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Editorial

Immunotherapy in Neurological Diseases

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In the last century, the disease pattern has shifted the gears. With the widespread availability of the antibiotics, the mortality from the communicable diseases has dropped precipitously. This has increased the longevity, which in turn, at least partly, has led to plethora of non-communicable diseases (NCD). Among these NCD, there is a huge share of non-communicable neurological disorders. In 2106, neurological disorders were the major cause of disability-adjusted life-years (DALYs). Migraine, Alzheimer's, and other dementias were only second and third after stroke contributing to DALYs [1]. Further, the Migraine Research Foundation estimated that U.S. employees take 113 million sick days per year because of migraines, creating an annual loss of $13 billion [2].

Such a substantial burden of neurological diseases underscores the need for the development of more effective therapy. Before the advent of some of the newer therapies, many of the neurological diseases were treated with drugs that were developed for some other diseases. For example, many of the drugs used to treat migraine initially came out as anti-epileptics and anti- depressants. Even with the addition of more targeted therapies, like serotonin 5-HT1B/1D receptor agonists, only a third of patients had meaningful relief of symptoms [3]. Similarly, Multiple Sclerosis (MS) was first recognized as a new disease entity in 1868, but it was not until 1993 that the first drug for its long-term management was approved. Till then, only the MS flares could be treated with cortisone [4]. However, with year over year advancements in the field of neuroimmunology, several promising treatments have now become available which have decreased the morbidity and increased the quality of lives of patients. In May 2018, the first monoclonal antibody targeting calcitonin gene receptor peptide (CGRP) was introduced for migraine and so far, has shown to significantly decrease the number of migraine headaches and its hampering effects on daily activities [3]. Ocrelizumab is another example which was approved by the FDA in 2017 for the treatment of relapsing forms of multiple sclerosis (MS) and primary progressive multiple sclerosis (PPMS). Studies have shown reduced relapse rates and reduced worsening of disability compared to interferon beta-1a [5]. Immunotherapy also has paramount role to play in field of neuro-oncology. Studies are already underway for using recombinant nonpathogenic polio-rhinovirus chimera (PVSRIPO) for treatment of recurrent WHO grade IV malignant glioma known to have poor prognosis. According to the study, survival rate was higher at 24 and 36 months among patients who received PVSRIPO immunotherapy compared to the historical controls [6].

While the results of immunotherapy seem promising, the possibility of side effects from non-specific manipulation of immune system are conspicuous. Taking example of the new anti-migraine drug, the inhibition of CGRP not only affects the migraine pathogenesis but may also interfere with some physiological processes. Hence theoretically, there is a possibility that these agents could inhibit that protective physiological response to cardiac or cerebrovascular ischemia [7]. In the same line, Alemtuzumab used for relapsing- remitting MS was shown in one study to be associated with secondary autoimmunity in approximately 48% of the treated individuals, with Graves' disease being the most common complication [8].

In the past, immunotherapy has decreased the morbidity and mortality from infectious diseases and has gone as far as eradicat-

ing a menace like smallpox. We now need to focus on similar goals for neurological disorders. Vaccination should be developed for the diseases whose etiological factors are known. For other diseases, tools for rapid diagnosis, and the adequate ways to monitor the disease course and response to therapy are of key importance. The availability of advanced molecular techniques such as next generation sequencing has opened the doors to the development of new biomarkers such as the genetic variants of neuroimmunological diseases. These biomarkers can then be used for targeted immune therapies. The goal of therapy should be to eliminate the disease and prevent the recurrence while minimizing the side effects. To develop such efficient drug therapies, researchers and clinicians should embrace the idea of artificial intelligence (AI). Using AI tools, patients' data can be analyzed to design algorithms for the development of targeted immunotherapies. Moreover, as a global community and society also have to look into the affordability of the drugs, so as not to bankrupt the financials. Cost-benefit needs to be weight when looking into the newer therapy and cost-benefits need to be assessed when offering the therapies.

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