007 to 2014 to women

Table. Maternal Characteristics for Singleton Infants Born to Women With Gastric Bypass Surgery and Matched Controls

Characteristics ^a	Women With Gastric Bypass Surgery (n = 2921)	Matched Controls (n = 30 573) ^b	Standardized Difference
Maternal age, mean (SD), y	31 (5)	31 (6)	0.028
Maternal body mass index, No. (%) ^c			
30-30.9	6 (0.2)	63 (0.2)	0.000
31-31.9	6 (0.2)	63 (0.2)	0.000
32-32.9	7 (0.2)	73 (0.2)	0.000
33-33.9	17 (0.6)	178 (0.6)	0.000
34-34.9	39 (1.3)	408 (1.3)	0.000
35-39.9	706 (24)	7389 (24)	0.000
40-44.9	1178 (40)	12 330 (40)	0.000
45-49.9	626 (21)	6552 (21)	0.000
≥50	336 (12)	3517 (12)	0.000
Pregnancy-related covariates, No. (%)			
Primiparous	1192 (41)	11 574 (38)	0.043
History of major birth defects ^d	67 (3.9)	701 (3.6)	0.007
Smoking ^e	427 (15)	4292 (14)	0.012
Year of delivery			
2007-2009	73 (2.5)	764 (2.5)	0.000
2010-2012	1148 (39)	12 016 (39)	0.000
2013-2014	1700 (58)	17 793 (58)	0.000
Comorbidity, No. (%) ^f			
Diabetes	283 (9.7)	2962 (9.7)	0.000
History of alcohol or substance use	149 (5.1)	1410 (4.6)	0.016
Drug use, No. (%) ^f			
Any psychiatric drug	873 (30)	9551 (31)	0.021
No. of unique prescription drugs			
0-1	300 (10)	3050 (10)	0.007
2-3	495 (17)	5283 (17)	0.006
4-5	504 (17)	5223 (17)	0.003
≥6	1622 (56)	17 017 (56)	0.002

^a All variables originate from the Medical Birth Register, except for presurgery body mass index (from the Scandinavian Obesity Surgery Register), history of major birth defects (from the National Patient Register and Causes of Death Register), diabetes and substance use (from the National Patient Register and Prescribed Drug Register), and drug use (from the Prescribed Drug Register).

^b Exact matching by presurgery body mass index and diabetes (early-pregnancy body mass index and preconception diabetes used for controls), maternal history of major birth defects in previous pregnancies, delivery year, and a propensity score based on maternal age, alcohol/substance use, smoking, parity, psychiatric drug use, and number of prescription drugs.

^c Presurgery data for the surgery group; early-pregnancy (body mass index) or preconception (comorbidity and drug use) data for controls. Body mass index calculated as weight in kilograms divided by height in meters squared.

^d Only possible for parous women. Percentages were calculated based on births to parous women.

^e The 0.9% missing data on smoking status (surgery: n = 127; controls: n = 284) was imputed using the mode.

^f During the 24 months before surgery for the surgery group and during the 24 months before conception for controls.



Figure. Major Birth Defects in Infants Born to Women With Gastric Bypass Surgery and Matched Controls

	Total No.		Events, No. (%)		Risk Ratio (95% CI)	P Value
	After Gastric Bypass	Matched Controls	After Gastric Bypass	Matched Controls		
Primary analysis						
Any major birth defect	2921	30573	98 (3.4)	1510 (4.9)	0.67 (0.52-0.87)	.002
Sensitivity analysis						
Excluding chromosomal abnormalities	2916	30516	93 (3.2)	1470 (4.8)	0.66 (0.51-0.85)	.001
First birth after surgery	2436	20045	75 (3.1)	1058 (5.3)	0.58 (0.44-0.77)	<.001
Excluding coarsened exact matching weights >20	2587	30463	85 (3.3)	1387 (4.6)	0.72 (0.56-0.91)	.007

Matched controls: exact matching by maternal presurgery body mass index and diabetes (early-pregnancy body mass index and preconception diabetes used for controls), history of major birth defects in previous pregnancies, delivery year, and a propensity score based on maternal age, alcohol and substance use, smoking, parity, psychiatric drug use, and number of prescription

drugs. For first birth after gastric bypass surgery, restriction was performed to avoid clustering effects (13% of mothers had >1 birth after surgery). Weights from coarsened exact matching were used to account for different sizes of matching strata.

receiving Roux-en-Y gastric bypass surgery during the same period (ascertained from the Scandinavian Obesity Surgery Register) and to women without bariatric surgery.

Using coarsened exact matching, controls were matched by major birth defects in previous pregnancies, presurgery BMI and diabetes (early-pregnancy BMI and preconception diabetes used for controls), delivery year, and a propensity score (estimated using logistic regression) including maternal age, smoking, alcohol/substance use, parity, psychiatric drugs, and number of prescription drugs.

Major birth defects, excluding genetic syndromes, defined according to the EUROCAT classification (which does not include minor defects), were identified via the National Patient Register (including inpatient and hospital-based outpatient care) and Causes of Death Register through 2015, permitting 1 year of follow-up.

Using generalized linear models with robust sandwich estimators in SAS version 9.4 (SAS Institute Inc), we estimated risk ratios in infants born after gastric bypass surgery vs control infants assuming a binomial distribution. A 2-sided $P < .05$ indicates statistical significance. Sensitivity analyses were conducted excluding infants with chromosomal abnormalities, restricting analysis to the first postsurgery birth, and excluding strata with high coarsened exact matching weights (>20).

The study was approved by the regional ethics committee in Stockholm, Sweden. Informed consent was not required.

Results | Matched controls were found for 97.4% (2921/2998) of postsurgery-born infants. The groups were well balanced on maternal characteristics (Table). In the surgery group, mean presurgery BMI (calculated as weight in kilograms divided by height in meters squared) was 43.5 and mean body weight was 122 kg; median surgery-to-conception interval was 1.6 years; mean weight loss was 40 kg, resulting in a body weight of 82 kg; and diabetes drug use decreased from 9.7% before surgery to 1.5% during the 6 months before conception.

Major birth defects were recorded in 3.4% (98/2921) of infants born to mothers with gastric bypass surgery vs 4.9% (1510/30 573) of controls (risk ratio, 0.67 [95% CI, 0.52-0.87]; risk difference, -1.6% [95% CI, -2.7% to -0.6%]) (Figure). Major heart defects accounted for 60% ($n = 58$) of birth defects among postsurgery-born infants. There were no cases of neural tube defects in the surgery group and 20 cases (0.07%) among controls. The lower risk remained in sensitivity analyses (Figure).

Discussion | In this nationwide matched cohort study, infants born to women with Roux-en-Y gastric bypass surgery had lower risk of major birth defects than infants born to matched control women.

Obesity is associated with poor glucose control, which is teratogenic.^{1,2} In this study, after bariatric surgery, women lost weight and diabetes drug use decreased. If the observed association is true, a mechanism could be that surgery-induced improvements in glucose metabolism, and potentially other beneficial physiologic changes, led to a reduction of major birth defect risk to a level similar to that of the general population (3.5%).¹

Concerns were raised by case series that gastric bypass-induced folate deficiency could increase risk of neural tube defects.⁴ In this study, no neural tube defects were found in postsurgery-born infants.

A systematic review of bariatric surgery and birth defects⁵ could not draw conclusions from available studies because of inadequate statistical power,⁶ a mix of procedures with different physiologic effects, unclear outcome ascertainment, and limited confounder control. The current study had sufficient statistical power, analyzed gastric bypass surgery only, used a well-established birth defect classification applied to prospectively recorded outcome data including defects detected after delivery hospital discharge, and matched for a range of potential confounders.

Limitations include that pregnancy termination data were not available, stillbirths were not included, and individual birth defects could not be analyzed because of small numbers.

BANTING AND BEST

Frederick Banting (an unsuccessful orthopedician) went to the University of Toronto, where, (although he had neither salary nor research budget) Professor John J. R. Macleod, gave him permission to use his physiology laboratory while he was on a three-month holiday in Scotland. Before he left, Macleod off-handedly instructed his assistant Charles Herbert Best, then 22, to help Banting.

He and Best finally obtained a dog's degenerated pancreas by tying off its pancreatic ducts; when they opened it, they found the islets of Langerhans still intact. After making an extract from this, Banting injected some into a diabetic dog that was close to death. Then the two young men waited. Within a few hours, the dog sat up, wagged its tail and barked. For their discovery to be a success, they had to find a source from which large quantities of insulin could be produced. A local slaughterhouse supplied them with a large number of immature pancreases, and enough insulin was extracted from these to keep their diabetic dogs alive and healthy indefinitely.

When Banting and Best's insulin began to produce toxic reactions, Macleod turned to a talented biochemist, James B. Collip, for help. In 1923, Collip devised a method of further purifying the extract and it was this purified insulin that made the control of diabetes possible.



JOHN J R MACLEOD



JAMES B. COLLIP

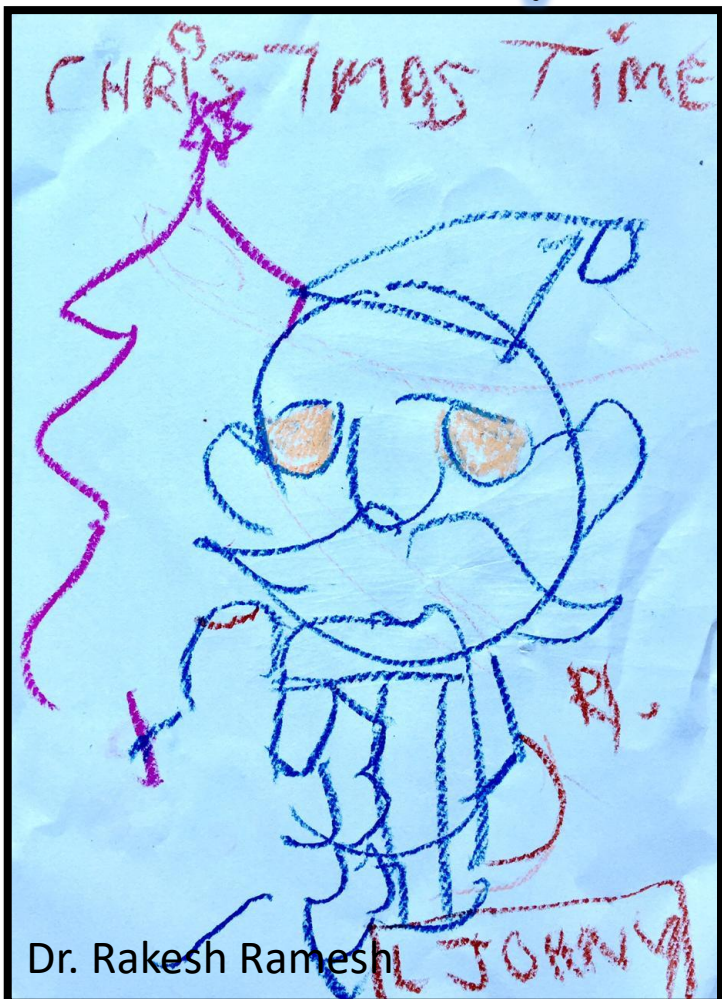


Charles Best (left) and Frederick Banting, with the first dog to survive as a result of Banting



The laboratory where insulin was discovered

L Johnny



Dr. Rakesh Ramesh

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