ELECTIVE (SSC5b) REPORT (1200 words)

A report that addresses the above four objectives should be written below. Your Elective supervisor will assess this.

Objective 1: To understand the pattern of haematological conditions in the USA and discuss this in the context of global health

The NIH Clinical Center is a quaternary healthcare institution, which exists solely to further clinical research. All patients are enrolled in a clinical research protocol, in whom novel approaches to diagnosis, management or monitoring of illnesses developed from the scientific research laboratories are trialed upon for use in clinical practice. All kinds of diseases are encountered at the Clinical Center, not only the common but also rare; the scientific discoveries behind the rare diseases that are rarely seen anywhere else are often applied to common diseases to further knowledge in the management of the common diseases. Patients come from all over the nation and world; for example, in hematology, most research trials on aplastic anemia takes place at the Clinical Research Center at NIH. The outcomes of these trials, mainly Phase I and II, influence not only the nation's practice in managing the hematological conditions but also in many cases, clinical practice worldwide. Patients also come for 2nd opinion from world-renowned experts in the field that work at NIH and to get investigations that are not readily available in local or even tertiary hospitals. For example, a patient with chronic history of menorrhagia and epistaxis may be investigated locally for complete blood counts including platelets, and clotting times but NIH is one of only a few places in the US that offers platelet aggregation studies.

Objective 2: To understand the pattern of health provision in the USA and compare this to the UK

The pattern of health provision in the USA and UK is largely different. In the US, patients pay for their healthcare with around 80% of the population possessing health insurance, personal or private. The private health insurance system is provided for by the individual's employment which has a mutual contract with a health insurance company. Around 25% of the population are covered by the government-funded system of Medicare and Medicaid. Medicare applies to those who are elderly or have certain disabilities while Medicaid helps those with low income. The degree of coverage for the different aspects of clinical care would vary depending on the state the patient lives in. Around 15% of the population have no health insurance at any point in time. There are local public hospitals and health programs for such portion of the population, which are funded by charities or private companies that shift the cost to other paying patients. However, these patients still face having to pay large sums of money for their clinical care and are often put in financial hardship as a result.

In contrast, the UK healthcare system is entirely government funded, the National Health Service (NHS). The patient does not need to pay for their healthcare costs, except for eye tests, dental care and prescriptions. Less than 10% of the population have private health care insurance, mostly provided by their employment, however, this tends to be used as a top-up to the NHS.

The NIH however runs under a different system to the standard American Healthcare system. Since most patients are enrolled to a research protocol, all the costs for clinical care is funded for by the US Congress and the patients do not pay for any aspect of clinical care that is part of their research protocol. At the same time, if the patient leaves their protocol for personal reasons or because they are deemed no longer eligible for research, there is no compensation that the patient is entitled to. Similarly, if the

outcome of the research is in the form of a new drug, neither the patient nor their relatives are entitled to any financial benefit.

Objective 3: To explore the costs of managing multiple myeloma, in developing and developed countries, considering the emergence of new immunotherapeutic management of myeloma

Multiple myeloma is currently an incurable illness that requires long-term management not only due to the haematological complications but also the systemic sequelae of the disease, such as renal impairment and bony lesions. Patients are given strong chemotherapeutic drugs and also in some patients, hematopoietic stem cell transplant which itself carries a whole host of complications and hence requires careful long-term monitoring by doctors. Such complex medical management means that the financial costs for the patients can often be overwhelming over the long journey of the illness in countries where healthcare is privately funded in the majority of the population.

New methods of potentially curing multiple myeloma is under development, in particular a type of immunotherapy called chimeric antigen receptor T-cell (CAR-T) therapy. This involves extracting the patient's own T-lymphocytes, engineering them in vitro with viral vectors to express the receptor against the surface antigen found on their malignant cells, and reinfusing these engineered cells to the patient. The modified T cells then binds to the malignant cells using the chimeric antigen receptor and destroy the malignant cells.

Such treatment would require the installation of technologically advanced biomedical laboratories, machines, and trained staff to manufacture, administer and monitor the effects of the treatment. Weighing up the pros and cons of this emerging treatment, the costs of installing the technicalities is likely to be initially substantial, however, considering that this can potentially cure the disease, it can shorten the journey of the illness. Therefore, once the technical aspects are well-established and stabilized, it may offer both economically and clinically superior alternative to the current mode of management.

Objective 4: To explore a variety of hematological conditions and immunotherapies

During my time at NIH, I witnessed the management of a range of hematological conditions, both benign and malignant. One of the most frequent reasons for referral to the hematology consult service was for recommendation in anticoagulation. This involved weighing the patient's individual risk factors for thrombosis versus bleeding should they be started/continued on anticoagulation. Patients would often have a malignancy or be on a treatment for their research protocol, which increase the risk of thrombosis. In some patients, recommendation was needed as to which bridging anticoagulant will be used pre-op, in a setting of prior thrombotic history that was being treated as secondary prophylaxis. Having to determine the optimal solution for anticoagulation in these patients, based on their individual risk factors, was a thought-provoking and learning experience.

What made the experience at NIH even more valuable however is the exposure to various immunotherapies for both solid organ cancers and hematological malignancies, either through teaching conferences or work-up of patients. In the conferences, new findings about the disease course of the hematological malignancies and their management were discussed. In the clinical setting, I had the

opportunity to do literature search on patients' illnesses and their treatment to look for any associations with the reason for which the hematology consult service was required. From such experience, I learnt about not only the illness and the new treatment but also the complications the new treatments can bring, such as the cytokine-medicated severe inflammatory syndrome in CART cell therapy, autoimmune phenomenon associated with pembrolizumab etc