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In this issue we have papers on the causes and rate of adherence to inhaler therapy in patients with bronchial asthma in Jordan. The authors found non-adherence was found to be significant and due to non-drug related causes and mainly caused by poor patient understanding of their condition and treatment. Education of patients is required to improve rates of adherence.

A paper from Turkey looks at whether or not there are some positive correlations between leg ulcers and severity of sickle cell diseases (SCDs). The authors concluded that SCDs are chronic destructive processes on capillaries initiating at birth, and terminate with early organ failures in life. Probably leg ulcers are found among the terminal consequences of the inflammatory processes that may indicate shortened survival.

A joint paper from Australia and Iran looks at virus mutation and spread. When there is still so little known about viruses it is important to know patterns of spread and mutation so that medical practitioners remain alert for new mutations and outbreaks and the global spread of existing viruses.

A paper from Iraq looks at the burden of war and particularly the use of degraded uranium during regional conflicts, causing short term and long term genetic damage to populations where it has been used.
Poor adherence to inhaler therapy in patients with bronchial asthma: Rates and causes

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ABSTRACT

Objective: To assess adherence rates to inhaler therapy in bronchial asthma patients, and to find out the most common causes of non-adherence.

Method: prospective study of 295 patients diagnosed to have bronchial asthma in King Hussein Medical Center (KHMC) in the period between March 2014 and January 2015. Patients were followed up for 15 weeks, after which adherence to their inhaler therapy was assessed, and the causes of non-adherence were investigated.

Results: It was found that 138 patients from the 295 patients included in our study were non-adherent to their inhaler therapy, which equals 47% of the patients in this study. The most common cause for non-adherence was the patients’ fear that using inhalers would be habit forming, and would be associated with a social stigma. This cause accounted for 46% of the causes for non-adherence in our study group.

Conclusion: Non-adherence rates to inhaler therapy in bronchial asthma were shown to be significant in our study. The fact that the most common causes for non-adherence in our study were found to be due to non-drug related causes, and mainly caused by poor patient understanding of their condition and treatment, makes patient’s education very important, and emphasizes the significance of doctor-patient communication to answer all the questions that might cause non-adherence to inhalers.

Key words: Bronchial asthma, Inhaler therapy, Adherence, Jordan
**Introduction**

Bronchial asthma is one of the most common chronic diseases in the world. The incidence and prevalence of bronchial asthma is increasing, and studies show that bronchial asthma affects 5-10% of the population worldwide. (1,2) Being a chronic and common medical condition, proper management of bronchial asthma is a very important goal to achieve. Inhaler therapy is the cornerstone in bronchial asthma management. (3,4) Inhalers have the advantage of delivering high concentration of the medications to the airways with minimal systemic side effects. (5) A common issue which is usually faced and prevents proper management of bronchial asthma is non-adherence to the inhaler therapy. Some studies show adherence rates of around 50% in bronchial asthma patients.(6) This means that about half the patients diagnosed to have bronchial asthma are non-adherent to their inhaler therapy.

Poor adherence to inhaler therapy increases the risk of morbidity and mortality from bronchial asthma. (7,8) It was shown that poor asthma control is a frequent cause of Emergency Department (ER) presentation and hospital admission.(9)

Another important aspect that shouldn’t be overlooked is the economic burden of uncontrolled bronchial asthma to the health care system. This aspect has been studied and documented in industrialized countries.(10) It was shown that 1/3 of all asthma costs in the United States of America come from ED use for managing bronchial asthma.(11)

In our study, the aim was to follow up patients diagnosed with bronchial asthma for 15 weeks, for whom inhaled therapy was given. We assessed the rates of adherence to these inhalers by the end of the 15-week period. The causes of non-adherence were also investigated in these patients, hoping that by knowing the causes of non-adherence we can maximize our efforts to target these causes and increase adherence rates to inhaled therapy in bronchial asthma patients.

**Methods**

In our study, 295 patients who were diagnosed to have bronchial asthma in KHMC, Respiratory Medicine Division, between March 2013 and January 2015, were enrolled for the study. All of these patients were prescribed inhaler therapy according to the GINA guidelines. Initially, proper education about their disease, the types of inhalers to be used and proper technique were explained to the patients. Follow up every 3 weeks for the next 15 weeks was done in the clinic. By the end of the 15 weeks, adherence to the inhaler therapy was assessed.

Adherence day was defined as a day in which the exact number of puffs of the prescribed inhalers was taken. Patients were labeled as adherent if they fit the above definition for more than 80% of the days of the study (>84 days).

During each visit to the clinic, the patients were asked about their adherence to inhalers during the 3 week period preceding their appointment, and the number of adherent days was recorded in their files. By the end of the 15 weeks, the number of adherent days was calculated by reviewing the patients’ files.

In the non-adherent group, the cause for non-adherence was investigated by asking the patients about the major reason that prevented them from adhering to their inhaler therapy.

**Results**

From the 295 patients with bronchial asthma who were enrolled in our study, 138 patients were found to be non-adherent to their inhaler therapy. This represents 47% of the patients in our study.

The cause was investigated in the non-adherent group. 63 patients (46% of the patients in the non-adherent group) stated that the major cause was that they were afraid that by using their inhalers regularly they will form a habit, which will be associated with a social stigma according to them. 54 patients (39% of the patients in the non-adherent group) said that they were non-adherent because they had doubts regarding the efficacy of inhalers, and they thought that oral treatment is superior to inhalers in treating bronchial asthma. 13 patients (9%) said that the cause was their fear of side effects. The remainder of the non-adherent patients (8 patients, 6%) gave other causes such as forgetfulness, difficulty in using their inhalers and refusing the concept of being asthmatics.

<table>
<thead>
<tr>
<th>Cause</th>
<th>Number of patients</th>
<th>% to non-adherent group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Habit forming and social stigma</td>
<td>63</td>
<td>46%</td>
</tr>
<tr>
<td>Inhalers are non efficient, and prefer oral treatment</td>
<td>54</td>
<td>39%</td>
</tr>
<tr>
<td>Fear of inhalers side effects</td>
<td>13</td>
<td>9%</td>
</tr>
<tr>
<td>Others*</td>
<td>8</td>
<td>6%</td>
</tr>
</tbody>
</table>

*Other causes such as forgetfulness, difficulty in using their inhalers and refusing the concept of being asthmatics.
Discussion

Bronchial asthma is a common chronic medical condition. Adherence to bronchial asthma treatment, of which inhaled therapy forms the cornerstone, decreases morbidity and mortality caused by this disease, and adherent patients are less likely to experience exacerbations than less adherent patients.(12)

However, adherence rates to inhaled therapy in bronchial asthma have been shown to be less than satisfactory. The WHO recorded adherence rates to treatment in chronic diseases to be around 50%.(13) Many other studies assessing adherence to inhaled therapy in bronchial asthma specifically showed non-adherence rates between 20-80%.(14)

In our study, it was found that 138 patients from the 295 patients with bronchial asthma enrolled in the study were non-adherent to their inhaled therapy, with non-adherence percentage of 47%.

This high percentage of non-adherence is worrisome and the causes of which should be investigated thoroughly.

In our study, it was found that the main causes for non-adherence were not related to the drugs per se, rather it was due to poor understanding by the patient about their disease and treatment choices and strategies.

We found that 46% of non-adherent patients were not adhering to their inhaled therapy because they were afraid that using the inhalers will form a habit, which is associated with a social stigma according to these patients. 39% of the patients in the non-adherent group stated that they were non-adherent because they preferred to use oral treatments because they thought it was superior to inhaled therapy. Other less common causes included fear of side effects of the inhaled therapy (9%), and forgetfulness, difficulty in using their inhalers and refusing the concept of being asthmatics (6%).

As it is clearly shown in our study, the main causes for non-adherence stem from poor understanding by the patient about bronchial asthma as a chronic, non curable disease, that needs lifelong treatment, and the significant role that inhaled therapy plays in managing bronchial asthma.

These causes for non-adherence were investigated thoroughly in various other studies. Gupta & Gupta found in their study that up to 76% of bronchial asthma patients consider inhaled therapy inferior to oral medications.(15) Another study done by Bedi found that 42% of the patients didn’t adhere to their inhaled therapy because they were afraid that it would be habit forming.(16)

The fact that the majority of the non-adherent patients stated causes which stemmed from poor understanding of their disease and treatment choices, makes patients’ education and doctor-patient communication of upmost importance in trying to improve adherence rates of bronchial asthma patients to inhaled therapy.
Conclusion

Non-adherence to inhaled therapy in patients with bronchial asthma is common. This emphasizes the need to regularly assess patients’ adherence to their inhaled therapy during their regular clinic visits.

The fact that non-adherence in bronchial asthma patients is mostly caused by non-scientific ideas by the patients about their disease and treatment methods, makes an informative doctor-patient relation very important, where patients should be educated about their disease, and the therapeutic strategies, of which inhaled therapy forms the cornerstone, discussed in detail with them.

References


3. G. Crompton A brief history of inhaled asthma therapy over the last fifty years Prim Care Respir J, 15 (2006), pp. 326-331


Leg ulcers in severity of sickle cell diseases

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ABSTRACT

Objective: Background: We tried to understand whether or not there are some positive correlations between leg ulcers and severity of sickle cell diseases (SCDs).

Methods: All patients with SCDs were taken into the study.

Results: The study included 346 patients with the SCDs (175 males). There were 50 cases (14.4%) with leg ulcers. Interestingly, the male ratio was significantly higher in patients with leg ulcers (74.0% versus 46.6%, p<0.001). Additionally, mean ages of the patients with leg ulcers were significantly higher than the patients without (35.0 versus 28.5 years, p<0.000). Prevalence of associated thalassemia minor was similar in both groups (64.0% versus 66.5%, respectively, p>0.05). On the other hand, smoking was significantly higher in patients with leg ulcers (28.0% versus 11.8%, p<0.05). Although the mean white blood cell and platelet counts of the peripheric blood were similar in both groups (p>0.05 for both), the mean hematocrit value was significantly lower in patients with leg ulcers (21.7% versus 24.0%, p= 0.002). On the other hand, although the painful crises per year, priapism, pulmonary hypertension, chronic obstructive pulmonary disease, coronary heart disease, rheumatic heart disease, and avascular necrosis of bones were all higher in patients with leg ulcers, the differences were only significant for digital clubbing, chronic renal disease, and stroke (p<0.05 for all).

Conclusion: SCDs are chronic destructive processes on capillaries initiating at birth, and terminate with early organ failures in life. Probably leg ulcers are found among the terminal consequences of the inflammatory processes that may indicate shortened survival.

Key words: Sickle cell diseases, leg ulcers, chronic capillary inflammation
Introduction

Atherosclerosis may be the major underlying cause of aging by inducing cellular hypoxia all over the body. As an example for the hypothesis, cardiac cirrhosis develops due to the prolonged hepatic hypoxia in patients with pulmonary and/or cardiac diseases. Probably whole afferent vasculature including capillaries are involved in atherosclerosis. Some of the currently known accelerator causes of the systemic process are smoking, physical inactivity, and overweight for the development of terminal consequences including obesity, hypertension, diabetes mellitus (DM), peripheral artery disease (PAD), chronic obstructive pulmonary disease (COPD), chronic renal disease (CRD), coronary heart disease (CHD), cirrhosis, mesenteric ischemia, osteoporosis, and stroke, all of which terminate with early aging and were researched under the title of metabolic syndrome in the literature (1-3). Similarly, sickle cell diseases (SCDs) are chronic destructive processes on capillaries. Hemoglobin S (HbS) causes loss of elastic and biconcave disc shaped structures of red blood cells (RBCs). Probably, loss of elasticity instead of shapes of RBCs is the major problem, since sickling is rare in the peripheral blood samples of SCDs patients with associated thalassemias, and human survival is not so affected in hereditary elliptocytosis or spherocytosis. Loss of elasticity is probably present in whole life, but exaggerated with conditions showing increased metabolic rate of the body. The hard RBCs may take their normal elastic natures after normalization of the metabolic rate, but they become hard bodies in time, permanently. The hard cells induced prolonged inflammation, edema, and fibrosis at capillary walls may terminate with tissue infarcts all over the body (4,5). On the other hand, obvious vascular occlusions may not develop in greater vasculature due to the transport instead of distributory functions of them. We tried to understand whether or not there are some positive correlations between leg ulcers and severity of SCDs.

Material and Methods

The study was performed in the Medical Faculty of the Mustafa Kemal University between March 2007 and December 2014. All patients with SCDs were taken into the study. The SCDs are diagnosed by the hemoglobin electrophoresis performed via high performance liquid chromatography (HPLC). Patients’ medical histories including smoking habit, regular alcohol consumption, painful crises per year, operations, priapism, leg ulcers, and stroke were learnt. Cases with a history of one pack-year were accepted as smokers, and one drink-year were accepted as drinkers. A check up procedure including serum iron, total serum iron binding capacity, serum ferritin, serum creatinine, hepatic function tests, markers of hepatitis viruses A, B, and C and human immunodeficiency virus, a posterior-anterior chest x-ray film, an electrocardiogram, a Doppler echocardiogram both to evaluate cardiac walls and valves and to measure the systolic blood pressure (BP) of pulmonary artery, an abdominal ultrasonography, a computed tomography of brain, and a magnetic resonance imaging (MRI) of hips was performed. Other bones for avascular necrosis were scanned according to the patients’ complaints. So avascular necrosis of bones was diagnosed via MRI (6). Cases with acute painful crises or any other inflammatory event were treated at first, and then the laboratory tests and clinical measurements were performed on the silent phase. Stroke is diagnosed by the computed tomography of brain. Acute chest syndrome is diagnosed clinically with the presence of new infiltrates on chest x-ray film, fever, cough, sputum production, dyspnea, or hypoxia in the patients (7). An x-ray film of abdomen in upright position was taken just in cases with abdominal distention and discomfort, vomiting, obstruction, and lack of bowel movement. The criterion for diagnosis of COPD is post-bronchodilator forced expiratory volume in 1 second/forced vital capacity of less than 70% (8). Systolic BP of the pulmonary artery of 40 mmHg or higher during the silent phase is accepted as pulmonary hypertension (9). CRD is diagnosed with a serum creatinine level of 1.3 mg/dL or higher in males and 1.2 mg/dL or higher in females during the silent phase. Cirrhosis is diagnosed with hepatic function tests, ultrasonographic findings, and histologic procedure in case of indication. Digital clubbing is diagnosed with the ratio of distal phalangeal diameter to interphalangeal diameter which is greater than 1.0 and with the presence of Schamroth’s sign (10,11). Associated thalassemia minors are detected with serum iron, total serum iron binding capacity, serum ferritin, and hemoglobin electrophoresis performed via HPLC. Stress electrocardiography is performed for cases with an abnormal electrocardiogram and/or angina pectoris. Coronary angiography is taken for the stress electrocardiography positive cases. So CHD was diagnosed either angiographically or with the Doppler echocardiographic findings as the movement disorders in the cardiac walls. Rheumatic heart disease is diagnosed with the echocardiographic findings, too. Ileus was diagnosed by the General Surgeons with the consultations in case of indication. Eventually, cases with leg ulcers and without were collected into the two groups, and they were compared. Mann-Whitney U test, Independent-Samples t test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 346 patients with the SCDs (175 males and 171 females). There were 50 cases (14.4%) with leg ulcers. Interestingly, the male ratio was significantly higher in patients with leg ulcers (74.0% versus 46.6%, p<0.001). Additionally, mean ages of the patients with leg ulcers were significantly higher than the others (35.0 versus 28.5 years, p<0.000). Prevalence of associated thalassemia minor was similar in both groups (64.0% versus 66.5%, respectively, p=0.05). On the other hand, smoking was significantly higher in patients with leg ulcers (28.0% versus 11.8%, p<0.05) (Table 1). Although the mean white blood cell (WBC) and platelet (PLT) counts of the peripheric blood were similar in both groups (64.0% versus 66.5%, respectively, p>0.05). On the other hand, smoking was significantly higher in patients with leg ulcers (28.0% versus 11.8%, p<0.05) (Table 1). Although the mean white blood cell (WBC) and platelet (PLT) counts of the peripheric blood were similar in both groups (p>0.05 for both), the mean hematocrit (Hct) value was significantly lower in patients with leg ulcers (21.7% versus 24.0%, p=0.002) (Table 2). On the other hand, although the painful crises per year, priapism, digital clubbing, pulmonary hypertension, COPD, CHD, CRD, rheumatic heart disease, avascular necrosis of bones, and stroke were all higher in patients with leg ulcers, the differences were only significant for digital clubbing, CRD, and stroke (p<0.05 for all), probably due to the small sample size of the group with leg ulcers (Table 3). Additionally, there were four patients with regular alcohol consumption who are not cirrhotic at the moment. Although antiHCV was positive in seven of the cirrhotics, HCV RNA was detected as positive just in two by polymerase chain reaction.
### Table 1: Characteristic features of the study patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients with leg ulcers</th>
<th>p-value</th>
<th>Patients without leg ulcers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>14.4% (50)</td>
<td></td>
<td>85.5% (296)</td>
</tr>
<tr>
<td>Male ratio</td>
<td>74.0% (37)</td>
<td>&lt;0.001</td>
<td>46.6% (138)</td>
</tr>
<tr>
<td>Mean age (year)</td>
<td>35.0 ± 8.8 (16-58)</td>
<td>0.000</td>
<td>28.5 ± 9.9 (6-59)</td>
</tr>
<tr>
<td>Thalassemia minors</td>
<td>64.0% (32)</td>
<td>Ns*</td>
<td>66.5% (197)</td>
</tr>
<tr>
<td>Smoking</td>
<td>28.0% (14)</td>
<td>&lt;0.001</td>
<td>11.8% (35)</td>
</tr>
</tbody>
</table>

*Nonsignificant (p>0.05)

### Table 2: Peripheric blood values of the study patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients with leg ulcers</th>
<th>p-value</th>
<th>Patients without leg ulcers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Hct# value (%)</td>
<td>21.7 ± 5.2 (11-34)</td>
<td>0.002</td>
<td>24.0 ± 4.8 (12-42)</td>
</tr>
<tr>
<td>Mean PLT§ counts (µL)</td>
<td>445.810 ± 237.502 (56.000-1.142.000)</td>
<td></td>
<td>455.680 ± 227.874 (48.800-1.827.000)</td>
</tr>
</tbody>
</table>

*White blood cell †Nonsignificant (p>0.05) ‡Hematocrit §Platelet

### Table 3: Associated pathologies of the study patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients with leg ulcers</th>
<th>p-value</th>
<th>Patients without leg ulcers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Painful crises per year</td>
<td>5.2 ± 7.2 (0-36)</td>
<td></td>
<td>5.0 ± 8.2 (0-52)</td>
</tr>
<tr>
<td>Tonsillectomy</td>
<td>4.0% (2)</td>
<td></td>
<td>5.4% (16)</td>
</tr>
<tr>
<td>Priapism</td>
<td>6.0% (3)</td>
<td></td>
<td>2.0% (6)</td>
</tr>
<tr>
<td>Ileus</td>
<td>2.0% (1)</td>
<td></td>
<td>2.3% (7)</td>
</tr>
<tr>
<td>Digital clubbing</td>
<td>24.0% (12)</td>
<td>&lt;0.001</td>
<td>7.0% (21)</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>16.0% (8)</td>
<td></td>
<td>10.8% (32)</td>
</tr>
<tr>
<td>COPD†</td>
<td>20.0% (10)</td>
<td></td>
<td>12.8% (38)</td>
</tr>
<tr>
<td>CHD‡</td>
<td>12.0% (6)</td>
<td></td>
<td>5.7% (17)</td>
</tr>
<tr>
<td>CRDS</td>
<td>16.0% (8)</td>
<td>&lt;0.05</td>
<td>7.0% (21)</td>
</tr>
<tr>
<td>Rheumatic heart disease</td>
<td>10.0% (5)</td>
<td></td>
<td>6.0% (18)</td>
</tr>
<tr>
<td>Avascular necrosis of bones</td>
<td>26.0% (13)</td>
<td></td>
<td>20.2% (60)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>4.0% (2)</td>
<td></td>
<td>4.3% (13)</td>
</tr>
<tr>
<td>Acute chest syndrome</td>
<td>2.0% (1)</td>
<td></td>
<td>4.7% (14)</td>
</tr>
<tr>
<td>Stroke</td>
<td>16.0% (8)</td>
<td>&lt;0.05</td>
<td>7.4% (22)</td>
</tr>
<tr>
<td>Mortality</td>
<td>4.0% (2)</td>
<td></td>
<td>4.7% (14)</td>
</tr>
</tbody>
</table>

*Nonsignificant (p>0.05) †Chronic obstructive pulmonary disease ‡Coronary heart disease §Chronic renal disease
Atherosclerosis is the most common type of vasculitis all over the world, and it is the leading cause of morbidity and mortality in elders. Probably the whole afferent vasculature including capillaries are involved in the body. Chronic endothelial injury and inflammation due to the much higher BP of afferent vasculature may be the major underlying cause, and effenter vessels are probably protected due to the much lower BP in them. Vascular walls become thickened due to the chronic endothelial injury, inflammation, edema, and fibrosis, and they lose their elastic natures which can decrease the blood flow and increase BP further. The hard RBCs induced chronic endothelial injury, inflammation, edema, and fibrosis mainly at the capillary level build up a prototype of an advanced atherosclerosis in younger ages in the SCDs.

SCDs are life-threatening genetic disorders affecting nearly 100,000 individuals in the United States (12). They keep vascular endothelium mainly at the capillary level (13), since the capillary system is the main distributor of the hard RBCs to tissues. In other words, SCDs are mainly chronic inflammatory instead of obstructive disorders, and the major problem is probably endothelial injury, inflammation, edema, and fibrosis rather than the hard RBCs induced occlusions in the capillary lumen. As a result, the lifespans of females and males with the SCDs were 48 and 42 years in the literature (14), whereas they were 33.3 and 29.9 years in the present study, respectively. The great differences may be secondary to initiation of hydroxyurea therapy much earlier in developed countries. On the other hand, the prolonged lifespan of females with SCDs and longer overall survival of females in the world cannot be explained by the atherosclerotic effects of smoking alone, instead it may be explained by more physical power requiring role of male sex in life (15,16).

Leg ulcers occur in 10 to 20% of patients with SCDs, and they are more common in males (17). The incidence increases with age and they are very rare before the age of 10 years (17). They are the most common in sickle cell anemia (HbSS) cases (17). They have an intractable nature, and around 97% of healed ulcers return in less than one year (18). The ulcers occur in distal areas with less collateral blood flow in the body (18). The most common location for these ulcers to develop is above the medial malleolus (the Gaiter area). The lateral malleoli are involved secondly in frequency. The pathogenesis of leg ulcers may be complex including mechanical obstruction by the hard RBCs, abnormal autonomic control with excessive vasoconstriction when in the dependent position, in situ thrombosis, anemia with decreased oxygen carrying capacity, and decreased nitric oxide bioavailability leading to impaired endothelial function (19,20). Venographic studies have shown that venous insufficiency is not a primary cause of the ulcers (17). Chronic damage to microcirculation of the skin via the hard RBCs is probably the major cause of leg ulcers in the SCDs (17). Increased exposure to the causative factors due to the blood pooling in the lower extremities by the effect of gravity may also explain the leg but not arm ulcers in the SCDs. Probably the same mechanism is also present for the diabetic ulcers, Buerger’s disease, and varicose veins. On the other hand, smoking may have an additional role for the leg ulcers of the SCDs (21), since its atherosclerotic effects are well known in CHD, PAD, COPD, and cancers (22,23). The effects are the most obvious in COPD and Buerger’s disease. Buerger’s disease is an inflammatory process characterized by obliterative changes in small and medium-sized arteries, and it has never been reported in the absence of smoking. COPD may also be thought of as a localized Buerger’s disease of the lungs. Similarly, smoking was higher in patients with leg ulcers in the present study (28.0% versus 11.8%, p<0.05) that may not be explained by the higher prevalence of smoking in men alone (22,23).

Hydroxyurea (hydroxycarbamide) is the only drug that was approved by Food and Drug Administration for the SCDs (12). It is an oral, cheap, safe, and highly effective drug for the SCDs that blocks cell division by suppressing formation of deoxyribonucleotides which are building blocks of DNA (13). Although the action of hydroxyurea is thought to be the increase of gamma globin synthesis for fetal hemoglobin (HbF) (24), its main action may be suppression of hyperproliferative WBCs and PLTs in the SCDs. Although there is presence of a continuous damage of hard RBCs on capillary endothelium, severity of the destructive process is probably exaggerated by the patients’ own WBCs and PLTs. So mechanism of tissue damage of the SCDs may mimic autoimmune disorders, and suppression of excessive proliferation of patients’ own WBCs and PLTs by the drug may limit the capillary endothelial injury, inflammation, edema, and fibrosis all over the body. Similarly, lower neutrophil counts were associated with lower crises rates, and if a tissue infarct occurs, lower neutrophil counts may decrease severity of pain and tissue damage (25). Furthermore, final HbF levels did not differ in hydroxyurea users (25). Due to the same reason, hydroxyurea is also used to suppress hyperproliferative cells in chronic myeloproliferative disorders and psoriasis, effectively. According to our practices during the eight-year period, the only side effect of hydroxyurea is a deep anemia. Although hydroxyurea increases Hct level in smaller doses, it may cause a deep anemia when used as a dose of 35 mg/kg/day. But this effect is usually harmless, and Hct level increases rapidly by decreasing the daily dose of the drug. On the other hand, although some authors suggest that hydroxyurea does not prevent or even augment the development of leg ulcers (26-28), some others have demonstrated that hydroxyurea is effective for the treatment of leg ulcers in the SCDs (29). According to our eight-year experiences again, due to the microvascular nature of the SCDs, as in microvascular complications of DM, complete healing of leg ulcers can frequently be achieved with hydroxyurea in children and adolescents, but it may be difficult due to the excessive fibrosis around the capillary walls later in life. Similarly, recalcitrant ulcers that have failed to epithelialize may benefit from an autologous skin graft. However, vascular insufficiency and circulatory difficulties lead to high rates of skin graft failure in the SCDs (29).
transfusions are stopped. They decrease sickle cell concentrations in blood, suppress their production in bone marrow, and prevent hard RBCs induced endothelial injury, inflammation, edema, and fibrosis in brain, lungs, liver, bones, kidneys, and other organs (32,33). Since the main pathology is disseminated and prolonged tissue ischemia in the SCDs (34), simple and repeated RBC transfusions are highly effective to restore tissue oxygenation. For example, ileus is also a common pathology in the SCDs’ patients probably due to their atherosclerotic nature (36), and all of the ileus cases were able to be treated with simple and repeated RBCs transfusions in the present study. But transfusions have to be given early in ileus and other severe conditions rather than too late when the patient is clearly comatose. According to our experiences, simple and repeated RBC transfusions are superior to RBC exchange in the SCDs. First of all, simplicity of the procedure provides advantages to clinicians. Secondly, preparation of one or two units of RBC suspension in each time rather than preparation of several units provides time for clinicians to prepare more units by preventing sudden death of such patients. Thirdly, transfusion of RBC suspensions in secondary health centers can prevent some deaths developed during transport to tertiary centers for RBC exchange.

As a conclusion, SCDs are chronic destructive processes on capillaries initiating at birth, and terminating with early organ failure in life. Probably leg ulcers are found among the terminal consequences of the inflammatory processes that may indicate shortened survival.

References


Virology vigilance - an update on MERS and viral mutation and epidemiology for family doctors

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ABSTRACT

This paper reviews aspects of virus mutation and spread generally as well as providing a review of the major viruses affecting people in the MENA and MESA regions.

Key words: virus, mutation, Middle East Respiratory Syndrome (MERS), Severe acute respiratory syndrome (SARS), Human Immunodeficiency Virus (HIV), rotavirus, Chikungunya, Ebola, avian flu, Marburg virus, rabies, dengue

Introduction

Viruses have been with mankind and the animal kingdom since recorded history and their aetiology is still not fully known.

Viruses are not cellular organisms and they may have either developed separately, or have been a precursor to cellular life; probably they are developing ‘genetically’ according to their own innate structure.

Throughout history the influenza viruses particularly, (having connections to simian life), have been the greatest everyday concern to man and Dengue viruses also take large numbers of lives in endemic areas.

Some viruses like smallpox, now eradicated, had been around for as long as recorded history - along with childhood viral complaints like rotavirus. Some scientists believe the Black Death (Bubonic plague) may have been an Ebola type virus.

While there are viruses specific to humans and particular animal species, the problematic viruses have become those that have spread from animals to humans due to mutation. Some of these mutations have then gone on to human to human transmission.

Even given better global communications has there been an actual increase in virus mutation and spread? In this past 100 years dramatic new viruses such as HIV, and Ebola, have emerged and spread rapidly among humans and have caused global concern; new strains of corona viruses such as SARS and MERS have been shown to spread rapidly and dramatically into new populations. We are yet to quantify if viruses spreading into new host populations may have an advantage and therefore greater impact on human health in geographical areas other than those in which the viruses originated.
The question for scientists and doctors to answer is, are these outbreaks just part of normal historical viral epidemiology or do they represent an advanced state of viral infection due to the virus’s own increased virility or due to, for example, changes in our biosphere and the ecosphere of carriers (animals and birds) providing the virus better access into human hosts. Does human over-population of the planet, and human’s greater proximity to concentrated animal populations (intensive animal husbandry) provide a new opportunity for both development of mutant strains and or the spread of such mutations globally into human populations in greater numbers?

If yes, we need to look generally at development and spread patterns in animal and human hosts of existing viruses and look equally at the possibility of development of new strains in certain environments.

It remains an ongoing problem and ongoing work for doctors, technicians and public health personnel, as well as global health organisations. Family doctors who are usually the first contacted and who live in the patient’s local environment where the outbreak may have originated, particularly need to be alert not just for evidence and symptoms of existing strains but for pockets of new viral strains/mutations.

No part of the world is immune to either locally developed viral outbreaks or strains of viruses brought by travellers, or migrant workers into the local population.

Ideally and with proper scientific application we should be able to start to pinpoint risk factors/areas of risk of development of outbreaks (agricultural areas, specific climatic conditions, migration paths of wild animal and bird species) and put in strategies on the community level to contain, or better, prevent, outbreaks.

In this paper we also provide an update on MERS and other globally circulating viruses for regional family doctors who may have patients travelling to the Hajj, going on Ramadan holidays, and for those who will see patients who have travelled from endemic areas overseas.

### Virus mutation

Accurate estimates of virus mutation rates are important to understand the evolution of the viruses and to combat them. However, methods of estimation are varied and often complex.

The mutation rate is a critical parameter for understanding viral evolution and has important practical implications. For example, the estimate of the mutation rate of HIV-1 demonstrated that any single mutation conferring drug resistance should occur within a single day and that simultaneous treatment with multiple drugs was therefore necessary. (1)

Slight changes of the mutation rate can also determine whether or not some virus infections are cleared by the host immune system and can produce dramatic differences in viral fitness and virulence, clearly stressing the need to have accurate estimates. (1)

Future mutation rate studies should fulfil the following criteria:

- the number of cell infection cycles should be as low as possible,
- the mutational target should be large,
- mutations should be neutral or lethal or a correction should be made for selection bias.

Adhering to these criteria will help us to obtain a clearer picture of virus mutation patterns. (1)

There have been many laboratory-based investigations since the emergence of the new coronaviruses in 2012, but most of the parameters required for establishing scientifically the control measures that will protect against them have yet to be determined. Equally, the global distribution of the viruses in their animal reservoir has yet to be established. The approach to monitoring of virus mutation is to highlight particular questions that need to be answered for the purposes of preventing or treating these infections and diseases.

Tables 1-3, on the following page, provide a summary of data and investigations required for control or mitigation of virus spread.
Table 1: Information required from investigations for control or mitigation of a novel respiratory virus affecting humans

<table>
<thead>
<tr>
<th>Information required</th>
</tr>
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<tbody>
<tr>
<td>Reservoir of infections: animal, human, environmental</td>
</tr>
<tr>
<td>Modes of transmission to humans and effective prevention of transmission</td>
</tr>
<tr>
<td>Survival of the viruses in infectiousness doses in the environment</td>
</tr>
<tr>
<td>Method of spread: human-to-human</td>
</tr>
<tr>
<td>Setting when infections take place and procedures associated with transmission</td>
</tr>
<tr>
<td>Those at risk of infection: risk factors for transmission</td>
</tr>
<tr>
<td>Those most likely to transmit</td>
</tr>
<tr>
<td>Those at highest risk of severe disease</td>
</tr>
<tr>
<td>Population susceptibility</td>
</tr>
<tr>
<td>Incubation period</td>
</tr>
<tr>
<td>When cases are infectious and how this relates to symptoms</td>
</tr>
<tr>
<td>Reproductive number and serial interval</td>
</tr>
<tr>
<td>Clinical presentation and clinical spectrum</td>
</tr>
<tr>
<td>Antiviral susceptibility if any</td>
</tr>
<tr>
<td>Effectiveness of specific treatment and care strategies</td>
</tr>
<tr>
<td>Proportionate and effective infection control procedures</td>
</tr>
</tbody>
</table>

Table 2: What parameters are involved in virus spread?

<table>
<thead>
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<th>Parameters involved in virus spread</th>
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<tbody>
<tr>
<td>Modes of transmission</td>
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<tr>
<td>Method of spread</td>
</tr>
<tr>
<td>Those at risk of infection</td>
</tr>
<tr>
<td>Setting when infections take place</td>
</tr>
<tr>
<td>Incubation period</td>
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<tr>
<td>When infectious</td>
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<tr>
<td>Reproductive number</td>
</tr>
<tr>
<td>Clinical presentation</td>
</tr>
<tr>
<td>Effective control measures</td>
</tr>
<tr>
<td>Those at highest risk of severe disease</td>
</tr>
</tbody>
</table>

Table 3: Specific public health questions regarding novel corona viruses that need to be answered

<table>
<thead>
<tr>
<th>Public health questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Where geographically are the human infections occurring worldwide?</td>
</tr>
<tr>
<td>2. What is the reservoir of the virus infection?</td>
</tr>
<tr>
<td>3. The estimated incubation period (from exposure to symptoms) and serial interval?</td>
</tr>
<tr>
<td>4. How infectious are these cases and what are the sources of infectious virus?</td>
</tr>
<tr>
<td>5. When are these cases infectious to others?</td>
</tr>
<tr>
<td>6. Are there any super-spreading events?</td>
</tr>
<tr>
<td>7. What do cases look like?</td>
</tr>
<tr>
<td>8. Who are the high risk groups?</td>
</tr>
<tr>
<td>9. How best to manage and treat the patients</td>
</tr>
</tbody>
</table>
Dealing with virus outbreaks

Viruses cannot exist on their own and for survival they need to spread to another host. This is because the original host may either die or eliminate the infection. Some important routes of viral transfer include:

<table>
<thead>
<tr>
<th>Route</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin contact</td>
<td>HPV (warts)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>SARS, Cold viruses, influenza, measles, mumps, rubella</td>
</tr>
<tr>
<td>Faecal-oral</td>
<td>Polio, Coxsackie, Hepatitis A, Rotavirus</td>
</tr>
<tr>
<td>Milk</td>
<td>HIV, HTLV-1, CMV</td>
</tr>
<tr>
<td>Trans-placental</td>
<td>Rubella, CMV, HIV</td>
</tr>
<tr>
<td>Sexually</td>
<td>Herpes 1 and 2, HIV, HPV, Hepatitis B</td>
</tr>
<tr>
<td>Insect vector</td>
<td>Yellow fever, Dengue fever</td>
</tr>
<tr>
<td>Animal bite</td>
<td>Rabies</td>
</tr>
</tbody>
</table>

Global and regional virus updates

MERS

Middle East respiratory syndrome coronavirus (MERS-CoV) maps and epicurves

Global update

Corona viruses are a large and diverse family of viruses that include viruses that are known to cause illness in humans. Middle East Respiratory Syndrome coronavirus (MERS-CoV) has never previously been detected in humans or animals but appears most closely related to coronaviruses previously found in bats. It is genetically distinct from the SARS coronavirus, and appears to behave differently.

The World Health Organization (WHO) first reported cases of Middle East Respiratory syndrome (MERS) coronavirus on 23 September 2012.

While Saudi Arabia has still recorded the highest number of MERS deaths, (over 400) the outbreak continues in South Korea with 33 deaths and 183 cases to mid June 2015.
All cases have lived in or travelled to the Middle East, or have had close contact with people who acquired the infection in the Middle East.

MERS Symptoms
- Most people become unwell quickly, with fever, cough, shortness of breath, leading to pneumonia.
- Other symptoms include muscle pain, diarrhea, vomiting and nausea.
- There have also been people with mild symptoms or no symptoms at all. These people had close contact with others who were seriously ill.

How MERS spreads
- It appears to spread from an infected person to another person in close contact. The virus does not appear to spread easily from person-to-person and appears to spread only from people who are sick.
- Some people in the Middle East appear to have caught the disease from infected camels and bats. How this occurred is not well understood.

People with underlying illnesses that make them more vulnerable to respiratory disease may be at a higher risk.

How it is diagnosed
A laboratory test on fluid collected from the back of the throat or the lungs can diagnose MERS-CoV.

How it is treated
There is no vaccine for MERS-CoV but early and careful medical care can save lives.

Key facts
- Middle East respiratory syndrome (MERS) is a viral respiratory disease caused by a novel coronavirus (MERS-CoV) that was first identified in Saudi Arabia in 2012.
- Coronaviruses are a large family of viruses that can cause diseases ranging from the common cold to Severe Acute Respiratory Syndrome (SARS).
- Typical MERS symptoms include fever, cough and shortness of breath. Pneumonia is common, but not always present. Gastrointestinal symptoms, including diarrhea, have also been reported.
- Approximately 36% of reported patients with MERS have died.
- Although the majority of human cases of MERS have been attributed to human-to-human infections, camels are likely to be a major reservoir host for MERS-CoV and an animal source of MERS infection in humans. However, the exact role of camels in transmission of the virus and the exact route(s) of transmission are unknown.
- The virus does not seem to pass easily from person to person unless there is close contact, such as occurs when providing unprotected care to a patient.

Between 1 and 4 June 2015, the National IHR Focal Point for the Kingdom of Saudi Arabia notified WHO of 5 additional cases of Middle East respiratory syndrome coronavirus (MERS-CoV) infection, including 1 death.

Contact tracing of household and healthcare contacts is ongoing for these cases.

In patients with suspected pneumonia or pneumonitis with a history of recent residence or travel (in the 14 days prior to symptom onset) in the Middle East*, or close contact with confirmed or probable cases, the following is recommended:

1. The patient should be placed in a single room if available and standard and transmission-based precautions implemented (contact, droplet and airborne), including the use of personal protective equipment (PPE).
2. The relevant state/territory public health unit/communicable diseases branch must be notified urgently of any suspected (and probable or confirmed) cases in order to discuss patient referral and coordinate management of contacts.

Note: Transiting through an international airport (<24hours duration, remaining within the airport) in the Middle East is not considered to be risk factor for infection.

Are GPs/FPs at risk from MERS-CoV?
Many confirmed cases have occurred in healthcare-associated clusters, and there have been a large number of cases in healthcare workers, but mainly in hospital settings as has predominantly, if not exclusively, been the case in South Korea.

The particular conditions or procedures that lead to transmission in hospital are not well known. However, lapses in infection control were known to have occurred for seven healthcare workers who acquired the infection from cases in Saudi Arabia.

Patient Pre-travel advice, travel restrictions, periods of peak travel
The WHO does not currently recommend any restrictions to travel due to the MERS-CoV outbreak.

Travellers should be aware of the importance of personal hygiene including frequent hand washing, avoiding close contact with animals and with people who are suffering from acute respiratory infection, and should be advised to seek medical attention as soon as possible if they feel unwell. They should also follow usual food hygiene practices for travellers, including avoiding drinking raw milk or eating food that may be contaminated with animal secretions or products unless they are properly washed, peeled or cooked.

What are the recommended isolation and PPE recommendations for patients in hospital?
In summary, transmission-based precautions for suspected, probable and confirmed cases should include:

- Placement of confirmed and probable cases in a negative pressure room if available, or in a single room from which the air does not circulate to other areas
- Airborne transmission precautions, including routine use of a P2 respirator, disposable gown, gloves, and eye protection when entering a patient care area
- Contact precautions, including close attention to hand hygiene
• If transfer of the confirmed or probable case outside the negative pressure room is necessary, asking the patient to wear a surgical face mask while they are being transferred and to follow respiratory hygiene and cough etiquette.

Ebola

Ebola is spread through contact with blood or other body fluids, or tissue from infected people or animals. The known strains vary dramatically in their fatality rates. The Bundibugyo strain fatality rate is up to 50 percent, and it is up to 71 percent for the Sudan strain, according to WHO.

Less than two months after Liberia was declared Ebola-free by the World Health Organization, the virus is back in the country.

Even when the outbreak diminished in Liberia, neighboring Guinea and Sierra Leone have continued to see 20 to 27 cases a week since late May 2015, according to the WHO. There have been more than 11,000 total deaths from the outbreak since it began in March 2014.

Ebola Situation Report - 8 July 2015
There were 30 confirmed cases of Ebola virus disease (EVD) reported in the week to 5 July 2015: 18 in Guinea, 3 in Liberia, and 9 in Sierra Leone.

Ebola Situation Report - 1 July 2015
There were 20 confirmed cases of Ebola virus disease (EVD) reported in the week to 28 June, the same as the previous week. Weekly case incidence has been between 20 and 27 cases for 5 consecutive weeks. In Guinea, 12 cases were reported from 3 prefectures: Boke, Conakry, and Forecariah.

Chikungunya virus

While not fatal, this virus can have a chronic disabling effect and it has spread rapidly around the globe.

Chikungunya is ravaging the Caribbean, having affected 24 Caribbean nations and possibly more than 850,000 people worldwide, including 185 Americans (in New Jerseyans). Chikungunya virus is most often spread to people by Aedes aegypti and Aedes albopictus mosquitoes. These are the same mosquitoes that transmit dengue virus.

• The only way to prevent chikungunya is to prevent mosquito bites, such as by using repellant.
• Several vaccines are in the developmental stage but none are in the licensing stage.
• Generally, more South Jersey counties have a higher risk because they have more Asian Tiger Mosquitoes.

It is predicted that chikungunya virus will spread through rest of the globe this year (2015).

• Prior to 2013, chikungunya virus outbreaks had been identified in countries in Africa, Asia, Europe, and the Indian and Pacific Oceans.

• In late 2013, the first transmission of chikungunya virus in the Americas was identified in Caribbean countries and territories. Local transmission means that mosquitoes in the area have been infected with the virus and are spreading it to people.
• Since then, local transmission has been identified in 44 countries or territories throughout the Americas with more than 1.2 million suspected cases reported to the Pan American Health Organization from affected areas.

Symptoms
• Most people infected with chikungunya virus will develop some symptoms.
• Symptoms usually begin 3–7 days after being bitten by an infected mosquito.
• The most common symptoms are fever and joint pain.
• Other symptoms may include headache, muscle pain, joint swelling, or rash.
• Chikungunya disease does not often result in death, but the symptoms can be severe and disabling.
• Most people feel better within a week. In some people, the joint pain may persist for months.
• People at risk for more severe disease include newborns infected around the time of birth, older adults (>65 years), and people with medical conditions such as high blood pressure, diabetes, or heart disease.
• Once a person has been infected, he or she is likely to be protected from future infections.

SARS
Severe acute respiratory syndrome. No outbreaks since May 2004 China

Avian Flu
Avian influenza A (H7N9) is a subtype of influenza viruses that have been detected in birds in the past. This particular A (H7N9) virus had not previously been seen in either animals or people until it was found in March 2013 in China.

However, since then, infections in both humans and birds have been observed. The disease is of concern because most patients have become severely ill. Most of the cases of human infection with this avian H7N9 virus have reported recent exposure to live poultry or potentially contaminated environments, especially markets where live birds have been sold. This virus does not appear to transmit easily from person to person, and sustained human-to-human transmission has not been reported.

WHO risk assessment of human infection with avian influenza A (H7N9) virus
On 23 February 2015 WHO conducted a risk assessment in accordance with the WHO recommendations for rapid risk assessment of acute public health events the summary can be found below.

Risk assessment
This 23 February 2015 risk assessment was conducted in accordance with WHO’s published recommendations for rapid risk assessment of acute public health events and will be updated as more information becomes available.
Overall, the public health risk from avian influenza A(H7N9) virus has not changed since the assessment published on 2 October 2014.

What is the likelihood that additional human cases of infection with avian influenza A (H7N9) viruses will occur?
The understanding of the epidemiology associated with this virus, including the main reservoirs of the virus and the extent of its geographic spread among animals, remains limited. However, it is likely that most human cases were exposed to the H7N9 virus through contact with infected poultry or contaminated environments, including markets (official or illegal) that sell live poultry. Changes to hygiene practices in live poultry markets have been implemented in many provinces and municipalities. Since the virus source has not been identified nor controlled, and the virus continues to be detected in animals and environments in China, further human cases are expected in affected and possibly neighbouring areas.

What is the risk of international spread of avian influenza A (H7N9) viruses by travellers?
On 27 and 31 Jan 2015, Canada reported 2 cases of human infection with avian influenza A (H7N9) in travellers returning from China. These travellers had mild symptoms and only reported indirect contact with poultry. On 12 February 2014, Malaysia reported one human case with avian influenza A (H7N9) virus infection. The patient was a Chinese resident who travelled to Malaysia while sick, and was most likely exposed in China. No further cases were reported in Malaysia linked to this case.

It is possible that further similar cases will be detected in other countries among travellers from affected areas, although community-level spread in these other countries is unlikely.

Flu viruses

During a typical flu season, up to 500,000 people worldwide will die from the illness, according to WHO. But occasionally, when a new flu strain emerges, a pandemic results with a faster spread of disease and, often, higher mortality rates.

There are four types of virus that cause seasonal flu in humans. Every year, drug developers try to predict which strains are likely to dominate in the next flu season so as to create an effective flu vaccine.

A good understanding of the rate and pattern of virus evolution helps these predictions, as one of the authors, Dr. Ian Barr, of the World Health Organization (WHO) Collaborating Centre for Reference and Research on Influenza in Melbourne, Australia, explains:

“This work represents another piece in the complex puzzle of influenza virus circulation and human infections and provides insights that will help develop better influenza vaccines that match strains circulating in the community.”

The four viruses that cause seasonal flu in humans are: influenza A viruses H3N2 and H1N1, and influenza B viruses Yamagata and Victoria.

The viruses cause similar symptoms - for instance sudden fever, tiredness and weakness, dry cough, headache, chills, muscle aches, sore throat - and they evolve in similar ways.

But what has not been well understood is their different patterns of spread around the world and what influences them.

H1N1 and B viruses persist locally between epidemics.

Marburg virus

Scientists identified Marburg virus in 1967, when small outbreaks occurred among lab workers in Germany who were exposed to infected monkeys imported from Uganda. Marburg virus is similar to Ebola in that both can cause hemorrhagic fever, meaning that infected people develop high fevers and bleeding throughout the body that can lead to shock, organ failure and death.

The mortality rate in the first outbreak was 25 percent, but it was more than 80 percent in the 1998-2000 outbreak in the Democratic Republic of Congo, as well as in the 2005 outbreak in Angola, according to the World Health Organization (WHO).

Rabies

Although rabies vaccines for pets, which were introduced in the 1920s, have helped make the disease exceedingly rare in the developed world, this condition remains a serious problem in India and parts of Africa.

It destroys the brain, but there is a vaccine against rabies, and we have antibodies that work against rabies, so if someone gets bitten by a rabid animal they can be treated,

If a patient doesn’t get treatment, there’s a 100 percent possibility they will die.

HIV

In the modern world, the deadliest virus of all may be HIV. It is still the biggest killer. An estimated 36 million people have died from HIV since the disease was first recognized in the early 1980s.

Powerful antiviral drugs have made it possible for people to live for years with HIV. But the disease continues to devastate many low- and middle-income countries, where 95 percent of new HIV infections occur. Nearly 1 in every 20 adults in Sub-Saharan Africa is HIV-positive, according to WHO.
Dengue

Dengue virus first appeared in the 1950s in the Philippines and Thailand, and has since spread throughout the tropical and subtropical regions of the globe. Up to 40 percent of the world’s population now lives in areas where dengue is endemic, and the disease - with the mosquitoes that carry it - is likely to spread farther as the world warms.

Dengue sickens 50 to 100 million people a year, according to WHO. Although the mortality rate for dengue fever is lower than some other viruses, at 2.5 percent, the virus can cause an Ebola-like disease called dengue hemorrhagic fever, and that condition has a mortality rate of 20 percent if left untreated.

Rotavirus

Two vaccines are now available to protect children from rotavirus, the leading cause of severe diarrheal illness among babies and young children. The virus can spread rapidly, through what researchers call the fecal-oral route (meaning that small particles of feces end up being consumed).

Although children in the developed world rarely die from rotavirus infection, the disease is a killer in the developing world, where rehydration treatments are not widely available.

The WHO estimates that worldwide, 453,000 children younger than age 5 died from rotavirus infection in 2008. But countries that have introduced the vaccine have reported sharp declines in rotavirus hospitalizations and deaths.

The future

The severity of viral outbreaks will largely depend on the local, regional and global response to them. Early vigilance by public health authorities and family doctors in endemic areas, particularly, are the greatest preventive measure along with hygienic practices of people, especially those living in close proximity to animal or bird carriers and those in hospital situations.

Global measures will need to be enacted early and up to date information made available to limit spread when it does occur.

Ideally, as in the case of smallpox which was declared eradicated in 1980 following a global immunization campaign led by the World Health Organization, we can start to tackle both the initial outbreaks and the spread of the more life threatening viruses.

This takes money and global will.

References

(1) Nicoll A. Short communication. Public health investigations required for protecting the population against novel coronaviruses
(2) WHO Disease Outbreak
(3) http://www.cdc.gov/chikungunya/symptoms/index.html
(4) http://www.who.int/csr/don/en/

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Art of killing?

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Iraq within the past three decades has been subjected to 3 large wars and to off and on military episodes in between. Recently another open end war was launched against the ISIS and the output is the same: senseless killing, abject suffering, large-scale displacement, and unprecedented destruction are occurring every day. The daily bloodshed devalues all people, not just those directly engulfed in it. This realization contradicts the guilt-relieving notion that there is nothing to be done.

With bitterness we recall the 23rd anniversary of the Desert storm battle outbreak and particularly the crime of using Depleted Uranium (DU) which was potentially involved in the recent upsurge of malignancies in populations exposed to war dust.

It is well-known that weapons containing natural uranium (NU), that is, ‘nuclear weapons’ are disqualified due to their radioactivity, prompt mass destructive power, and long lasting genotoxicity, which has a sustained effect through generations. However, as DU has not been globally and legally well-identified and studied, and as it formed a heavy disposal task on the nuclear industry, this allowed it to leak to the traditional weapon industry for deeper destructive effects instead of being buried costly in nuclear graveyards. In light of new reports tackling the disastrous outcome of DU on the health of exposed populations, a question arises, as to which extent may the weapons containing DU yet be considered conventional, and does DU still retain similarities with the “maternal” NU, regarding the toxic and carcinogenic effect, which the latter has.

It is important here to be reminded of the biodata of NU and DU. On average, approximately 90 (micrograms) of uranium exists normally in the human body, this is gained from normal intakes of water, food, and air. Approximately 66% is found in the skeleton, 16% in the liver, 8% in the kidneys, and 10% in other tissues. (http://www.who.int/mediacentre/factsheets/fs257/en) However, DU is a nuclear exhaust born as a byproduct of Uranium impregnation in the nuclear industry, and almost completely formed from Uranium-238 (U238), which has a 60% radiation power of NU. Physically, NU and DU consist of a mixture of 3 radioactive isotopes but in different ratios; NU contains U238 (99.27% by mass), U235 (0.72%), and U234 (0.0054%), whereas DU contains approximately 99.8% U238, 0.2% U235, and 0.001% U234 by mass. The main difference between DU and NU is that the former contains at least 3 times less U235 than the latter. Table 1 shows the half-lives and the specific activity of the 3 isotopes of NU and DU, the average energies per transformation emitted by these isotopes, and the percentages of isotopic abundance by weight and activity of NU and DU. (Data derived from URL: http://www.who.int/mediacentre/factsheets/fs257/en).

The DU behaves chemically, physically, and toxicologically similar to NU. As it was found to still retain an extra penetrative and destructive effect, it is presently involved in the manufacture of high-powered smart bullets/missiles, and thus it entered the armory of the arsenal as an anti-tank shell agent. Uranium-238 is pyrophoric, bursting after shooting into flame with 70% of the shell aerosolized into respirable particles less than 5 microns in diameter. Most DU particles are dispersed as dust on earth, which when it rains, penetrates into the soil to contaminate water resources, and consequently agricultural products. Uranium-238 is an alpha radioactive emitter. On degradation, it shoots mainly alpha, and to a lesser quantity beta particles. Man, in and around the battle field, is exposed to DU hazards by radiation, inhalation, swallowing, and wound contamination. In the human body, DU is nephro-toxic; it is mostly excreted via the kidney causing acute nephritis, however, it is also excreted in the semen, and uranyl ions infiltrate the testes, ovaries, placenta, embryo, and central nervous system. Naturally, children are more susceptible to radiation induced cancers than adults.

A mainstay report published in Saudi Medical Journal in 2003 by Al-Waiz et al from Baghdad University clearly shows that (Kaposi Sarcoma) KS has recently made an upsurge in southern Iraq, and it behaved in these particular cases quite divergently compared with the well-known classic KS, which existed before sporadically in Middle Eastern people including Iraqis. The report concluded that this KS outbreak might have been provoked and/or boosted by DU fallout. The differences between the new Iraqi KS outbreak and the known classic type may be concluded in:

1. **Age:** the mean age of patients in these series was 54 years compared with 68 years in classic KS, thus these patients were 14 years younger than the classic KS patients, that is, 14 years earlier presentation.

2. **Advanced presentation:** classic KS usually presents as macular lesions and progresses very slowly to plaques or nodules, but the disease in all these patients presented directly in the advanced plaque and nodular stage, none was in the macular stage. This is a major deviation from the classic KS, which
indirectly by DU. The alpha rays hit the DNA molecules and induce mutations and cell damage. Cells are attacked directly and indirectly by DU. The alpha rays hit the DNA molecules resulting in direct damage to the chromosomes, although this damage is not stationary, it passes via generations posing genomic instability of the damaged cells. Additionally indirect bystander effect occurs to the intact adjacent cells by uranyl ions, which bind avidly to DNA-clumped chromatin causing DNA damage and chemical toxicity, hence, their mutagenic capability. Hamilton inquires why adequate measures were not taken to ensure that good scientific evidence for later use was obtained at the onset of both Gulf and Balkan conflicts. It is possible that at the time of confrontations, circumstances were not fit, there were political or military limits, which made the recurrent publication and media comments on these events decades after their occurrence just serve in dissolving the confidence of the general public. Possible, however the lack of publication and media coverage serves also to obscure the problem rather than solving them, whereas it continues to exist inconspicuously with extra potential human sufferers. For fairness, it is worth mentioning that some studies showed leniency with DU and did not refuse using it in military, for instance, Patel in his article “Health in the Middle East: No strong link between depleted uranium and cancer”, and McDiarmid (“Depleted uranium and public health. Fifty years study of occupational exposure provides little evidence of cancer”) but circumstances of both are quite different. Uncontrolled occupational exposure is quite different from haphazard permanent residence of the whole society, including children and pregnant women inside the contaminated field. Yet, the authors could not deny the existence of an insidious link or evidence of malignant relation between DU and cancer, the term they used -no strong “link” - and -little “evidence” - ascertains the presence of a “link” with, and an evidence of cancer rather than denying it.

It is not the size of the “evidence” or the “link” between DU and cancer which accounts in human affairs, but the link itself; it is incriminated even if it kills one man only. Size can act in the field of materials not in humans.

We, in the medical field feel it is part of our medical mission and educational deputation as pioneering medical media in the region, to notify any malpractice against human health or life, share in protecting the common people from mass health disruption, and send a plea to whom it may concern, such as the WHO, United Nations, the Green Groups, and all concerned health authorities requesting them to consider research reports regarding KS originated from the Gulf and Balkan region as work paper, which is worthy of further investigation and follow up, that is:

1. Perform epidemiological studies with control groups and further mass population screening for any uprise in mortality and morbidity in general, and malignancy in particular and around the battle fields, prospectively and retrospectively, to document the old cases and discover the new ones as early as possible in order to have a larger statistical database to depend on in the next steps.

2. Perform further in vitro laboratory research and animal studies -although not ideal with battle field medium to clear any suspicion regarding DU - human health relation on radiological, toxic, and molecular basis. 3. Until a final conclusion is issued, to ban the use of DU in any means until full knowledge of its safety and hazards is evident. Military experts should obtain a safety certificate of DU before taking it to the field but not after. Safety should never be proved retroactively or provisionally, as long as man is not a laboratory rat to start with.

suggestions a rather aggressive nature, and more rapid course probably related to a new potential factor.

3. **Visceral involvement:** KS patients (25%) had lung and liver involvement, and 10% of them had lymph node involvement within a short period of the disease course. Considering that the visceral dissemination occurs very lately and infrequently in classic KS reflects again a comparatively more florid type of KS than the classic one.

4. **High mortality rate:** The mortality rate was 15%, and death was due to systemic dissemination of the tumor. Whereas, classic KS patients enjoy a rather normal life span, approximately 10-20 years in average and death is very rarely related to KS.5. The southern geographic predilection: one case of KS only came from northern Iraq, which is comparatively calm and far from the battle field, versus 15 cases that came from the central Baghdad region, and 4 that came from the south; this suggests some geographical polarization of KS distribution consistent with the battle field - Baghdad and south Iraq. Considering that Baghdad is relatively closer to the south increases the polarization to one case north versus 19 middle/south.

This southern:northern ratio of KS cases is far bigger than that of the populace distribution. The northern people alone are approximately 8 million. From the Wikipedia almost 75% of Iraq’s population lives in the flat, alluvial plain stretching southeast from Baghdad to Basra, and the Arabian Gulf. Possibly, approximately one quarter of Iraqi population lives in the north, and one KS case came only from the North, and 19 from the Midsouth. This inconsistent geographical distribution of KS cases which are not parallel with the populace distribution suggests a Southern related factor incriminated in KS epidemic, and it existed in the Middle South, that is the focus of the battle field during successive wars. 6. The epidemic occurrence: This is highlighted via a cluster of 20 KS cases diagnosed within a short (one year) period, and perhaps, this number has jumped up later. Literature review shows that this compact episode of KS is probably the first recorded in Iraq, and in all the neighboring countries. Fortunately, there was an Iraqi study of 21 cases of classic KS 15 years before, that is, before the Gulf war era but with a quite different clinical behavior. Thus, the current report involves almost the same number of patients but within a tenth of the period of the previous study.

Reports from southern Iraq have documented a steep rise in the incidence of cancers since the 1990s, especially in children. According to the Cancer Treatment Centre of Basra, in the far Southern Iraq and the focus of the Gulf wars, local cancer incidence raised from 11 cancers per 100,000 in 1988 to 75 in 1998, and 116 in 2001, approximately 11 fold in 13 years, rising almost one fold each year. In Fallujah, Busby et al found that the results qualitatively support the existence of serious mutation-related health effects as 80 deaths per 1,000 births were reported in Fallujah compared with only19.8 in Egypt. Caldicott recollected the mechanisms, by which depleted uranium induces mutations and cell damage. Cells are attacked directly and indirectly by DU. The alpha rays hit the DNA molecules resulting in direct damage to the chromosomes, although this damage is not stationary, it passes via generations posing genomic instability of the damaged cells. Additionally indirect bystander effect occurs to the intact adjacent cells by uranyl

MIDSOUTH. This inconsistent geographical distribution of KS - and - little “evidence” - ascertains the presence of a “link” with, and an evidence of cancer rather than denying it.

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in death trials, and as long as prevention is better than cure as we always say, noticing that once DU is blasted, it will never vanish, it will finally pollute the water, agriculture, and human life in an everlasting circle.

International health authorities who care should undergo regular check up on the factories of death materials to see what is up, they should not wait and see, but should move -prophylactic wise- there to face the death engineers in the pre-manufacturing stage in order to control the obsessive killing drive in that media, and suppress the explosive fatal craving. Performing all these preventive measures is crucial -particularly at this very time with new launch of wars, in order to clear the relation between DU and uprising malignancies, and to clean this perpetual hazardous contaminant of human life. When NU is disqualified for its non-conventional mass destructive effect, DU with 60% radiation of NU, and with everlasting environmental contaminating effect is a genuine suspect, it should not at all be justified and passed, and should not be simply considered as conventional until proven otherwise by unbiased evidence-based science. There seems to be a thick wall separating militarists and health preachers. Each is working separately and independently, one with death and the other against it, without minimal coordination and harmony. This wall should be knocked down so that they might work together like a smart surgical team when this does a legal operation. Yes, bombs are made to kill, but they should not do this randomly, they should first earn a health certificate before going to war and before killing. Materials involved in them should not be used until safety measures are confirmed, and preserved in terms of effects, adverse effects, and contra effects, exactly like poisons, and pharmaceutical materials. The side effects of these materials are as vital as the effects. In fact, they are effects on the long run. In another way, they should not kill massively beyond the range of their pre-decided legal claw, and “hiddenly” through mutagenicity, which works deeply across decades and generations. In terms of DU, allow the manufacturers to first prove its conventionality and then use it, but not before. The capacity of death should be callipered precisely in extent, mass and duration so that no undesirable hidden killing would silently take place. Illegal instruments should not be used, even in killing, although the taste of death is finally alike. Instruments also should be compatible with -but not above- the morals and ethics of wars, and nothing should be there above ethics and norms.

Leaving a sustained agendum of death to act insidiously and deeply at the level of molecules and chromosomes, and ignoring it is an immoral behavior, and should not occur in the claimed era of human rights and in the current advanced health and war technology. We believe until proven otherwise, that semi-nuclear is nuclear as well, and nucleotides and genes do not read well these accumulative quantitative gradients of radiology, but we do. Scientific silence is a hypocritical act, and it is the other face of the coin of death.

Table 1: The half-lives* and specific activity of the 3 isotopes of Uranium

<table>
<thead>
<tr>
<th>Isotope</th>
<th>U238</th>
<th>U-35</th>
<th>U234</th>
</tr>
</thead>
<tbody>
<tr>
<td>Half life, million years</td>
<td>4510</td>
<td>710</td>
<td>0.247</td>
</tr>
<tr>
<td>Specific activity</td>
<td>12.4</td>
<td>80</td>
<td>231000</td>
</tr>
<tr>
<td>Average energy emitted per transformation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alpha</td>
<td>4.26</td>
<td>4.47</td>
<td>4.84</td>
</tr>
<tr>
<td>Beta</td>
<td>0.01</td>
<td>0.048</td>
<td>0.0013</td>
</tr>
<tr>
<td>Gamma</td>
<td>0.001</td>
<td>0.154</td>
<td>0.002</td>
</tr>
<tr>
<td>Relative isotopic abundance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natural Uranium (%)</td>
<td>(99.28)</td>
<td>(0.72)</td>
<td>(0.0057)</td>
</tr>
<tr>
<td>Depleted Uranium (%)</td>
<td>(48.8)</td>
<td>(2.4)</td>
<td>(48.8)</td>
</tr>
<tr>
<td>By weight</td>
<td>(83.7)</td>
<td>(1.1)</td>
<td>(15.2)</td>
</tr>
</tbody>
</table>

*The half life of a radioactive isotope is the time needed to decay to half of its original radioactivity.

Reference

Travel Medicine: A Case of Multiple Sclerosis

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ABSTRACT

Travel medicine concerns the in depth evaluation of multiple and different environmental and personal factors impacting on travellers’ health. Those with the disease of multiple sclerosis (MS) however, require different and more intensive health needs to improve their quality of life whilst travelling. MS is chronic, progressive and disabling. Therefore, it is crucial to understand the symptoms experienced by travellers with MS in order to enhance quality therapeutic care provided by carers and the traveller.

Travelling patients affected by MS need to be very cautious whilst travelling. This includes minimising their exposure to heat, having a healthy nutrient based diet and limiting their alcohol consumption. Due to the rapid change of environmental conditions whilst travelling, patients need to avoid situations of stress that may lead to later depression and as a result, the experience of fatigue. Therefore, patients should have a clear understanding of their needs and the risk factors associated with MS. They should also not try to push the boundaries of their health or energy capacity as such things lead to the exacerbation of MS symptoms. Above all, before travelling or intending to travel, patients should seek consultation with a physician to understand the conditions that they may experience while travelling and co-evaluate them with their health, needs, requirements and preparations. In regards to this, all travel agents have facilities for MS patient use. The government also has established and implemented policies for MS travelling patients, safeguarding their overall health and wellbeing.

Key words: Multiple sclerosis, travel, travel medicine
Introduction

Travel medicine is a fundamental discipline addressing the complex ecology of travellers. As geographical regions greatly differ, travellers become more susceptible to being affected with multiple health factors. In some situations, such affects lead to critical health conditions where emergency medical attention must be available to meet the health needs and requirements for patient recovery(1). To avoid such situations, it is important that prior to travelling, MS patients undertake a travel health examination assuring their health compatibility. To support this, further clinical evidence suggests that MS patients are as equally susceptible to implications that relate to travel.

Main Objective of the Study

The objective of this study is to further explore and evaluate previously suggested implications of MS. These will be further applied in this study to address the measures that can be undertaken in future situations of MS travellers through the evaluation and counterbalancing of the negative and positive effects that may be experienced by MS patients during travel. This will enhance precautions that can be undertaken to enhance the holistic welfare of patients. MS is a neurological disease that affects the nervous system as it damages the myelin sheath of neurons(2). This results in the inability of the nervous system. Impairment of the nervous system is caused by damage to the myelin sheath of neurons which acts to enhance the neurological transmission of electrical information travelling to and from the brain and body. Hence once damaged so is movement, sensation and cognition(1).

Although the condition or severity of each MS patient’s symptoms differ, care and management of the disease is crucial. This includes taking medications, therapy, lifestyle, and diet. Results of managing and caring for patients’ health and well-being relies on appropriate timing of implementing engagement in essential therapeutic activities. Statistical evidence indicates that females are more susceptible to MS(3). It is also claimed that MS is caused by both genetic and environmental factors.

This suggests that the disease can lead to death. For this reason, exploration of MS and its facets in relation to travel is very crucial, in fact, lifesaving. This will be explored in this study, regarding patient and carers in relation to understanding the relative concerns of MS and acting on them with ease instead of having minimal knowledge of how to address such a disease during travel which may also assist in daily life.

The progression of the disease may exacerbate whilst travelling. It is therefore important to ensure that emergency preparations and plans are considered before travelling and practiced in emergency. Information from doctors is also important in order to avoid incidences in an adequate timely manner to avoid and recover from life threatening situations(4).

Having emergency plans and preparations including information concerning patients’ medical condition and history is effective in avoidance of shock or trauma during travel for patients, carers and the people around them. It is also important that a medical history or description of current health conditions of patients is known by those close to them and is readily accessible in emergency cases where patients may be in shock or unable to move or communicate. Regarding travelling patients with extreme MS medical conditions, it is vital to arrange the storage or transportation method of medications(2). Some medications such as copaxane require refrigeration at certain temperatures. Therefore, patients and caregivers should arrange their medication in a manner suitable for travelling by seeking advice from a pharmacist or physician trained in the field of travel medicine.

Methodology

In this study, MS is considered through the presentation of extensive information obtained from various primary and secondary sources which include; journal articles, websites, books and research papers published over the years by physicians, including clinical practitioners. The combination of resources presented in this study presents efficient information on MS, and applies and evaluates information that has been put
into practice. This will be carried out to determine MS patient travel needs, evaluate them and provide recommendations to improve the holistic welfare of travellers suffering from MS. As well as this, the role of stakeholders will also be considered in countering the negative impacts MS may have on a travellers health conditions and how they can be managed and treated.

Understanding Multiple Sclerosis

Multiple sclerosis (MS) is a chronic auto immune disease that is a common disease of the nervous system affecting people of all ages around the world(5). However, it commonly affects people in higher latitudes and females within the age of 45-54 years in comparison to males.

Despite the fact that it is not inherited but involves genetic susceptibility, early discoveries of the disease were made in the 19th century where scientists were not really sure of the nature of the disease. The first recognizable case of the disease was the case of her Majesty Queen Victoria’s cousin because he documented his signs and symptoms in his diary(2).

In 1868 Jean Martin made his description of the disease when he was attending to a patient. He tried to establish a treatment for the disease and was frustrated because it was thought to be due to the resistance of drugs. However, it was due to the lack of knowledge on the pathology of the disease. The first drug treating MS symptoms was discovered in 1993. The drug was interferon beta-1b and was approved by the Food and Drug Administration(6).

Some of the signs and symptoms associated with MS include; lack of sensation and general weakness on one side of the body, optical problems that can lead to blindness, blurred visualization, tiredness, and problems with speech, faintness and issues with urinary incontinence.

Factors associated with the spread of MS

Causes of the disease are not really known but factors that are associated with MS include an immunological factor where the immune system attacks Myelin coating that is normally based around the nervous system. When the myelin coating is destroyed this causes some malfunction of the nervous system, leading to MS(7). Current research is still exploring why this happens and how to prevent further pathology.

Environmental factors indicate that people who are geographically far from the equator are at greater risk of acquiring MS because they do get enough sunlight which acts as immunity to the disease. Smoking has also been suggested to be one of the factors that lead to the acquirement of the disease. If an MS patient stops smoking, the symptoms of MS are lowered(8).

Regarding infectious factors, bacterial infections in children indicate that children can develop the disease in later years as supported by research. Infections may include Chlamydia, Canine Distemper among many others(2).

Figure 2: A graph presenting MS across age groups

![Figure 2: A graph presenting MS across age groups](image-url)
Genetic factors of MS are hereditary. Studies have indicated that if one has a close relative who has MS, there is high risk of also being affected or being a carrier. Some families may have some genes that are at a higher risk of reacting with ecological conditions than others(9).

Some of the risk factors associated with MS include; ethnicity, age, gender, climatic conditions, smoking, lifestyle, and family history among many others. The diagnosis for the disease is a combination of different techniques such as tests, MRI and spinal tap. All tests assist in establishing the correct diagnosis which assists in prescribing the relevant and correct medication, and the implementation of suitable therapeutic treatments(2).

There is no cure for MS. However, medication is normally prescribed for treatment. Medication slows down the symptoms and progression of the disease. The treatment given to patients may include medication and therapy that will assist in slowing down the effects of the disease(10). However, as symptoms and severity of the disease varies from one patient to another, so does the treatment as medication is normally based on the types of symptoms the patient experiences.

Medications treating MS Symptoms

Different symptoms require different medication. There are those for physical treatment such as painful muscle stiffness while others are modified drugs that assist in controlling the rates of relapse in the disease and the severity of attacks(1). Occupational and physical therapy is an important factor of treating MS patients.

(See Figure 3 next page)

Travel Medicine

Traveling for patients with MS may be difficult and stressful causing complications to the patients’ health. Neurologists have indicated that this should not occur and that patients’ medical conditions should not be an issue causing travel restrictions. For the patient to not have their medical condition or symptoms restrict their traveling or be an issue, some planning ahead is effective(6).

It is essential to carry the right medications, in the right amount, and in the correct storage while traveling. It is also vital to communicate with a physician to ensure that you are fit to travel and find out the requirements for the storage of medications. The physicians should issue a travel medicine certificate with a medical history of the patient, indicating the type of medicine that should be taken with correct dosage and time which is useful in times of emergency.

Starr(7) suggests that it is important to make pre-travel inquiries on the geographical area patients are visiting to make sure they have necessary facilities such as refrigeration and if there is a medical center nearby in case of emergency or need. The contacts of the patients’ doctors should always be accessible if there are any medical related inquiries; it becomes easier in cases of emergencies. It is also advisable for the patients to carry a flash drive that holds all their medical records.

Patients with MS should avoid risk factors that can lead to aggressive symptoms such as heat, fatigue, stress, and depression(4).

In modern times things have changed and many traveling agencies are making special arrangements for people with disabilities and various illnesses. MS patients should make arrangements with travel agents that adequately provide support services to meet MS patient’s health and wellbeing needs. Prior to travel, it is recommended for travel agencies to have the passengers’ updated medical records. By establishing this, it is easier to distinguish travelers that require special care and meet their needs.

The importance of travel medicine

Travel medicine practitioners should have an evaluative awareness campaign to be put in place to assist in educating MS patients about how to travel safely whilst ill(9). Travel medicine practitioners should work collaboratively with multidisciplinary health institutes and governments to provide support for MS patients(9).

Prior to travelling, patients need to seek consultations from a physician to make sure that they get all the details and advice that they will require during their journey(7). During consultation, it is important for patients to give all their correct travelling details to the physician to receive correct medications and advice according to the environmental conditions of the geographical area they are visiting.

Travel agencies should be equipped with necessary requirements needed by MS patients while they travel. This will increase the efficiency in travel medicine. These agencies should ensure their patients are first priority with regards to providing health care as well as mobility facilities such as wheelchairs(4).

Clinics should be equipped with vital medical resources essential in addressing emergent problems. This is compounded by the realisation that conditions tend to worsen with time. This may include the development of severe symptoms caused by various reasons such as changing climates, diets, fatigue, stress and depression(8).

Providing these services during traveling can aid in dealing with emergency cases. This would also ease the ensuing tension that has diverse implications on other passengers as well as patients(7).

During travel it is equally important for patients to consult with physicians in case of any changes in their symptoms, so that they can ensure they are safe and can be guided on how to stay healthy(8). Understanding the advancement of their condition aids in timely verdict making, regarding measures assumed to counter any depressing effects.
<table>
<thead>
<tr>
<th>Class</th>
<th>Mechanism of Action</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recombinant interferons</td>
<td>IFN-beta has many effects on the immune system. Exact mechanism of action in MS unknown.</td>
<td>Interferon-beta-1b, Interferon-beta-1a</td>
</tr>
<tr>
<td>Altered Peptide ligands</td>
<td>Ligands either templated on sequence of myelin basic protein, or containing randomly arranged amino acids (e.g., ala, lys, glu, tyr) the structure resembles myelin basic protein. Believed to be an antigen that plays a role in MS. Binds to T-cell receptor but do not activate the T-cell because they are not presented by an antigen-presenting cell.</td>
<td>Glatiramer acetate, MBP 8298, Tiplimotide, AG-284</td>
</tr>
<tr>
<td>Chemotherapeutic agents</td>
<td>Immunosuppressive, MS believed to be an autoimmune disease. Chemotherapeutics that suppress immunity can improve MS.</td>
<td>Mitoxantrone, Methotrexate, Cyclophosphamide</td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td>Act via mechanisms to dampen immune response.</td>
<td>Azathioprine, Teriflunomide, Oral Cladribine</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Induce T-cell death and may up-regulate expression of adhesion molecules in endothelial cells on the lining walls of cerebral vessels. Also decrease CNS inflammation.</td>
<td>Methylprednisolone</td>
</tr>
<tr>
<td>Monoclonal Antibodies</td>
<td>Bind to specific targets in autoimmune cascade that produces MS, e.g., bind to activated T-cells</td>
<td>Natalizumab, Daclizumab, Alemtuzumab, BMS 188667, E-6040, Rituximab, M1 MAb, ABT 874, T-0047</td>
</tr>
<tr>
<td>Chemokine Receptor Antagonists</td>
<td>Prevent chemokines binding to specific chemokine receptors involved in attraction of immune cells in CNS of MS patients, and inhibiting immune cell migration into CNS.</td>
<td>BX-471, MLN-3897, MLN-1202</td>
</tr>
<tr>
<td>AMPA Receptor Antagonists</td>
<td>AMPA receptors bind to glutamate, an excitatory neurotransmitter, which is released in excessive quantities in MS. AMPA antagonists suppresses damage caused by glutamate.</td>
<td>E-2007</td>
</tr>
<tr>
<td>Recombinant Human Glial Growth Factor (GGF)</td>
<td>GGF is associated with the promotion and survival of oligodendrocytes and protect myelin sheath covering axon.</td>
<td>Recombinant Human GGF2</td>
</tr>
<tr>
<td>T-cell Receptor Vaccine</td>
<td>Mimic part of receptor in T cells that attack myelin sheath, which activates regulatory T cells to decrease pathogenic T-cells.</td>
<td>Neuro Vax</td>
</tr>
</tbody>
</table>

Figure 3: A table indicating medications used in reducing MS symptoms
Other practitioners in the area of destination can also keep contact with the patients’ physicians at home to communicate on the progress and changes in patients symptoms. This can assist in providing very insightful understanding by patient’s physicians on elements of the patient’s ailment with regards to the environment of their new destination(2).

These measures are very beneficial as physicians have a better understanding of the impacts of multiple factors to patients residing in their areas. This knowledge allows physicians to provide adequate advice to future patients(7).

All countries should provide adequate education to travellers, ensuring MS patient travellers’ health needs are considered. Different health centers around the world should be established with the specialty in MS. They should have all the facilities that are needed in ensuring that MS patients’ health needs are met. The development of health facilities in health centers and the establishment of specialty in MS around the world will assist, and expand further research exploring where in the human body acceleration of MS symptoms occurs and the reasons behind symptom acceleration. Travel medicine is a very important part of establishing a world that is free and easy to survive in, because it gives patients a chance to go along with daily activities and careers. The help of many organizations that deal with sick people makes it easier for patients to be comfortable in their daily activities(2).

MS patients should rely on themselves in making an effort to stay healthy and putting into practice the advice they are given from their physicians. This would allow patients’ health to improve following the management plan developed by their physicians(9).

**Conclusion**

As indicated in this study, MS is a disease that affects the neural system. It is very dangerous, progressive and chronic. The main cause of MS remains idiopathic. However, the risk factors associated with MS include; smoking, low levels of vitamin D, excessive exposure to heat, excessive alcohol consumption, and many others factors. These factors contribute to the development of the disease and the exacerbation of symptoms. Travel medicine is an area of medicine that takes care of travellers who may or may not have medical or health ailments such as MS.

Travel medicine and its advances around the world have made it easier to travel safely and effectively without any fears of difficulties or complications. Information regarding travelling is very accessible and available on the internet since there are websites on various diseases that offer advice on traveling tips for travellers and travelling MS patients. Travel agents have also contributed to ensure that traveling as an MS patient is easy and safe as they provide good medical care. They also ensure that travel destinations are equipped with correct medical centers that have updated medical facilities.

The role of the government is also very important. Countries should ensure that medical centers in their areas are well equipped with facilities that assist MS patients at all times. They should also ensure that there are facilities that have been put in place to advise MS patients on how to travel safely and take care of their health while travelling. There are also policies put in place to ensure that all organisations that deal with travelling or hosting tourists have comprehensive medical care, taking care of the needs of any traveling MS patients. The implementations discussed in this study will assist in improving the quality of life of traveling MS patients.

**References**


Author’s Answers and feedback on Question 2

U+E’s, CR

The authors disagree.

This would give some indication as to whether her renal function had deteriorated further. Renal failure causes anaemia.

Serum iron and ferritin

The authors disagree.

Iron deficiency is the commonest cause of anaemia in the community, usually with loss of blood from the GIT. This would be an appropriate test but not the ONE most useful.

FBE with film

The authors agree.

This is the best test—the film will tell you the red cell size and morphology, suggesting therefore whether any of the following are likely: iron deficiency (small cells), folate deficiency (large cells), or B12 deficiency (large cells). Other forms of anaemia may also be suggested; the anaemia of chronic renal failure is normochromic, normocytic (normal size cells).

Reticulocyte count

The authors disagree.

An elevated reticulocyte count would suggest either recent bleeding or haemolysis, and this could be useful.

B12 and Folate levels

The authors disagree.

Deficiency of these vitamins is less common and probably these tests should only be ordered on the basis of macrocytosis on the blood film.

Serum protein immuno-electropheresis

The authors disagree.

This will detect myeloma. This is not uncommon in elderly patients but a hint might be pancytopaenia on the blood film rather than just anaemia, although this is not absolute. Probably best as a second line test.

Continuing history

You make a further appointment for Mrs. Hussain to return in a few days for test results.