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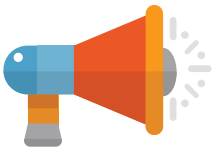
Medical Bulletin

News You Can Use



Gazette Notification on Tuberculosis

Q. What is the Gazette Notification on Tuberculosis about?

A. The latest gazette notification dated 19th March, 2018 by Ministry of Health & Family Welfare (MOH&FW), Govt. of India is to ensure proper tuberculosis diagnosis and its management in patients and their contacts and to reduce tuberculosis transmission and further to address the problems of emergence and spread of drug resistant tuberculosis.

Q. What does the said notification want from Doctors?

A. Through the notification, the Govt. of India wants to collect complete information of all tuberculosis patients from Doctors and Chemists.

Q. To whom is it applicable / who has to notify a case of Tuberculosis?

A. Every clinical establishment as defined under the Clinical Establishment Act, 2010 (C.E.A.). In short, every Doctor of any pathy of medicine (allopathy/AYUSH), Laboratory and Chemist running a Pharmacy.

Q. Is the notification applicable to the entire country / all States?

A. Yes.

Q. Which type of patients have to be notified?

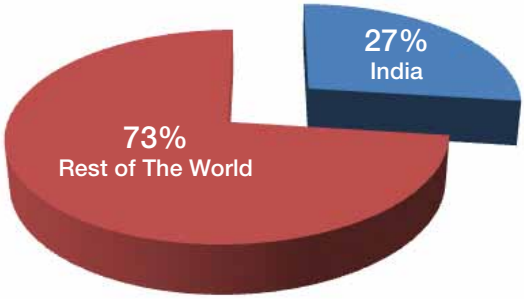
A. All patients who are diagnosed to be suffering from Tuberculosis or initiated on anti-tubercular drugs, whether by clinical, microbiological or radiological diagnosis.

Q. Do I have to notify all cases of Tuberculosis –

- **whether diagnosed by me or by anyone else?**
- **whether on treatment from me or on treatment by anyone else?**
- **who are already on treatment?**

A. Yes.

Global Incidence of TB in Year 2017 (10 million cases)



Worldwide India is the country with the highest burden of both TB and MDR-TB. In 2017, an estimated 27 lakh cases of tuberculosis occurred in India. **India also has more than a million "missing" cases every year** that are not notified.

Reference: WHO Global Tuberculosis Report Executive Summary 2018.

Greetings from Blue Cross Laboratories!

Dear Colleagues,

Hope all of you are in the best of health and spirit! It gives me immense pleasure and satisfaction to present you with the first issue of the Blue Cross Medical Bulletin for the new financial year of 2019.

This issue will have you updated on a few recent medical developments, and novel clinical insights involving diverse therapeutic facets. I am happy to include a tutorial on Peptic Ulcer and Its Management. The medical news section comprises of breakthrough case of getting rid of HIV infection. The topics have been chosen keeping your needs in mind. Besides this, we have also included succinct on notification of TB Cases.

We hope all these topics make for interesting reading and you shall enjoy reading this edition of Medical Bulletin as in the past. Please feel free to send in your feedback, so that we can incorporate the same in future editions.

Happy Reading!

Best wishes & Warm regards,

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Q. Do I have to notify cases of Tuberculosis who have fully completed their treatment and are in consultation with me for other medical issues?

A. The notification is silent on this aspect. A careful reading of the notification leads to a logical conclusion that it needs to be reported. Although, a clarification is needed from the MOH&FW regarding the issue that whether cases of past history of tuberculosis need to be reported or not.

Q. Can a patient self-notify?

A. Yes. The patients are encouraged to self-notify themselves as well as the details of their treating physicians to the Govt. of India.

Q. How and where do I notify?

A. Can be reported electronically at the website - https://nikshay.gov.in through Annexure-II for Doctors. (Annexure-I is for medical laboratories, Annexure-III is for Chemists) Or, by hard copy to District Health Officer or Chief Medical Officer of a District and Municipal Health Officer of urban local bodies. You should receive a SMS on completing the process of online reporting. You need a Govt.-issued I.D. of the patient (mandatory) for the reporting process.

Q. What happens if I fail to notify?

A. One could be liable for committing an offence under Section 269 and Section 270 of the Indian Penal Code.

Section 269 IPC – Negligent act likely to spread infection of disease dangerous to life – Whoever unlawfully or negligently does any act which is, and which he knows or has reason to believe to be, likely to spread the infection of any disease dangerous to life, shall be punished with imprisonment of either description for a term which may extend to six months, or with fine, or with both.

Section 270 IPC – Malignant act likely to spread infection of disease dangerous to life – Whoever malignantly does any act which is, and which he knows or has reason to believe to be, likely to spread the infection of any disease dangerous to life, shall be punished with imprisonment of either description for a term which may extend to two years, or with fine, or with both.

Q. What happens after such notification to the government?

A. The information on tuberculosis notification received by Public Health Staff, shall be used only for extending the care and support, take appropriate public health action; including financial and non-financial incentives to patients, like free drugs and diagnostics, screening for co-morbidities, drug susceptibility testing, information technology based treatment adherence support system for improving quality care, etc., and providing feedback to the respective treating medical practitioner: provided that the confidentiality of the individual identity of the tuberculosis patients shall be maintained.

Efficacy and Safety of Teneligliptin in Patients with Type 2 Diabetes Mellitus:

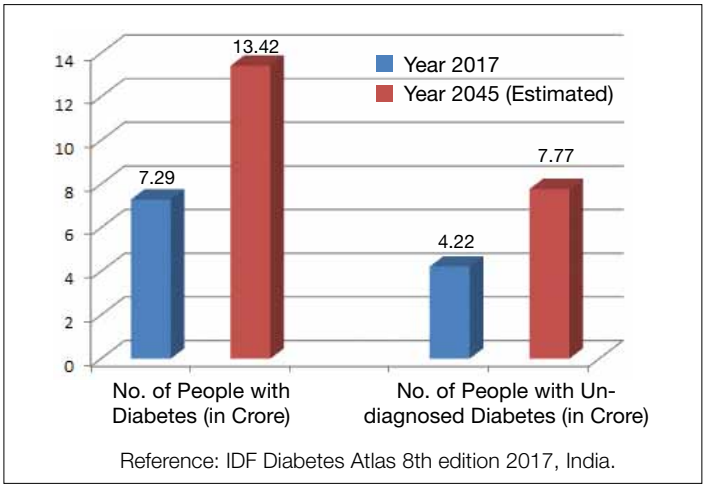
A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Li X, et al. Front Pharmacol. 2018 May 4; 9:449.

Background: Teneligliptin is a 3rd generation dipeptidyl peptidase-4 (DPP-4) inhibitor. There is limited evidence regarding the effect of teneligliptin. Therefore, this study is to assess the efficacy and safety of teneligliptin in type 2 diabetes mellitus (T2DM) patients with inadequately glycemic controlled.

Results: Ten trials with 2119 patients were analyzed. Teneligliptin produced absolute reductions in glycated hemoglobin A1c (HbA1c) levels by 0.82% compared with placebo. Teneligliptin led to greater decrease of fasting plasma glucose (FPG) level (–18.32%) vs. placebo. Teneligliptin also significantly decreased the 2 h post-prandial plasma glucose (2 h PPG) level by –46.94% and area under the glucose plasma concentration-time curve from 0 to 2 h (AUC_{0-2h}) for PPG by –71.50% compared with placebo. Patients treated with teneligliptin achieved increased homeostasis model assessment of beta-cell function (HOMA-β). However, there was no significant difference between teneligliptin and placebo in overall adverse effects (risk ratio 0.96). The risks of hypoglycemia were not significantly different between teneligliptin and placebo.

Conclusion: This meta-analysis suggests that treatment of teneligliptin provided clinically and statistically significant reductions in HbA1c and FPG levels in patients with T2DM. These effects were associated with significant improvements in beta-cell function. Furthermore, the incidences of adverse events were not significantly in patients treated with teneligliptin compared to placebo. Therefore, the present study demonstrated that teneligliptin exhibits beneficial effects in T2DM patients.



Reference: IDF Diabetes Atlas 8th edition 2017, India.

Number of Deaths due to Diabetes in India in 2017: 10 Lakh

1 out of 10 Indian Adults have Diabetes

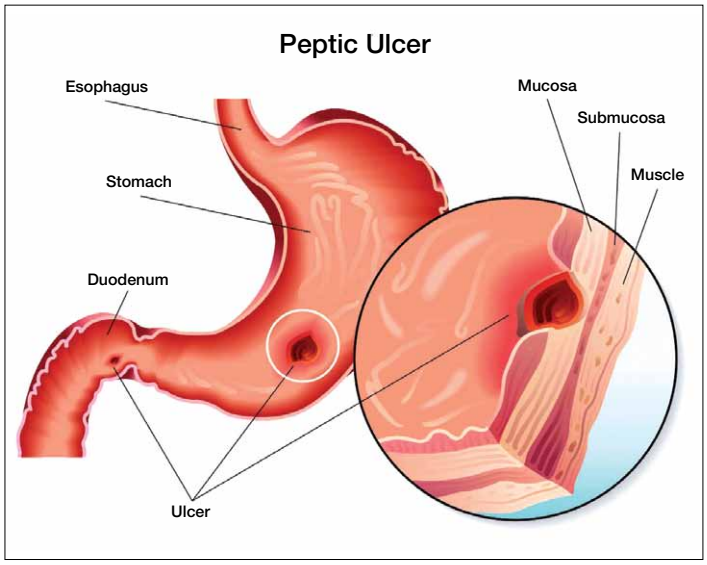
Reference: International Diabetes Federation (IDF) Diabetes Atlas 8th edition 2017, Country Reports – India.

Peptic Ulcer Disease And Its Management

Peptic Ulcer Disease (PUD) is a term used to include ulcerations and erosions in the stomach and the duodenum from a number of causes. **These lesions are called "peptic" because of the enzyme pepsin** which plays a major role in causing the mucosal breaks, regardless of the inciting agent.

There is a role of gastric acid secretion and the effects of stress, personality type, and genetics in the pathogenesis of PUD. Role of *H. pylori* infection, aspirin and other NSAIDs in development of peptic ulcer disease is also well established.

Most common complication of peptic ulcer is bleeding. Patients can also develop perforation and strictures. Malignancy can occur especially in gastric ulcer.



MANAGEMENT OF PEPTIC ULCER DISEASE (PUD)

Diet

For years it is suggested that certain foods including spicy food can induce ulcers in the gastrointestinal (GI) tract. There are many food items that can induce or exacerbate symptoms in patients with PUD. These include: coffee, chocolate, spicy food, alcohol, acidic foods, such as citrus and tomatoes. Overeating and eating within two to three hours before bed may also worsen symptoms. Patients themselves can identify such food items and should refrain from using these foods.

Research shows that a high fibre diet decreases the risk of developing ulcer disease. Although, both insoluble and soluble fibres demonstrate this association, there is a stronger association between diets high in soluble fibre and a decreased risk for developing ulcers. Foods that are high in soluble fibre include oats, psyllium husk, legumes, flax seeds, barley, nuts, and certain vegetables and fruits, such as oranges, apples, and carrots.

Antacids

Antacids have been shown to be superior to placebo in healing peptic ulcers, their efficacy in ulcer healing is modest, and their use is limited by adverse effects. Antacids neutralize gastric acid, but their precise mechanism in healing ulcers is still unclear. Side effects of antacids can include diarrhoea or constipation depending upon the salts viz. Mg or Al /Ca respectively.

All antacids must be used with caution, if at all, in patients who have chronic kidney disease.

Histamine (H2) Receptor Antagonists (H2RAs)

H2RAs are safe, well tolerated and moderately effective for healing of gastric and duodenal ulcers. They inhibit basal as well as meal stimulated gastric acid output significantly. Ranitidine (150 to 300 mg twice daily) and Famotidine are generally available as H2RAs. However, tolerance to the anti-secretory effects of H2RAs develops quickly and frequently.

Proton-Pump Inhibitors (PPIs)

PPI are mainstay of therapy for management of PUD. These agents are prodrugs that must be activated by acid to inhibit the H^+,K^+-ATPase. There is genetic polymorphism in CYP2C19 – the isoenzymes involved in PPI metabolism. Approximately 25% Asians have deficient CYP2C19 activity which leads to substantially higher plasma levels of Omeprazole, Pantoprazole, Lansoprazole, but not Rabeprazole. PPI bind predominantly to those proton pumps that are actively secreting acids, so dosing before meals is most effective. Omeprazole 20mg, Esomeprazole 40mg, Pantoprazole 40mg, Rabeprazole 20mg, Lanzoprazole 30mg once or twice a day 30 minutes before meals is the recommended dose. Tolerance generally does not develop to PPI. PPIs are safe and well tolerated.

Overall, superiority of one PPI over the other in healing of peptic ulcer has not been proved consistently in various clinical studies. So choice of specific PPI depends upon the availability, cost, and drug-drug interaction profile.

Mucosal Protective Agents

These agents are used sometimes in non-healing recurrent and large ulcers. Sucralfate, colloidal bismuth preparations, misoprostol, rebamipide, troxipide are used with varying success in various studies. Misoprostol is best reserved for prophylaxis of non-steroidal anti-inflammatory drug (NSAID)-induced ulcers, but the side effect profile precludes its routine use.

Helicobacter Pylori (H. Pylori)-Related Ulcers

Most duodenal ulcers are associated with *H. Pylori* infection, so *H. Pylori* test is compulsory in a confirmed case of duodenal ulcer. If duodenal ulcer is

diagnosed on endoscopy, gastric biopsy for *H. Pylori* should be taken, and if positive, 10-14 day course of anti *H. Pylori* treatment should be initiated. *H. pylori* treatment should consist of two antibiotics like amoxycillin and clarithromycin with one PPI.

NSAID-Related Ulcers

PPI are superior to H2RAs in healing peptic ulcers related to NSAID use. In general, 80-90% response rate is documented after 8 weeks of therapy with PPI. Even if patients continue to take NSAIDs, 70% response rate is expected with PPI. H2RAs are less effective than PPIs and misoprostol has significant side effects and hence is used in selective cases only. Prophylaxis for NSAID induced ulcers includes co-prescription of PPI and use of COX-2 inhibitors like etoricoxib.

Conclusion

Morbidity and mortality due to PUD can be prevented if diagnosed early and treated aggressively. Many effective and safe options are now available for treatment of peptic ulcers. Proper dose and duration of treatment and identification of the underlying etiological conditions can help physician to deal with the peptic ulcer disease in the best possible way.

Second Patient is HIV-Free after Stem-Cell Therapy

Breakthrough suggests first case was not a one-off and could pave way for future treatments for HIV patients.

A person with HIV seems to be free of the virus after receiving a stem-cell transplant that replaced their white blood cells (WBCs) with HIV-resistant versions. The patient is only the second person ever reported to have been cleared of the virus using this method.

The patient - whose identity hasn't been disclosed (called as 'London patient') - was able to stop taking antiretroviral drugs, with no sign of the virus returning 18 months later. The stem-cell technique was first used a decade ago for HIV-infected patient, known as the 'Berlin patient', who is still free of the virus.

Like 'Berlin patient', the latest 'London patient' also had a form of blood cancer that wasn't responding to chemotherapy. They required a bone-marrow transplant, in which their blood cells would be destroyed and replenished with stem cells transplanted from a healthy donor. But, rather than choosing just any suitable donor, the investigators picked a donor who had two copies of a mutation in the CCR5 gene that gives people resistance to HIV infection. Both patients received stem cell transplants from donors with the rare genetic mutation known as 'CCR5 delta 32.' CCR5 is the most commonly used receptor by HIV-1. This specific mutation - CCR5 delta 32 - prevents the virus from using CCR5 as a receptor to enter host cells. In other words, the HIV-1 virus cannot exist without normal CCR5 receptors.

This gene codes for a receptor which normally present on the surface of WBCs involved in the body's immune response. Normally, the HIV binds to these receptors and attacks the cells, but a deletion in the CCR5 gene stops the receptors from functioning properly. About 1% of people of European descent have two copies of this mutation and are resistant to HIV infection.

The researchers report that the transplant successfully replaced the patient's WBCs with the HIV-resistant variant. Cells circulating in the patient's blood stopped expressing the CCR5 receptor, and in the lab, the researchers were unable to re-infect these cells with the patient's version of HIV.

The team found that the virus completely disappeared from the patient's blood after the transplant. After 16 months, the patient stopped taking antiretroviral drugs, the standard treatment for HIV. In the latest follow-up, 18 months after stopping medication, there was still no sign of the virus.

For those who need a transplant to treat leukaemia or other diseases, it seems reasonable to try and find a donor with the CCR5 mutation. Many doctors believe that replacing the host's immune cells with donor cells that do not contain the CCR5 receptor seems to be way to prevent the HIV from returning after treatment.

However, scientists agree that this kind of treatment could only ever be used for a small group of patients. But he hopes that the research will stimulate a renewed interest in gene therapies that target CCR5, which could be applied to a much broader group. "The real breakthrough, we are still waiting for," they added.

[References: Published in the journal 'Nature' on 5th March, 2019. https://www.nature.com/articles/d41586-019-00798-3. https://newzealandworldnews.worldnewsnetwork.co.in/2019/03/05/second-patient-free-of-hiv-after-stem-cell-therapy-nature-com/.]

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