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EDITORIAL

TMU: Tuberculosis at a Glance

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1. Introduction

1.1. Background

Two dreaded diseases demand and receive international attention from the biomedical community. It is of pervasive interest with respect to our globalized welfare that there is ongoing concern about these two infectious diseases—tuberculosis (TB) and malaria. I call attention to three sources of current efforts all informative in various degrees and reflecting the source. Rather conveniently, my sources of information come from May, June and July 2010 publications. The May 14 issue of *Science* devoted a special section to the two diseases titled “Tuberculosis & malaria. Landscapes of infection”.¹ I regularly receive the newsletter *Illuminate* from the Director (Douglas Hilton, Ph.D., F.A.A.) of the Walter and Eliza Hall Institute of Medical Research, Australia. In the Winter 2010 issue, there is a short article titled “Blood-thinning copycat enters malaria fight”.² Another source perhaps closer to the public is found in the *Wall Street Journal* dated July 10–11, 2010, which published an article titled “The Tenacious Buzz of Malaria” with the interesting subtitle “Humans have underestimated the disease for millennia: new research and new worries”.³ After reading these articles, I deemed it interesting to briefly examine the research at TMU (Taipei Medical University) with respect to the two diseases, with a focus only on one.

1.2. Examining current publications

For the subject of this editorial, I did a PubMed search. “Tuberculosis” and “Taipei Medical University” turned up

48 references, with only four from TMU published in the narrow period of 2009–2010. “Malaria” and “Taipei Medical University” turned up nothing. So here I limit the presentation to the four that reveal respectable interest in the problem of TB as attacked from the angle of biomedical research, not demographic or epidemiological. These clinical and basic science investigations concern four states of health that are affected by TB: pregnancy; ischemic stroke; use of anti-TB therapy; and the fourth, which impinges on another difficult disease that is approaching a global crisis, especially in developed countries—TB and the interface with diabetes.

2. Relationship Between TB and Fetal Outcomes

The relationship between TB and fetal outcomes remains unclear. Thus, a team from the School of Health Care Administration led by Lin used a 3-year nationwide population-based dataset to determine the risk of adverse pregnancy outcomes: low birth weight (LBW), preterm birth and small for gestational age (SGA) infants among women with TB.⁴ Conditional logistic regression analyses were performed to compare the risk of LBW, preterm birth and SGA for mothers with TB and unaffected mothers. According to the results, mothers diagnosed with TB had significantly higher percentages of LBW (8.5% vs. 6.4%, $p=0.033$) and SGA (19.7% vs. 16.7%, $p=0.048$) infants than unaffected mothers. However, there was no significant difference in preterm birth (8.0% vs. 8.0%, $p=0.961$) between the two groups. The adjusted odds ratios of having LBW and SGA infants for mothers with TB were 1.35 (95% CI,

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1.01–1.81) and 1.22 (95% CI, 1.00–1.49) compared with unaffected mothers. Lin and colleagues concluded that women diagnosed with TB during pregnancy are at increased risk of having LBW and SGA babies compared with unaffected mothers. Because of the implications of the work, the investigators suggest that clinicians increase the awareness of women with TB of the potential risks before family planning.

3. Risks of Ischemic Stroke

From the Department of Neurology, and published in the journal *Stroke*, Sheu et al estimated the risk of ischemic stroke during a 3-year follow-up period after TB diagnosis using a nationwide, population-based study and a retrospective cohort design.⁵ There were 2283 patients who had received treatment for TB, except TB of the meninges and central nervous system, between 2000 and 2003; 6849 randomly selected subjects comprised the comparison cohort. Cox proportional hazard regressions were performed to compare the 3-year ischemic stroke-free survival rate between these two cohorts. Of the 9132 sampled patients, 392 (4.3%) experienced ischemic stroke during the 3-year follow-up period: 136 (6.0% of the TB patients) from the study cohort and 256 (3.7%) from the comparison cohort. After adjusting for patient age, sex, hypertension, diabetes, coronary heart disease, hyperlipidemia, malignancy, monthly income, and the geographical region and urbanization level of the community in which the patient resided, the hazard ratio of ischemic stroke for TB patients was 1.52-times (95% CI, 1.21–1.91; $p < 0.001$) higher than for comparison patients. The investigators concluded that patients with TB are at an increased risk for ischemic stroke but not hemorrhagic stroke in the next 3 years.

4. Diagnosing Tuberculous Meningitis

In another study from the Department of Neurology, but this time published in the *American Journal of Medical Science*, Sheu et al considered the challenging disease of tuberculous meningitis (TBM).⁶ The main problem confronting clinicians is the difficulty in making an early diagnosis, which is then followed by the serious consequences of delayed treatment. They examined 105 adult patients with TBM between 1997 and 2006 in a retrospective analysis. They defined treatment delay as progression of stage, and physician delay as the time between the initial presentation and initiation of anti-TB therapy. Two factors played a key role in the outcome: progression of stage and prolonged physician delay were evaluated using univariate and multivariate analyses. Clearly, rapid diagnosis and early treatment before progression of stage are crucial for

good outcome in TBM. Other observations are crucial. When TBM is acute and when discrimination from bacterial meningitis is difficult, it is mandatory to begin anti-TB and antibacterial therapy simultaneously. Or, treatment can lower the threshold for early anti-TB therapy when persistent fever, deteriorated consciousness status, or progression of stage occurs during antibacterial therapy.

5. Linkage Between TB and Diabetes Mellitus

Finally, the next research concerns a linkage between TB and another disease that is becoming an international epidemic. In the past, extrapulmonary TB (EPTB) has not been analyzed with respect to the impact of diabetes mellitus. From the Department of Internal Medicine, a team led by Weng conducted a retrospective study to investigate differences between EPTB patients with and without diabetes.⁷ EPTB patients who received initial treatments between January 2003 and March 2008 were recruited and grouped as “with-diabetes” or “non-diabetes” and their characteristics compared. The prevalence of hypertension and chronic liver diseases, the incidence of tuberculous peritonitis, and the total bilirubin levels were higher in EPTB patients with diabetes than in those without diabetes. The results are significant since theirs is the first investigation concerning the impact of diabetes on EPTB.

6. Perspectives

All three of the more popular articles end with promising hope. Stella Hurtley, Caroline Ash and Leslie Roberts advocate “careful well-funded R and D, combined with political will and strong health care systems that will help to lessen the impact of these terrible diseases of poverty”.¹ More specifically, Beeson, Boyle and Richards from the Walter and Eliza Hall Institute of Medical Research’s Infection and Immunity Division have identified a new approach that could stop the parasite (*Plasmodium falciparum*) infecting red blood cells. Heparin-like carbohydrates bind to MSP1, which stops the parasite from properly attaching to the red blood cell and therefore from invading. This finding supports the prospect of developing new anti-malarials that are based on the structure and activity of heparin-like molecules. Finally, the very long and astute article by Sonia Sham in the *Wall Street Journal* ends: “As countries with heavy malarial infections prosper and develop, the day will surely arrive when those still vulnerable to the bites of malarial mosquitoes will live in screened domiciles, more than a stone’s throw away from stagnant, mosquito-infested waters—or will suffer the brief sting of a highly

effective malaria vaccine—and malaria will be no more. Until then, let the abracadabra (i.e. hocus-pocus, open sesame, hey presto) cures continue!”

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