



## Tuberculosis: Case Studies from Southern India

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### INTRODUCTION

Tuberculosis (TB) is one of the oldest illnesses known to man, plaguing populations for centuries and claiming the lives of many notable historical figures. Despite the availability of a cheap and effective cure for over 70 years, TB still presents a significant global burden. In 1993 TB was declared a worldwide public health emergency, and the subsequent WHO strategy has been experiencing great success in reducing mortality from the disease.<sup>[1]</sup> However, the emergence of obstacles such as drug-resistance and the HIV epidemic mean that TB remains a major world killer, with 8.7 million new cases and 1.4 million deaths reported in 2011.<sup>[2]</sup>

Infection with *Mycobacterium tuberculosis* does not usually present a problem to a healthy individual, whose immune system should be capable of eliminating, or at least containing, the disease. In the latter cases TB is held in a dormant, non-infectious, state within the body, but the individual is at risk of developing active disease should their immune system weaken. TB is a disease of the ill and the poor, as they are less capable of building a strong immune defence. Because of this the highest incidence of TB is in developing countries, with India and China accounting for 26% and 12% of global incident cases respective,<sup>[2]</sup> yet it is not unknown to the West. In Europe TB is responsible for the deaths of 7 people every hour,<sup>[3]</sup> with increasing immigration from high-burden countries continually bringing new cases. In the UK case incidence was not insignificant at 8963 in 2011, a population rate of 14.4 per 100,000.<sup>[4]</sup> The majority of cases are reported in major cities with high immigration rates, and with the compounding factors of inadequate housing and poor healthcare in many migrant communities, it is not unlikely for many Western physicians to encounter the disease.

This report aims to increase the general knowledge of TB above the baseline taught in standard medical school courses. By presenting 4 case studies a personal element will be added to the review, illustrating more clearly the nature and treatment of TB. The histories discussed here will cover the topics of typical presentation, medical complications, drug-resistance and HIV co-infection.

### METHOD

With 2-2.5 million new cases in 2011, India has the highest incidence of TB in the world,<sup>[2]</sup> making it an ideal location for the study of the disease and the acquisition of a wide-range of cases. The Christian Medical College (CMC) in Vellore, South India, is one of the top medical institutions in India and cares for over 8,000 patients daily.<sup>[5]</sup>



Figure 1a: The main entrance to CMC, Vellore

I was offered a 2-week Clinical Observer posting at CMC in July. Here I was able to observe outpatient clinics, ward rounds and team meetings, and through this experience I met and talked with patients with TB, learning about their histories and treatment

Figure 1b: Busy outpatients department



### CONSENT

Verbal consent was gained from all patients before including their information in this report. All cases have been fully anonymised and identifying information removed.

A note on photographs of X-rays  
Photographs of chest x-rays have been included in this report to enhance understanding. However due to confidentiality limiting access to the system I was only permitted to take photographs from the computer screens, unfortunately resulting in fairly low quality images.

### Case 1: Ms N

Ms N presented to outpatient clinic following a 2-month history of cough with expectoration and a low-grade fever in the evenings. She also noted several episodes of haemoptysis within this time period, and was experiencing right sided chest pain. A chest x-ray and CT taken at a community hospital revealed a right sided pleural effusion.

On hearing her history Ms N's doctor immediately ensured that facemasks were worn by all medical staff and suggested that the patient do so as well. He explained to the patient that his immediate concern was of TB and he would need to analyse Ms N's sputum, take another chest x-ray and do a pleural biopsy. A follow-up appointment was arranged for 5 days later to discuss these results.

Ms N's sputum was positive for acid-fast bacilli and Xpert MTB/RIF analysis revealed the presence of TB with no resistance. Her pleural biopsy showed granulomatous inflammation whilst her chest x-ray was inconclusive. She was





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consequentially commenced on anti-tubercular treatment under management of the DOTS clinic.

Ms N's case provides us with an example of what an initial presentation of pulmonary TB can look like. A 'typical' case of pulmonary TB presents with chronic cough, haemoptysis, weight loss, intermittent fever, night sweats, reduced appetite and sputum production<sup>[6],[7]</sup>. The clinical picture can vary widely, however, and the presence of any one of 4 symptoms (weight loss, night sweats, fever or cough) has been shown to be 80% sensitive in warranting further investigation.<sup>[8]</sup>

When concerned about TB, diagnosis is typically made using sputum smear microscopy. Two samples are tested over two consecutive days and stained using the Ziehl-Neelson method, after which the patient can be classified as 'sputum-positive' or 'sputum-negative'.<sup>[9]</sup> Further analysis using Xpert MTB/RIF, a rapid, cartridge-based assay, can provide detection of TB within two hours, as well as identifying rifampicin resistance.<sup>[10]</sup> The WHO has recommended the use of Xpert since 2010, and it is currently the subject of a three-year global rollout programme, costing \$25.9 million (US).<sup>[10]</sup>

Chest x-rays are routinely taken, but as seen in the case of Ms N they can lack sensitivity and specificity, and therefore should not be relied on solely for diagnosis. However, studies evaluating the control of TB in India have identified an over-reliance on x-rays for diagnosis, resulting in under-detection of active cases.<sup>[11]</sup> Therefore the WHO endorses diagnosis through bacteriology: providing case-detection through smear microscopy is one of the five elements of DOTS, the treatment principle at the heart of the WHO's Stop TB Policy.<sup>[12]</sup>

Ms N's case also illustrates the scale of the epidemic in India. Her presenting history would not have sparked such immediate concern for TB in a Western country, highlighting the frequency at which Indian physicians see the disease. However, even in countries where TB is rare, there are particular patient sub-groups for which presentations such as

Ms N's should spark a similar response. These include immunocompromised patients, those with chronic illness or malnutrition, migrants from TB-endemic countries, and individuals living in poor quality, crowded accommodation.<sup>[6]</sup> If TB is not considered in these patients then not only will they not be given effective treatment, but also they will remain infectious. Therefore keeping Ms N in mind may help to identify these uncommon cases earlier on, and save many lives in the process.

#### Case 2: Mr K

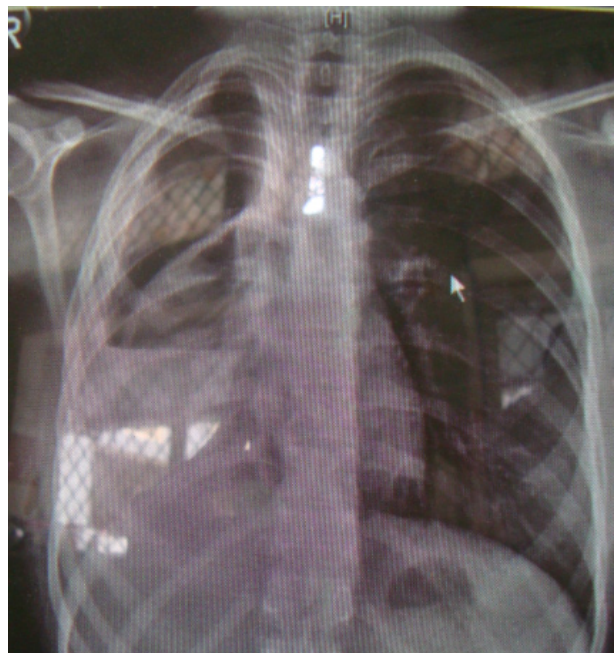
Mr K is a 19-year-old student. He was referred by a private clinic to the CMC following a three-week history of severe breathlessness at rest. Two months previously Mr K had been diagnosed with pulmonary TB by an outside facility due to a six-week history of low-grade fever and cough with expectoration. He had then been commenced on first line anti-tubercular treatment, following which his symptoms improved.

On examination Mr K was hypotensive (90/60 mmHg); tachycardic (108 BPM); tachypnoeic (26 RPM); and had decreased breath sounds with crepitations audible on the right side.

Mr K's sputum stain showed acid-fast bacilli and further Xpert MTB/RIF analysis revealed the presence of non-resistant TB. Chest x-ray showed a hydropneumothorax (see below).

Figure 2.

Mr K's chest x-ray taken on admission displays a right-sided hydropneumothorax:



Following the above results Mr K was admitted for intercostal drain insertion to drain the hydropneumothorax. This was successful, however he developed a grade 1 bronchopleural fistula and low-grade fever, and therefore remained in hospital for management. This impacted heavily on his studies and he was required to take further time out of his course.

The case of Mr K highlights several factors. Firstly, in India TB is not solely a disease of the old or chronically ill: it can have a devastating impact upon the young and healthy too. Secondly, despite adequate treatment complications can still develop. This can have a large impact upon the patient's life and, as for Mr K, it is important to maintain close follow-up of TB patients – a point of great difficulty in many developing countries.

Treating TB is a lengthy process. Mr K's first-line therapy would have been a 6-month course of 4 antibiotics (rifampicin, ethambutol, isoniazid and pyrazinamide), most likely taken thrice weekly. If this standard course is not closely complied with and completed then drug resistance can emerge,<sup>[13]</sup> as well as relapse or further complications of the disease (see below). It usually takes around 2 weeks for non-resistant sputum-positive pulmonary TB patients to stop being infectious, and at least 6 months to ensure all the bacteria are killed.<sup>[6]</sup> This treatment incurs a large cost to Indian patients even if their medication is subsidised, due to the working time lost during the illness period. Total cost has been estimated to represent 193% of a manual labourers' monthly income,<sup>[14]</sup> although this will vary from state-to-state. Comparatively the UK views TB treatment as relatively inexpensive if uncomplicated, but this cost can rise by over 25 times in complex or drug-resistant cases:<sup>[15]</sup> further motivation for stringent monitoring.

Unfortunately TB is a burden in precisely the countries where receiving and complying with this sort of treatment protocol is problematic. Poor infrastructure, poverty and lack of information make access to medication difficult for many, inspiring the WHO to develop





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the DOTS strategy.<sup>[16]</sup> This is an effective policy, with the Indian National TB Programme (RNTCP) reporting a cure rate of over 85% in new sputum positive patients since using a DOTS-based strategy.<sup>[11]</sup> Therefore all treatment of TB patients should comply with DOTS protocols, and physicians should be familiar with these when managing the illness.

Mr K is by no means unusual in developing a hydropneumothorax. Both pneumothoraces and pleural effusions are frequently observed complications of pulmonary TB,<sup>[17]</sup> and destruction and scarring of lung tissue can also cause long-term conditions such as bronchiectasis and recurrent pneumonia.<sup>[18]</sup> Furthermore, the influence of TB is not necessarily confined to the lungs. Amongst the myriad systemic complications of TB are hyponatraemia, syndrome of inappropriate ADH secretion,<sup>[19]</sup> altered mental state, haematological abnormalities,<sup>[20]</sup> tuberculous meningitis,<sup>[21]</sup> arthritis,<sup>[6]</sup> abdominal and pelvic inflammatory disease,<sup>[22]</sup> and lymphadenopathy.

Whilst thankfully not occurring in Mr K, extra-pulmonary tuberculosis can either be a complication of poorly treated pulmonary infection, or in fact be the primary infection. Whilst much less infectious than pulmonary strains, it can be tricky to diagnose with the milieu of symptoms often presenting a confusing picture. Furthermore, extra pulmonary TB occurs in between 10 and 42% of TB patients, depending on background,<sup>[23]</sup> and thus may be the answer to a patient's otherwise unexplained symptoms. <sup>[24]</sup>

#### Case 3: Mr D

Mr D was seen in an outpatient clinic, having initially presented 2 years ago with productive cough, haemoptysis and low-grade fever. He was diagnosed with TB, with further analyses revealing the strain to be resistant to both isoniazid and rifampicin. He was placed on second line anti-tubercular treatment and managed by a private clinic, and as such the exact details of his treatment are unknown. He was later referred to CMC with recurrence of his original symptoms. He was revealed to have an exten-

sively drug-resistant strain of TB: resistant to isoniazid, ofloxacin, rifampicin, ethionamide, streptomycin, capreomycin and ethambutol, but susceptible to kanamycin.

Mr D was admitted to the isolation ward and began an extensive regimen of second line anti-tubercular drugs. Despite subsequent discharge to DOTS clinic, Mr D has been frequently re-admitted to manage complications. He appeared tired although generally well in clinic, and is currently being treated daily with amikacin, cycloserine, moxifloxacin and kanamycin. Mr D has a sputum smear test 3 days every month, as well as a sputum culture every 3 months to check for sensitivity. He also has frequent follow-up chest x-rays, with one series revealing a massive left-sided pleural effusion and inadequate lung expansion following drainage: complications of his long-term disease.

tively low, with the more severe extensively drug-resistant (XDR-TB) cases - such as Mr D - accounting for a very small proportion.<sup>[11],[27]</sup> MDR-TB, with its lengthened infectious period and complicated treatment regimen,<sup>[6]</sup> presents a significant obstacle to TB control worldwide. It is estimated that only 10% of cases of MDR-TB are currently being diagnosed, and only half of these receive the appropriate treatment. <sup>[13]</sup> Therefore the WHO recommends that all patients receive rapid drug susceptibility testing when diagnosed;<sup>[28]</sup> a much-needed step to reduce MDR-TB, presupposing it is followed.

The causes of MDR-TB are multifactorial. Genetic mutations occur when the bacilli replicate, and these can make the bacteria resistant to certain medication. When the drug regimen is poorly or inadequately administered these bacilli can become dominant in the strain, causing resistant TB.<sup>[27]</sup>

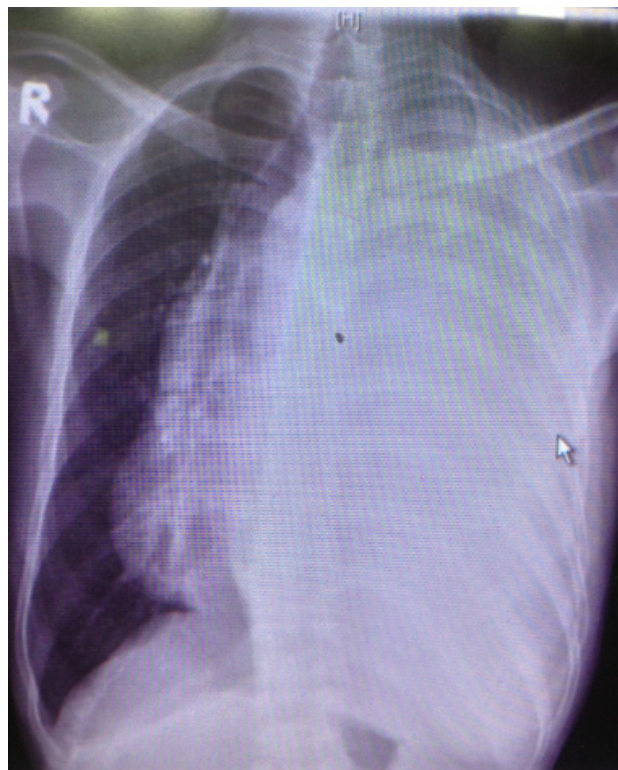


Figure 3a  
Chest x-ray showing Mr D's large left-sided pleural effusion:

Multi-drug resistant tuberculosis (MDR-TB) is defined as a strain of TB that is resistant to elimination by isoniazid and rifampicin, 2 of the most powerful first-line drugs.<sup>[25]</sup> Globally MDR-TB is estimated to account for 3.7% (650,000) <sup>[26]</sup> of new cases and 20% of those previously treated.<sup>[2]</sup> Fortunately the incidence of MDR-TB in India is rela-

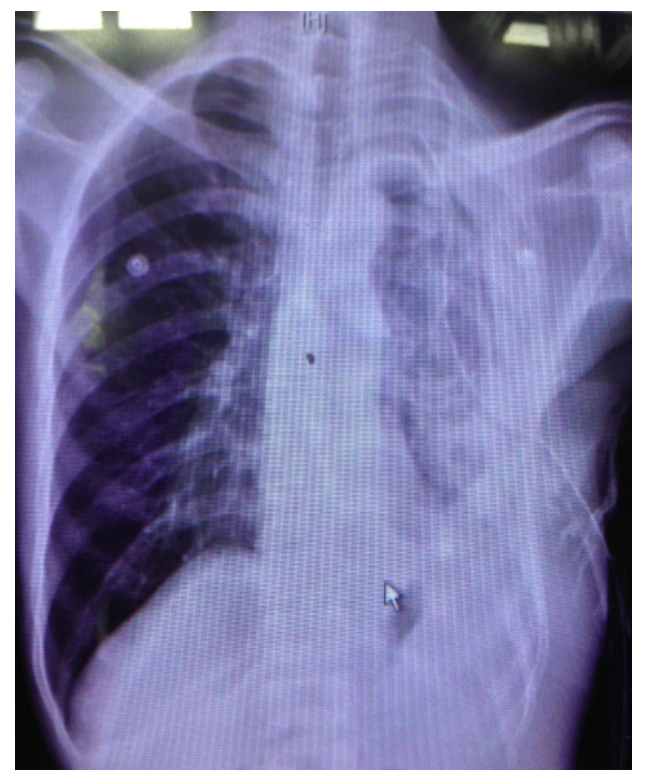


Figure 3b  
Mr D's Chest x-ray following drain insertion shows inadequate recovery:

Factors that can lead to a regimen being inadequate include, but are not limited to: non-compliance with guidelines; poorly monitored treatment; incorrect dosages or drugs used; poor quality and availability of medication; poor adherence to therapy course and lack of information regarding the risks.<sup>[27]</sup> A variety of socio-economic factors contribute to this, and whilst DOT acts to tackle these,



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they are still presenting a barrier to TB elimination. If inadequate drugs continue to be used in an MDR-TB patient this can create further resistance in the strain. This is a possible cause of Mr D's XDR-TB, and a problematic outcome of a fractured public/private medical system, highlighting the necessity of closely adhering to treatment guidelines.

As can be seen by Mr D's history, the treatment of MDR-TB is complex and prolonged. The WHO's 2011 revised guidelines suggest a combination of no less than 5 drugs, including an injectable, to be administered daily for a period of at least 8 months, followed by a further 12-20 months of tailored treatment.<sup>[28]</sup> This cocktail should include the first-line drug pyrazinamide, which may cause hepatotoxicity; a fluoroquinolone that risks GI and neurological disturbances; cycloserine, commonly causing CNS effects such as paranoia and psychosis; ethionamide, frequently resulting in nausea and vomiting; and a parenteral aminoglycoside, risking renal impairment and irreversible ototoxicity.<sup>[28]</sup> Simply the concept of this medication regime is off putting, let alone the practice of adhering to it for up to 20 months: it is easy to see how difficulties can arise in MDR-TB therapy. However, these recommendations do not necessarily apply to Mr D's strain of TB as there is a lack of evidence available on XDR-TB treatment<sup>[28]</sup>. Due to this, XDR-TB patients are likely to have further drugs added to their regimen, and a substantially increased treatment period<sup>[28]</sup>, complicating matters even further.

Despite this there is good news coming in from research in TB pharmacology. For the first time in 5 decades new drugs have been developed and are expected to be effective against MDR-TB, providing a shorter and better-tolerated treatment regimen, with a lower pill-burden.<sup>[26]</sup> Some of these medications are predicted to be available soon - late in 2013<sup>[29]</sup> - and so physicians need to keep abreast of these developments to ensure the best possible care, and reduce the risk of cases like Mr D's.

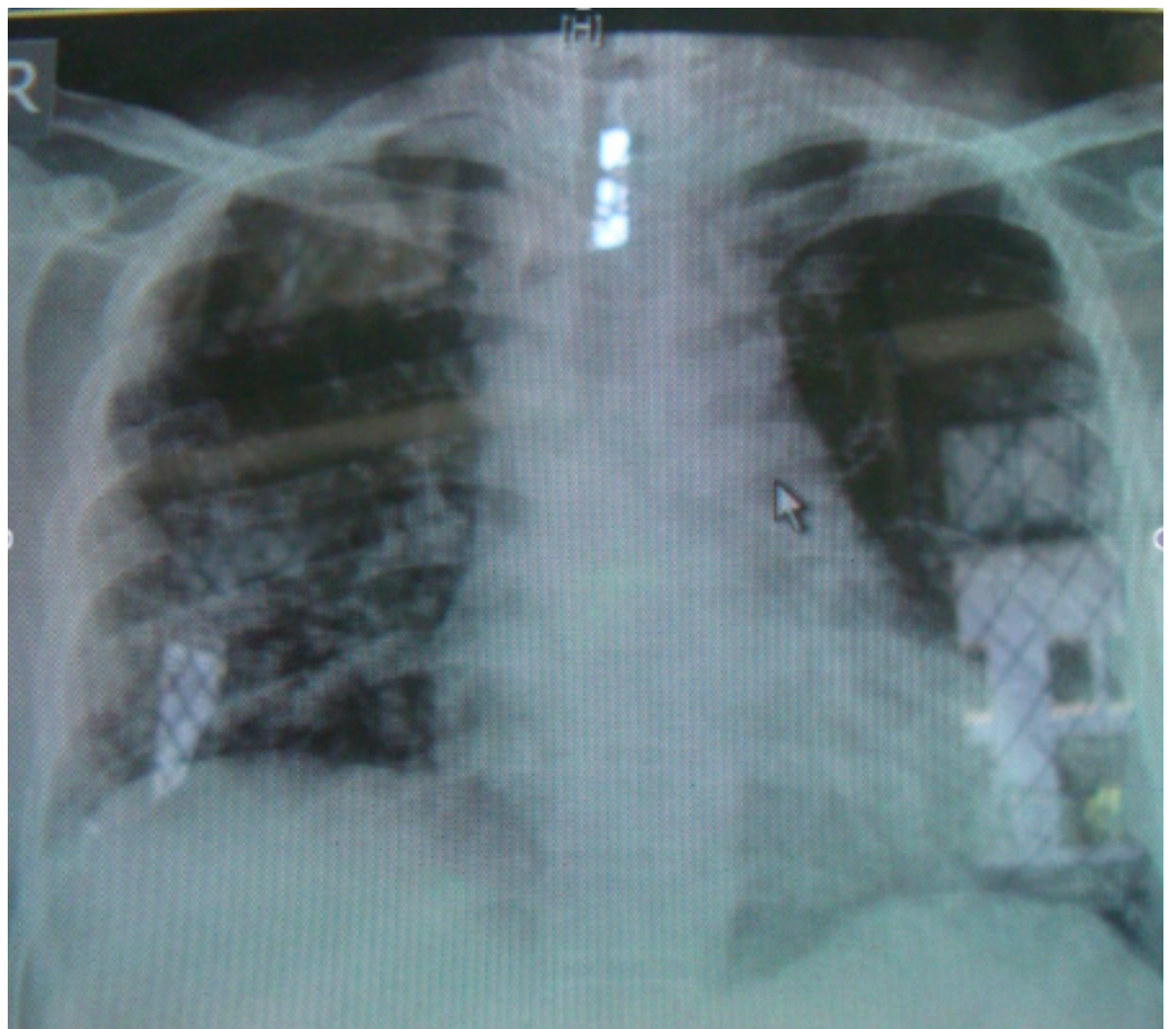
#### Case 4: Mr F

Mr F was a 43-year-old unemployed male with a standing diagnosis of HIV (WHO Classification Stage 4). He presented to outpatients with a 2-month history of low-grade fever and cough with expectoration. For the 2 days prior to presentation his fever had increased and he was experiencing intermittent chills and rigors, mild dyspnoea and a 'dull, aching' abdominal pain with distension. He had a history of chronic alcohol abuse and a 7-pack year history of cigarette smoking.

Examination found palpable left axillary, left supraclavicular and left posterior cervical lymph nodes. He was febrile at 101°F and tachypneic with a respiratory rate of 25.

Investigations revealed pancytopenia (Hb 6.0g/dL; WBC 3.5 x10<sup>9</sup>/L; Platelets <130 x10<sup>9</sup>/L); a decreased CD4 count (11%); granulomatous inflammation of pleura and bone marrow on biopsy (consistent with TB); the presence of non-resistant TB in sputum and bone marrow by Xpert MTB/RIF analysis;

Figure 4: Mr F's Chest x-ray showing a nodular pattern of disseminated tuberculosis



and multiple enlarged lymph nodes (on abdominal ultrasound). LFTs were not deranged.

A diagnosis of disseminated TB with concurrent HIV infection was made, and Mr F was started on first line anti-tubercular treatment as an inpatient. Due to the development of a rifampicin induced cholestasis Mr F's rifampicin was stopped and he was started on levofloxacin. He was also treated prophylactically with azithromycin due to his low CD4 count. His condition improved over 8 days and he was discharged to outpatient care.

Mr F's chest x-ray taken 2 days after admission showed a disseminated pattern of TB infection (see figure 4).

Globally 13% of all TB patients are HIV positive, with a vast majority (79%) of these individuals living in African countries.<sup>[2]</sup> Though in India HIV co-infection occurs in only 5% of all cases, in absolute figures this is nearly 10% of the worldwide burden<sup>[11]</sup>; further indicating the scale of the Indian epidemic.

In having HIV, Mr F's immune system had been drastically weakened, reduc-





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ing his ability to fight and contain infection by tuberculosis mycobacteria. Such individuals have increased susceptibility not only to new infection with TB, but also re-activation of latent bacteria. Considering that one-third of the world's population is postulated to have latent TB,<sup>[6]</sup> this is not an insignificant risk.

HIV and TB are a deadly combination. TB increases the rate of HIV replication and progression of infection, whilst HIV reduces the body's capability to fight the infection, dramatically increasing morbidity and mortality <sup>[30],[31]</sup>. Mr F's history makes this point clearly, with the infection spreading to his bone marrow and disseminating throughout his chest and abdomen. This synergy has led to TB being labelled as the leading cause of AIDS-related death worldwide.<sup>[32]</sup>

Rapid treatment for HIV-TB is essential in stopping these preventable deaths. Patients should be commenced on anti-retroviral therapy (ART) alongside standard tuberculosis medications, with studies showing that delaying ART can increase mortality by up to 100%.<sup>[33],[34]</sup> Recommendations currently state that ART should be started within 8-weeks of anti-tubercular treatment, and sooner in those with very low CD4+ counts. <sup>[31],[35]</sup> Unfortunately the concomitant use of these two treatment protocols is not without risk. Potential drug interactions complicate matters, with at least 10% of patients developing the immune reconstitution inflammatory syndrome (IRIS) after initiating joint treatment.<sup>[13]</sup> IRIS is a paradoxical worsening of tuberculosis, and other infectious conditions, following initiation of ART, and is more common in patients with low CD4+ count.<sup>[36]</sup> Furthermore, first-line drug rifampicin is an enzyme-inducer that will reduce the serum concentrations of medications used in ART. As such, rifabutin, a less-potent inducer, is recommended in HIV-TB cases. However this will only reduce, not remove, the influence. <sup>[26]</sup>

Considering the above it is worth bearing in mind TB prophylaxis. A patient such as Mr F could have been offered a 6-month course of isoniazid, as long as he had no signs of active infection. How-

ever, in this case Mr F's chronic alcohol abuse would have excluded him from receiving this treatment, as the combination incurs a high risk of hepatotoxicity.<sup>[37]</sup> Other inclusion criteria, such as availability to follow-up and good HIV/TB programmes, must also be met to provide preventative therapy. <sup>[37]</sup>

Prophylaxis for opportunistic infections in HIV-TB patients is available through the use of cotrimoxazole, a broad-spectrum antibiotic. It is a well-tolerated and cost-effective medication with a strong evidence base in reducing hospitalisation and mortality.<sup>[31]</sup> However, studies in India have shown limited efficacy, despite the drug being freely available at chemists, due to poor adherence and inadequate ART administration.<sup>[38]</sup> Thus the routine inclusion of cotrimoxazole as part of ART for HIV-TB patients is strongly recommended,<sup>[31]</sup> but this will rely upon the presence of good HIV programmes.

The complex, deadly interactions of these two epidemics provide a great deal more for consideration than discussed here. Expanding on this knowledge and collaborating closely with HIV and TB teams is essential for the effective support of cases such as Mr F.

#### CONCLUSION

Tuberculosis is a global killer. In order to care for its victims and assist in its eradication physicians need to be aware

of the numerous complications and obstacles involved in treatment. This report describes four case histories of TB, each highlighting a different aspect of the disease and expanding our knowledge of effective management. Awareness of TB presentation and at-risk patient groups is necessary for quick and accurate diagnosis, helping to reduce mortality, morbidity and abate the spread of the infection. Further consideration of the possible complications and co-morbidities that can arise over the lengthy course of treatment is necessary, as they are not uncommon and may considerably compound the affect of disease upon the patient's life. Close adherence to published treatment protocols is essential as drug-resistance can emerge, bringing with it increased morbidity and a vastly convoluted treatment regimen. Finally, the lethal synergy of HIV and TB means that co-infection must be consistently considered and actively prevented, with treatment administered rapidly and effectively when it occurs. By keeping these factors in mind doctors in every country, regardless of the disease prevalence, can help face and eliminate the burden of TB.

#### Reflection

I have really valued and enjoyed my time working on this eSSC project. I feel very lucky to have had the chance to witness the treatment of TB, an important global disease, in a country where it presents such a problem.



Figure 5: Cluttered corridors at CMC



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I can say without a doubt that the experience has drastically improved my knowledge of the illness and I would hope that I am much better equipped to manage these cases. Furthermore the perspective I gained has made me take stock of aspects of the English healthcare service I have taken for granted, such as freedom of access and dedication to patient privacy. Despite CMC having a very similar structure to UK hospitals and access to comparable medical therapies, I found the care provided different in several fundamental ways. Not nearly as much importance was placed upon cleanliness and patient privacy as it would have been in the UK, and what struck me most was the lack of working hand washing facilities in the toilets – even on the infectious diseases ward! Despite this, the driven and committed attitude of all of the staff - without exception - was inspiring, and there was no doubt that the patients felt safe and cared for in their hands. I would like to emulate this attitude in my career and hope this may make my patients feel the same way.

In having to find my way in a large, busy foreign hospital I believe that I have further developed my ability for independent learning. This will be of incredible use to me in Fourth Year, hopefully encouraging me to engage fully with the programme and actively gain experiences I may otherwise have been too timid to. As such I am very glad that I undertook such a project for my Third Year SSC. Furthermore, presenting case studies is an important method of communication amongst the medical profession, and in doing so I have improved and developed upon the skills I acquired in the Third Year Medicine and Surgery module. This SSC gave me the opportunity to gather new knowledge that does not sit within the core curriculum of the medical course. In producing it in this manner – as an overview for a medical student audience – I feel I made the most of this, and hope that it would be useful for other students to read.

Despite this, I feel slightly unfulfilled with the final report I have produced. In this project I gathered a wide span of



Figure 6: Broken sinks in the patient's toilet

information but was unable to delve into any aspect in much detail, despite very much wanting to. Ideally I would have produced a much larger, more in-depth final result, and would certainly be interested in expanding upon what I have gained here in the future. Furthermore I found it difficult to display a great deal of original, critical thought whilst trying to fulfil the aims of my project. Therefore, I feel I was unable to develop this aspect of my academic work as much as I would have liked, and will be looking to undertake a narrower brief for my next project in the hopes that I can rectify this.

In conclusion, I have relished the opportunity to learn about TB in such a first hand way, and have gleaned a great deal more from this than I would have in doing a library project on this topic.

#### REFERENCES

1. WHO, Global Health Observatory, Tuberculosis, Website Accessed via URL: <http://www.who.int/gho/tb/en/index.html/> on 24/07/2013
2. World Health Organisation. Global tuberculosis report 2012. Geneva: World Health Organization. WHO/HTM/TB/2012.6 (2012)
3. Kuehne J & Finch K. Bridging The Gap: Why the European Union must address the global fund's funding crisis to tackle the escalating HIV and TB epidemics in Eastern Europe and Central Asia, TB Europe Coalition. Position Paper. (September 2012)
4. Pedrazzoli D, Fulton N, Anderson L, et al, Tuberculosis in the UK: 2012 Report, Health Protection Agency. (5th July 2012)
5. Christian Medical College, Vellore. Facts and Figures. Website Accessed via URL: <http://www.cmch-vellore.edu/pdf/CMC-Year2012.pdf> on 21/07/2013
6. National Institute for Health and Care Excellence. (2011) Tuberculosis: Clinical diagnosis and management of tuberculosis, and measures for its prevention and control. (CG: 117). London: National Institute for Health and Care Excellence.
7. Lawn, SD, Zumla AI. Tuberculosis. *Lancet*. (2011). 278:57-72
8. Getahun H, Kittikraisak W, Heilig CM, et al. Development of a standardized screening rule for tuberculosis in people living with HIV in resource-constrained settings: individual participant data meta-analysis of observational studies. *PLoSMed*. (2011). 8:1]
9. Revised National Tuberculosis Control Programme. RNTCP At a Glance. Training Module. Accessed via URL: <http://www.tbcindia.nic.in/pdfs/RNTCP%20at%20a%20Glance.pdf> on 15/07/2013
10. World Health Organisation. TB Xpert Project. Information Leaflet. (2013). Ac-





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cessed via URL: [http://who.int/tb/features\\_archive/TBXpert\\_briefing\\_note.pdf](http://who.int/tb/features_archive/TBXpert_briefing_note.pdf) on 24/07/2013

11. Directorate General of Health Services. TB India 2012: Revised National Control Programme Annual status report. (March 2012). New Delhi: IG Printers Pvt.

12. World Health Organisation, Stop TB Partnership. The Stop TB Strategy: Building on and enhancing DOTS to meet the TB-related Millennium Development Goals. Geneva: World Health Organisation. WHO/HTM/TB/2006.368. (2006).

13. Zumla A, Raviglione M, Hafner R, Fordham von Reyn C. Tuberculosis. *NEJM*. (2013). 368:745-755

14. John KR, Daley P, Kincler N et al, Cost incurred by patients with pulmonary tuberculosis in rural India. *Int J Tuberc Lung Dis*. (2009). 13(10):1281-7

15. NHS, Tuberculosis, Accessed via URL: <http://www.londonhp.nhs.uk/services/tuberculosis/> on 22/08/2013

16. World Health Organisation. Treatment of tuberculosis guidelines: Fourth Edition. Geneva: World Health Organisation. WHO/HTM/TB/2009.420 (2010)

17. Shamaei M, Taharsi P, Poihan S et al. Tuberculosis-associated secondary pneumothorax: a retrospective study of 53 patients. *Respir Care*. (2011). Mar: 56(3):298-302

18. Salkin D. Tuberculosis as a cause of upper lobe bronchiectasis. *Calif Med*. (1950). 73(6):577-580

19. Jafari NJ, Izadi M, Sarrafzadeh F et al. Hyponatremia due to pulmonary tuberculosis: review of 200 cases. *Nephrourol Mon*. (2013). 5(1):687-691

20. Sharma R, Acharya K, Poornima V. A rare complication of pulmonary tuberculosis. *JACM*. (2007). 8(2): 179-81

21. Anderson NE, Somaratne J, Mason DF et al. Neurological and systemic complications of tuberculous meningitis and its treatment at Auckland City Hospital, New Zealand. *J Clin Neurosci*. (2010). 17(9):1114-8

22. Saaq M, Shah SA, Zubair M. Abdominal tuberculosis: epidemiologic profile and management experience of 233 cases. *J Pak Med Assoc*. (2012) 62(7):704-7

23. Caws M, Thwaites G, Dunstan S et al. The influence of host and bacterial genotype on the development of disseminated disease with *Mycobacterium tuberculosis*. *PLoS Pathog*. (2008). 4(3).e1000034

24. TB Europe Coalition. Extrapulmonary Tuberculosis - A Challenging Problem. (2013). Online Information Video. Accessed via URL: <http://www.tbcoalition.eu/2013/03/25/extrapulmonary-tuberculo->

<http://www.tbcoalition.eu/2013/07/18/2739/> on 22/07/2013

25. Iseman MD, Goble M. Multidrug-resistant tuberculosis. *NEJM*. (1996). 334(4): 267

26. Zumla A, Nahid P, Cole ST. Advances in the development of new tuberculosis drugs and treatment regimens. *Nature Reviews Drug Discovery*. (2013). 12:388-404

27. Directorate General of Health Services. TB India 2012: Revised National Control Programme: Guidelines on Programmatic Management of Drug Resistant TB (PMDT) in India (May 2012). New Delhi.

28. World Health Organisation. Guidelines for the programmatic management of drug-resistant tuberculosis: 2011 Update. Geneva: World Health Organisation. WHO/HTM/TB/2011.6 (2011)

29. TB Europe Coalition. Multi-drug Resistant Tuberculosis – No Promises. (2013). Online Information Video. Accessed via URL: <http://www.tbcoalition.eu/2013/07/18/2739/> on 22/07/2013

30. Churchyard GJ, Kleinschmidt I, Corbett EL et al. Factors associated with an increased case-fatality rate in HIV-infected and non-infected South African gold miners with pulmonary tuberculosis. *Int J Tuberc Lung Dis*. (2000) 4:705-12.

31. World Health Organisation. WHO policy on collaborative TB/HIV activities: Guidelines for programmes and other stakeholders. Geneva: World Health Organisation. WHO/HIV/2012.1 (2012)

32. TB Europe Coalition. TB-HIV Co-infection. Website accessed via URL: <http://www.tbcoalition.eu/what-is-tuberculosis/tb-hiv-co-infection/> on 22/07/2013

33. Gandhi NR, Moll A, Sturm AW et al. Extensively drug-resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural area of South Africa. *Lancet*. (2006). 368: 1575-1580

34. Dheda K, Shean K, Zumla A. et al. Early treatment outcomes and HIV status of patients with extensively drug-resistant tuberculosis in South Africa: a retrospective cohort study. *Lancet*. (2010). 375:1798-1807.

35. Havlir DV, Kendal MA, Ive P. et al. Timing of antiretroviral therapy for HIV-1 infection and tuberculosis. *NEJM*. (2011). 365:1482-1491.

36. Naidoo K, Yende-Zuma N, Padavtchi N et al. The immune reconstitution inflammatory syndrome after antiretroviral therapy initiation in patients with tuberculosis: findings from the SAPIt trial. *Ann Intern Med*. (2012). 157:313-324.

37. Department of Health Republic of South

Africa. Guidelines for tuberculosis preventative therapy among HIV infected individuals in South Africa. (2010). Report issued online. Accessed via URL [http://www.who.int/hiv/pub/guidelines/south\\_africa\\_hiv\\_tb.pdf](http://www.who.int/hiv/pub/guidelines/south_africa_hiv_tb.pdf) on 24/07/2013

38. Raizada N, Chauban L, Babu B. Linking HIV-Infected TB Patients to Cotrimoxazole Prophylaxis and Antiretroviral Treatment in India. *PLoS One*. (2009). 4(6):e5999

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