Narayana Health · Bangalore · India · Elective 2014

Describe the pattern of pulmonary disease in India, how does this differ from the U.K.

My original plan was to write about tuberculosis in India but that is what I expected to see. What would be more beneficial is talk about two conditions that took me by surprise and that is how environmental factors influences the epidemiology of asthma and chronic obstructive airways disease (COPD)

Where there is smoke, there is fire

Patients I saw in India that were diagnosed with COPD were not the same as the demographic seen in the U.K. Many were women who had never smoked cigarettes. Previously, COPD and significant tobacco use, was to me, synonymous. Then I learnt that they had an exposure to biomass fuel or other pollutants.

Almost half the world's population (3 billion) is exposed to biomass fuel exposure; 50% of all households and 90% of rural households [1]. In India, more than 80% of homes use bio-mass fuel [1]. In contrast, 1.01 billion people smoke tobacco [1]. Worldwide it seems pollutants such as, biomass, may be a bigger risk factor than smoking.

A study conducted in the slums of Pune, India, studied 12,055 people using a respiratory symptoms questionnaire and found an overall rate of COPD in 6.7%; 68.6% of those patients had never smoke [1]. The risk factors identified were biomass exposure. Interestingly, in England 8215 participants were studied using spirometry and found an overall prevelance of 13.3% of COPD; as a proportion 29.5% of those patients had not smoked [2]. However, the risk factors in this sub group was not identified.

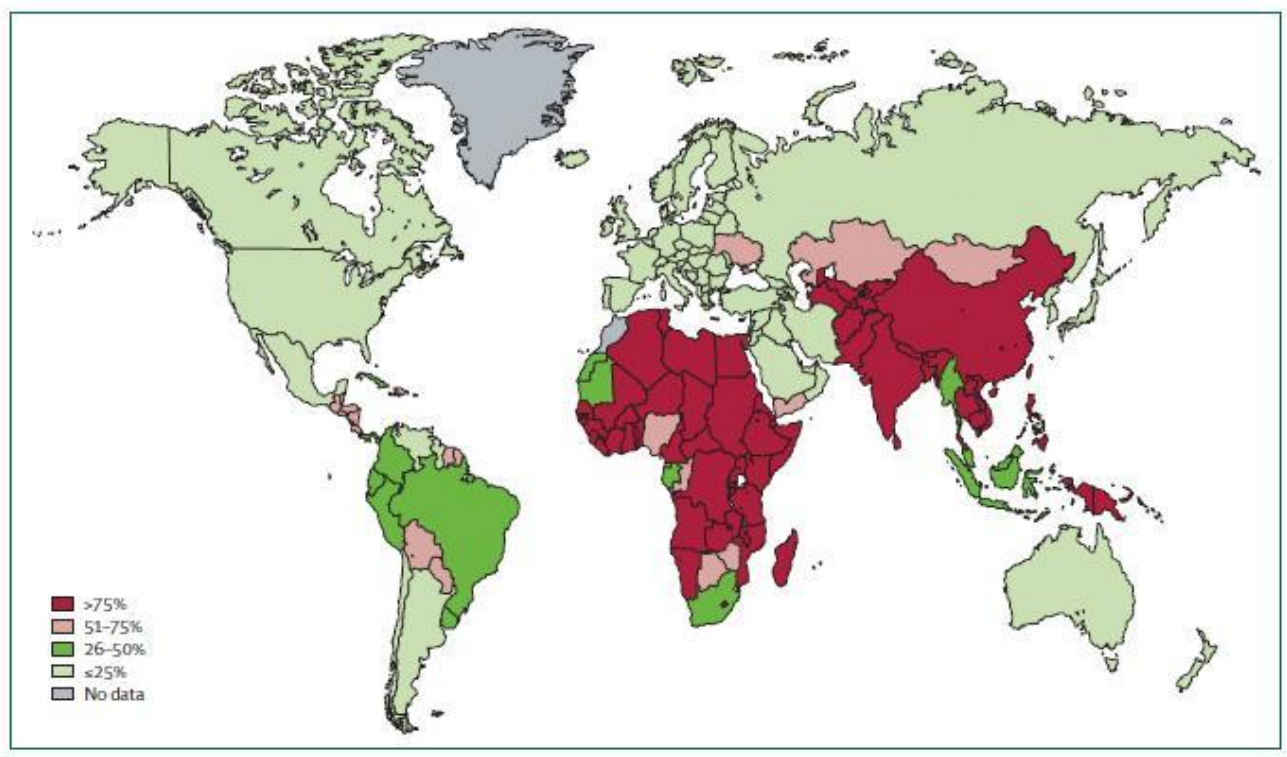

Figure 1: Proportion of households using biomass fuel for cooking worldwide [1]

Biomass is derived from plant or animal source, for example, cow dung patties. They provide energy inefficiently that leads to many pollutants harmful to health. In the economic struggles of rural areas in less affluent countries it is difficult to discourage its use. Nevertheless, raising its awareness may help with improved ventilation strategies.

Helminths, co-evolution and the hygiene hypothesis in asthma

One of my first experiences in the *out patients department* involved a young girl who came in for microcytic anaemia, the consultant put her on a course of anti-helminth medication. At this point I thought I missed something about her history but later on it occurred to me, world-wide parasitic infection is the leading cause of iron-deficiency. This consultation relates to another observation I had that is, compared to the U.K. there is drastically less asthma patients. The environment here in India is different. This being the leading theory to explain the comparatively low rates of asthma in India and other 'eastern' countries, one proposal called the *hygiene hypothesis*.

The hygiene hypothesis states that from birth our immune system is modulated with pathogenic pressure and this is essential for a healthy immune system. The trend in affluent countries is towards high levels of sterility, in the environment and the food we eat. Also, rural farming and livestock practices are uncommon. This with high levels of antibiotic use creates an immune system biased towards the TH_2 pathway [3,4], which will react to harmless antigens and create the various auto-immune conditions such as asthma. This is supported by epidemiological evidence that shows an inverse relationship between early childhood infection and asthma [4].

Another fascinating view is the "*old friends theory*" [5]. This is the explanation that over human evolution we have co-evolved our immune system with hunter-gatherer ancient micro-flora. Helminthes infections being a prominent "old friend" that exists in dead vegetation and mud. This is in contrast to "*crowd infections*" which are only recently evolved such as the common cold, when societies became much larger. With improved sanitary control we have helped eradicate cholera and thyphoid infections but possibly inadvertently lost the some important micro-flora. Indeed, IgE is responsible for reacting against helminth infections and also is raised in asthma. Therefore, there is some growing interest that helminth treatment may be beneficial in autoimmune diseases [6].

So it seems the young girl who came to the clinic to help her with a troublesome helminth infection may have been asking for an inhaler in the U.K.

1. Salvi S, Barnes P (2009). Chronic obstructive pulmonary disease in non-smokers. *Lancet* **374**:733-43
2. Shahab L, Jarvis MJ, Britton J, West R. Prevalence, diagnosis and relation to tobacco dependence of chronic obstructive pulmonary disease in a nationally representative population sample. *Thorax* 2006; **61:** 1043–47.
3. Peter J.M. (2000). Do common childhood infections 'teach' the immune system not to be allergic? *Immunology Today* **21** (3): 118–20.
4. Hertzen LC, Haahtela T (2004). Asthma and atopy – the price of affluence? *Allergy* **59**:124-137
5. Raz E (2010). Mucosal immunity: aliment and ailments. *Nature – mucosal immunology* **3**(1):4-7.
6. Leonardi-Bee J, Pritchard D, Britton J (2006). Asthma and current intestinal parasite infection: systematic review and meta-analysis. *American Journal of Respiratory and Critical Care Medicine* **174** (5): 514–523.

This hospital provides cost effective healthcare to a relatively deprived population & still produces a significant profit. How is this achieved?

England Vs India batting average

The National Health system (NHS) forged in 1948 is one of the biggest companies in the world, ranking 5th just below McDonalds in number of employees [1]. They provide for the 83% of the total health care spending in the U.K [2]. In India the figures are reversed, private health represents 73.8% of the money spent [3]. The U.K spends approximately double what India spends as a proportion of GDP (9.8% and 4.2% respectively) [3].

Nevertheless, health care in India has a significantly reduced cost. In cardiac surgery, the NHS tariff is placed between £8,226-11,757. The cost in India is somewhere between £3,100-4,340. At Narayana Health they have lowered the figure further to £1,116 [3].

Henry Ford of Healthcare

The founder of NH, Dr. Devi Shetty, has been likened to Henry Ford. Ford is famous for creating the assembly line and mass production in the Ford Motor Company. This utilizes *economies of scale* where the cost per unit of output generally decreases. This is because the fixed costs are spread over more units and this is true at NH where they have a 1,000 bed cardiac hospital.

Besides standard economic theory there are more esoteric comparisons that could be made. There is a legend that surrounds Henry Ford, where he has been described to send out his team to junk yards to see what parts tend to fail in scrapped cars. Many parts showed fatal signs of wear but one part was always in pristine condition, that being the *kingpins*. Ford instead of showing satisfaction of the kingpins, ordered that this part was in fact over-engineered, and has no value in outlasting the car so needs to be made to a lower specification. Dr. Devi Shetty challenges conventions and asks *"When somebody does an appendix operation the person who hands over the instrument has to be a BSc in Nursing. Is it required for that qualified person to do this?"* [4].

1. Alexander R (2012). Which is the world's biggest employer? *BBC News Magazine*. URL [http://www.bbc.com/news/magazine-17429786]. Accessed [01/04/14]

2. Nuffield trust (2013). UK spending on public and private healthcare. *Nuffield Trust*. URL [http://www.nuffieldtrust.org.uk/data-and-charts/uk-spending-public-and-private-health-care]. Accessed [03/04/14].

3. Cawston T (2011). High volume, specialist cardiac care in Bangalore, India. *Reform.* URL [moreforless.reform.co.uk/pdfs/Narayana_Hrudayalaya.pdf]. Accessed [03/04/14]

4. Dr Devi Shetty, in *Reform* (2011), A lot more for a lot less.

Discuss an interesting case seen during the placement

Case history

Mr. AB is a 19 year old previously fit and healthy gentleman who presented with a cough. The cough was present for four months and was to a certain degree productive of white sputum. This was associated with breathlessness that was worse at night. He also described a wheeze which came on and off. In addition, there were non-specific symptoms of tiredness, weight lost with a loss of appetite. He had no symptoms of orthopnoea, atopy or did not previously have tuberculosis. He has a brother that is healthy and does not have breathing difficulties or a cough.

On examination Mr. AB looked well although slightly underweight. His lung fields were clear, heart sounds normal and abdomen soft non-tender.

Initial investigation

Initial blood tests were taken and surprisingly the white cell count was at **25.5**. However, the differential was not done and so the physician instigated Augmentin and had the blood tests repeated. Two days later the white cell count now slightly up from last time came to be **26.9**, with a **72.4%** eosinophilia. Other abnormal tests included a macrocytosis with MCV at **104**, this was with a vitamin B_{12} of **102** and folate of **2**. The ALP was also raised at **225** and CRP was at **3.36**. The haemoglobin and platelets were in the normal range.

Further investigation

Further investigations revealed largely no abnormalities. Viral serology was negative (hepatits B&C and HIV), vasculitic screen was negative (pANCA, cANCA, ANA). The TSH came slightly elevated at 6.11, but with no free T4 for evaluation. The ECG was normal. On stool sampling ova and cysts were negative.

Spirometry testing revealed a non reversible restrictive lung disease:

	Pre bronchodilator	**Post bronchodilator**
FEV_1	**63%**	**61.9%**
FEV_1/FVC ratio	**91.7%**	**92.6%**

The chest x-ray was normal. However, the CT revealed subtle fibrotic strands and a small nodule in the anterior segment in the lung, likely to be inflammatory etiology, there was no significant mediastinal lymphadenopathy. The bone profile was completed and found eosinophilic proliferation but with no malignant changes. Genetic testing looking for the abnormal fusion gene encoding *FIP1L1-PDGFR* alpha protein found in 12-18% in patients with idiopathic hypereosinophilic syndrome compared to 0.4% in the normal population [3] was found to be negative.

Fourteen days after presentation the white cell count was persistently raised at 23.8. A provisional diagnosis of *primary idiopathic eosinophilic syndrome* was made and the patient started on steroid treatment.

Discussion

The role of eosinophils include defense against parasites, allergies and tissue inflammation. Eosinophilia can be *secondary* and raised due to a stimulus, or *primary* and so raised due to a bone marrow etiology [1] (see *figure 1*). In the case of Mr. AB there were no secondary causes to be found. In investigating primary causes the bone marrow biopsy shows hypereosinophilia but with no clonal expansion of malignant cells.

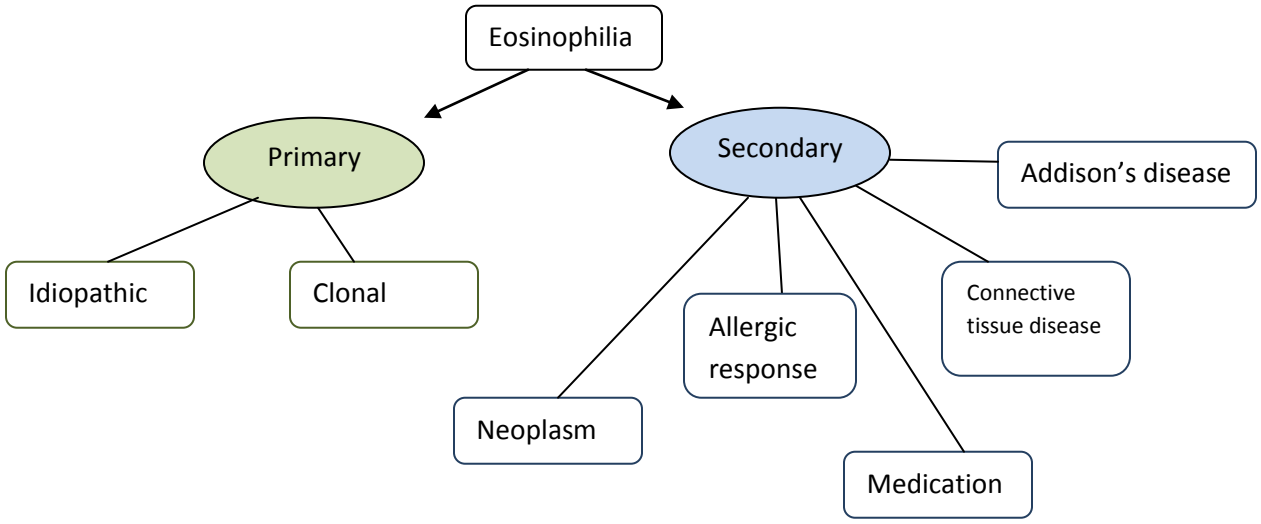

Figure 2: classification of eosinophilia

Therefore, a working diagnosis of idiopathic Eosinophilia is to be considered here, which is made as a diagnosis of exclusion. However, it is difficult diagnoses to make as in retrospect studies have shown patients to have malignant changes in the bone marrow [2]. Indeed, in the long term future these so called "idiopathic" patients may undergo malignant transformation.

Hypereosinophilic syndrome (HES) is a subset of idiopathic Eosinophilia, the syndrome is characterised by [3];

- A sustained absolute eosinophilic count (AEC) greater than >1500µl, persisting longer than 6 months.
- No identifiable etiology for eosinophilia is present.
- Patients must have signs and symptoms of organ involvement.

Although Mr. AB has an AEC of 20,444µl, this has not been proven to last greater than 6 months. On the other hand, his signs and symptoms may relate to the high eosinophilic count. The common signs and symptoms of HES are;

- Cardiac: chest pain, dyspnea, orthopnea
- Haematological: left upper quadrant pain due to splenomegaly
- Neurological: stroke, peripheral neuropathies
- Pulmonary: chronic persistent cough, usually non-productive
- Rheumatological: arthalgia

- Dermatological: pruritis, dermatographism and angioedema
- Gastrointestinal: diarrhea, nausea, vomiting
- Constitutional: fever and night sweats

HES can affect any system and Mr. AB has presented with a persistent cough, which could be attributed to HES. Other pulmonary eosinophilic conditions that could be considered, but does not fit the criteria, are Churg-Strauss syndrome, Loefflers syndrome, eosinophilic granuloma (Histiocytosis X)

Although no sinister causes of the eosinophilia can be found, the high levels of this white cell can itself cause problems, most notably cardiac disease such as, restrictive cardiomyopathy. Asymptomatic patients can be followed up and monitored with tropinin levels, echo and pulmonary function tests. The mainstay of treatment is suppression of the bone marrow using glucocorticoids and then second line with interferon alpha and hydroxyurea. However, those with a *FIP1L1/PDGFRA* mutation, which this patient does not have, imatinib is very effective [3].

1. Liss M (2013). Eosinophilia. *Medscape* URL [http://emedicine.medscape.com/article/199879-overview]. Accessed [04/05/14].

2. Guitart J (2000). Idiopathic eosinophilia. *N Engl J Med* **342**:659-661.

3. Samavedi V (2012). Hypereosinophilic syndrome. *Medscape* URL [http://emedicine.medscape.com/article/202030-overview]. Accessed [04/05/14].