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Chronic Hepatitis B in Asian Communities: Overcoming Barriers to Optimize Management

Slide 1 Hello. Today, I would like to welcome everyone, and thank you for participating in this educational program by Asian Health Foundation. We are excited to present and discuss this topic, West Meets East for hepatitis B, because a vast majority of hepatitis B patients in the world, as well as in the US, are from East Asia. We would like to focus on the Eastern and Western approaches to the management of hepatitis B. Slide 2 I would like to introduce our distinguished faculty, Dr. Joseph Lim, Director and Professor of Medicine from Yale University, Dr. Jian Zhang, a long-time hepatitis B care provider and CEO of Chinese Hospital in San Francisco, and Dr. Danny Chu, a long-time hepatitis B and leader in the Chinese community in New York area. We will have three topics today. One is understanding hepatitis B from Eastern and Western perspectives by Dr. Joseph Lim, herbal therapy and acupuncture vs pharmacotherapy for hep B with Dr. Jian Zhang, and the impediments to hep B care~~,~~ discussion by Dr. Danny Chu. Slide 3 So, I would like to first ask Dr. Joseph Lim if you could give us an overview of the epidemiology of hepatitis B, and what are some of the Eastern and Western perspectives with patients with hepatitis B?

Dr. Lim:
Absolutely. Thanks very much for the opportunity to share some thoughts about this very important topic. Slide 4 I think we all recognize that we need to be very mindful of the cultural differences and perspectives in how we approach human health, and specifically ~~to~~ chronic hepatitis B infection. As noted, the hepatitis B epidemiology is notable for global burden of approximately 290 million persons. Of this group, we believe that there are about 2 million persons infected here within the United States, and within this group in the US, a significant proportion of these individuals are believed to be foreign-born. Recent estimates by NHANES epidemiologic survey suggest an overall seroprevalence of approximately 0.35 percent, which constitutes approximately 1.15 million persons. Now, we recognize that NHANES is not optimal for estimation of chronic infections because it excludes some of the highest risk populations, and in this context, a number of studies suggested that when you take into consideration foreign-born persons, the true burden of chronic hepatitis B may be as high as 2.2 million persons. A recent consensus conference estimate suggests an overall burden of approximately 1.6 million persons, with an upper interval up to about 2.5 million persons.

Now, we recognize that the reason why we care about hepatitis B and the ultimate implication is that a significant proportion, up to one in four, may die of liver disease and/or liver cancer. Because of the unique relationship between chronic hepatitis B and carcinogenesis with hepatocellular carcinoma, hepatitis B is the number two carcinogen in the world after tobacco. And, approximately 70 percent of all hepatitis B related deaths are attributable to liver cancer.

Slide 5 Now, if you take a deeper look into the epidemiology among US individuals with chronic HBV, we see a disproportionate burden to ethnic groups, specifically, among Asian-Americans and non-Hispanic Blacks. We estimate that about 70 percent are foreign-born, and are predominantly Asian, about 60 percent of that group. Now, if you look at a comparison to the general population, again, two groups are higher than the general population, including Asians (about eightfold the general prevalence) and non-Hispanic blacks (about twofold general prevalence). And, as expected, there are some differences between US-born and foreign-born persons.

Slide 6 Now, as we think about this burden of disease that is concentrated in foreign-born persons, predominantly from the Asian continent, we must take into consideration differences in perspectives in our care of these patients. Eastern medicine approaches, such as Chinese Medicine and Complementary and Alternative Medicine, have been used for centuries. And, the theoretical

foundations really stem from ancient philosophies that rely on two therapeutic approaches of holism and syndrome differentiation. And, it's important to note that the human body is not viewed as an entity in which there are organs that are working interdependently, but really all part of a global universe interaction between human and the surrounding environment. And, in this context, human illness is actually viewed not in terms of dysfunction of organ systems, but an imbalance of Yin and Yang. Slide 7 Now, chronic hepatitis B and liver disease broadly do not easily fit within the definitions of traditional Chinese medicine. However, the components that are linked to chronic hepatitis B include the following concepts: Number one, weakening of Qi, which are biological substances and activities that preserve life; number two, blockage of meridians, which represent circulation channels of Qi by blood stasis; and number three, generation of dampness and heat, which suggests inflammatory pathogens.

Slide 8 Now, in this context, we need to highlight that this directly influences many of our patients in terms of how they view their health specific to hepatitis B and liver disease. Whereas in the West, we view the body as a machine, in the East, it's viewed as a garden. In the West, we view hepatitis B and liver disease as a diseased organ rather than a weakening of the Qi. In the East, we look at hepatitis B as a blockage of meridians. Liver inflammation in the West, generation of heat in the East. And, this directly influences therapeutic approaches. So, in the West, we focus on pharmacologic therapy with antivirals, with oral, nucleoside or nucleotide analogues, whereas in the East, the focus on restoration of balance, of pathogenic and Qi, including a focus on nutrition, herbal therapies and acupuncture.

Slide 9 Now, we do need to keep in mind that a lot of these traditional Chinese medical approaches have not until recently been validated using traditional Western scientific approaches but, there is an abundance of growing literature, particularly within the last ten years, to support the physiologic basis of traditional Chinese medicine and therefore, this has renewed interest in drug developments of herbal entities, and we are very excited. There have been important advances in the validation of inflammatory, antioxidant and antifibrotic properties of some of these key herbal components of traditional Chinese medicine and herbal therapies. There remain important challenges in drug development, predominantly due to the isolation and purification of the individual components of herbal therapies. But we know that with increasing attention, support by the NIH and rigorous methodology and clinical trial developments, we do anticipate that some of these traditional approaches may be validated using Western scientific methodology.

Slide 10 Now, if you think about modern medicine in the West, we think about the slide here towards the left bar, we think about treatments like pegylated interferon, oral nucleoside/nucleotide analogues such as entecavir and tenofovir. And on the right, we look at the approach in Eastern medicine, which focuses on manipulative body-based therapies, diet, herbal medicines and vitamins, and think about homeopathy, naturopathy and acupuncture. These are fundamental differences in perspectives and approaches to therapy between the East and West. Slide 11 Now, I want to highlight that this is not something that is concentrated in a very small proportion of patients with hepatitis B. We believe that up to 70 percent, based on current studies, of patients with chronic hepatitis B use complementary and alternative medicines. Therefore, it is important that we, as clinicians, routinely query our patients about the use of complementary or alternative medicines, or traditional Chinese medicine in our evaluation of patients. We need to have careful, mindful discussions with patients about what we know about the safety and efficacy of these approaches. And, I believe that we must think about these as complementary approaches between East and West so we can augment our understanding of these different perspectives to improve the quality of care of patients with chronic hepatitis B.

Slide 12 So, in conclusion, I hope I've been able to articulate that hepatitis B remains a very common global and local public burden with substantial morbidity and mortality due to its link to liver cirrhosis and liver cancer. Although current Western therapies are highly effective in suppression of HBV DNA with improvement in clinical outcomes, we must recognize that Eastern medicine approaches remain commonly used in our patients with chronic HBV, particularly in those from Asian communities. Therefore, clinicians should routinely query their patients regarding their use of these therapies and counsel them regarding known safety and efficacy. It is quite clear that additional investigation is needed to further define the potential utility of traditional Chinese medicine and complementary alternative medicines in future treatments of chronic hepatitis B. Thank you very much, Mindie, for this opportunity.

Dr. Nguyen:
Thank you so much, Dr. Lim. That was a very clear and helpful review and discussion of the foundational differences in the Eastern and Western approaches to hepatitis B management and perspective. That is very helpful for care. Slide 13 Now, I would like to turn to Dr. Jian Zhang in regards to the complementary care approach to hepatitis B. As Dr. Lim already alluded to, this would be herbal medication, acupuncture. Could you give us more information on some examples of herbal medicine, acupuncture versus the Western traditional pharmacotherapy for hepatitis B?

Thank you very much, Dr. Nguyen. Slide 14 I will talk a little bit about herbal therapy and acupuncture versus pharmacotherapy in treatment of chronic hepatitis B. in the United States. Sadly, only 18.6 percent of chronic hepatitis B is diagnosed with very low treatment rate of only 5.7 percent here. I want to point that out. And in the United States, there is a lot of herbal medicine that's used, about 30 to 50 percent, and more so in China and in Taiwan, with 80 percent. So, a lot of our patients are using herbal medications,

even those not approved, butcalled supplements.

Slide 15 The goals of pharmacotherapy in chronic hepatitis B. The primary goal is to sustain suppression of viral replication. And, the secondary goals:to achieve clinical remission, which includes ALT normalization, loss of hepatitis B e-antigen and surface antigen, and stabilize liver function, and also to prevent or delay progression to cirrhosis and liver cancer.

Slide 16 Herbal therapy in chronic hepatitis B. There are no herbal treatments proven to improve outcomes in patients with chronic hepatitis B. I know that there are a lot of studies, but a lot of them are poor quality and no control and protocol. That's why some of the medicines can cause serious liver toxicity, because it's not really going through clinical trials. A lot of them, it's considered a supplement. I had a patient who took the supplements and it caused elevation of liver enzymes--and ended up in the hospital. Herbal treatments are not recommended for patients with chronic hepatitis B. A lot of patients can buy it in a market, so, that's why it's really widely used by our patients.

Slide 17 Acupuncture in treatment of chronic hepatitis B is very common, too. It was first documented a long, long time ago, a hundred years B.C., in *The Yellow Emperor's Classic of Internal Medicine*. And so, widely used in clinical practice in a lot of the Asian countries to decrease discomfort, relieve symptoms like loss of appetite and nausea, right upper quadrant discomfort, typical chronic hepatitis B symptoms. Acupuncture can increase leukocyte counts, increase blood natural killer cell count and activity, and improve erythrocyte immune function, and reduce TNF-alpha and interleukin 1 beta in the serum. Acupuncture is very commonly used in China, ~~as~~ I have visited many clinics there, and here in United States, too.

Slide 18 So, if you would like to look into this Cochrane study by Kong and colleagues, they talk about eight randomized clinical trials with 555 patients, all in China, and compared acupuncture therapy versus no intervention. And again, a lot of the studies they used said that there's some improvement in patients' symptoms, and then some increase the conversion of hepatitis Be-antigen. But, a lot of the studies are not well controlled, so that's why some of them were saying that they have some reduction in detectable hepatitis B DNA levels. And, because there are no strict controls, we really don't know whether it's acupuncture or it's other treatments there.

Slide 19: Antiviral Therapies] The antiviral therapies, we know, are proven to decrease

Slide 20 In summary, I would like to point out that the effects of acupuncture for chronic hepatitis B, it's not clear and more controlled studiesshould be done to prove that. And, benefits of herbal treatments of chronic hepatitis B are really not proven. And so, I think again, more controlled studies should be done, and not just that it's not helpful; some of them are really harmful, because can cause liver toxicity. Certain herbal treatments can cause life-threatening liver failure, and so really not recommended at this point. I know a lot of patients say I want to try, but really should talk to their doctors and make sure that severe liver failure is not going to happen. Thank you very much.

Dr. Nguyen:
Thanks so much, Dr. Zhang, for giving us a very comprehensive and detailed review of this very important topic. Many of our patients use it, and many believe in it even more than the Western medicine that we are familiar with.

Slide 21 Next, I want to ask Dr. Chu if you could help review for us the current barriers for hepatitis B care, because the barrier is not just financial, as many people may think. Data from even patients with private insurance in the US show that only about 20 percent of US hepatitis B patients have been diagnosed, and even patients with very severe complications like cirrhosis and liver cancer, only about one-third or one-half have received treatment. So, Dr. Chu, could you help us understand more of the barriers and how we could help overcome some of these?

Dr. Chu:
Great, thank you very much. I've been practicing in New York City Chinatown for about 25 years. ~~so~~ A lot of the subject matter is something I've experienced, so maybe I can share some of that thought on the impediments to hepatitis B care.

Slide 22 Well, first, there's a lot of misconception and there's reality. So, whenever I see a patient, I try to gauge their understanding. The first thing I ask, how do you get hepatitis? And sure enough, a lot of people say well, you get it through sharing food and utensils, and in fact, some family member will say I have bowls in the house. Well, the reality is that it is transmitted through blood and body fluid and sex. I tell them that you can share the forks and knives, but don't share the razors and the toothbrushes. And have your family members tested, because obviously, they should be immunized or make sure they're not a carrier.

The second thing they always talk about is that well, my mother has it, I have it, so it must be inherited. The reality is that it is not a genetic disease, but it is something that can be given through vertical transmission, so that's something I go through with them, again, just to educate them. The third thing is they feel well, I have no symptoms, so do I really have hepatitis B? And, I think that they associate jaundice with liver diseases but the reality is that that only occurs with acute symptoms. But, when, I try to explain to them,

you have chronic hepatitis B, you'll be asymptomatic and for that reason, you should be followed with a doctor to make sure that your liver enzymes and your virus level is okay.

The last thing that they don't understand is that they don't think there's a treatment available. What I tell them is that the reality is that there is treatment. But I go further and say that there is no cure, especially if you're on any type of antiviral; there is no cure, and the fact that some doctor may give you medicine for three months, well, you can't stop it after three months. You have to continue taking it. So, these are a couple of points that I try to explain to the patient so that we can at least get to where they can understand it.

One of the biggest things is education; try to educate the patient from day one, when you start seeing the patient, to gauge what they know, and try to supplement what they know with some information so they can at least go home understanding a little bit about hepatitis B.

Now, after talking about~~, really,~~ the misconception, there's a lot of ~~also~~ bad perceptions about hepatitis B. Slide 23 Here we have a survey that was done in rural China, about 6,000 people who were found and were looked at. And this is a study from 2016, so this is not from the 1980s, right? You find that there's a lot of people who are unwilling to accept gifts from hepatitis B carriers, which is about 67 percent. About 78 percent of their family will not permit their children to play with hepatitis B carriers. 72 percent will not have dinner with hepatitis B carriers at this point. And, about 61 percent of the people will not even touch the patient with hepatitis B, whether it be a hug or a handshake.

Slide 24 Now, how about self-perceptions? What do patients themselves think about hepatitis B? A lot of them, more than 58 percent, think that hepatitis B brings trouble to the family. 36 percent think they should avoid close contact with other family, and 33 percent think they're not a desirable spouse. I just had this last week, where a man and a woman were going to get married. The man was here to see me for hepatitis B and I said, “Have your family members tested?” And the woman goes, “Well, I can't tell my family members because if they know he has hepatitis B, they won't let me marry him.” Well, that's a real thing that's happening these days, so these are some of the perceptions. Obviously, people have experienced discrimination from employers from having hepatitis B, so they don't want to reveal that because that'll be something that employers can use against them.

Slide 25 Now, again, in Asian countries, a lot of hepatitis B institutional stigma. In China, admission has been denied to school/university because you have hepatitis B. There has been unfair treatment from employers. In fact, it's only in the 2000s, 2007, there was anti-discrimination legislation to end termination of a worker with hepatitis B. In 2010, they banned testing for hepatitis B before starting school or work. So, this is actually some of the stuff that people have experienced as they're living in this Asian country. I have a patient who comes to see me from Minnesota every six months. And he speaks perfect English, so he doesn't have to come to see me for hepatitis B, but he does it because he owns two restaurants and he doesn't want the health department to know he has hepatitis B, because he's fearful that they're going to shut his restaurant down. So, there's a lot of stigma that's attached to that.

Slide 26 Now, in the community setting, maybe the socioeconomic status and language barrier, would hinder them from understanding hepatitis B. But, if you look at even American college students who are Asian, here's a study with 258 students and you ask them questions and only 22 percent of them knows that it is not hereditary, so 78 percent doesn't know. 61 percent believe that you can get it from a shared utensil. And, only 50 percent knew that you can get it from sex and blood. So, the last two slides are trying to raise ~~is~~ the point that we do need to do a lot of education in the community setting with our Asian patients.

Slide 27 Now, what does that mean? Well, this means ~~is~~ you get some clinical consequences, right? So, if there's a negative perception, you don’t understand what's going on, then you don't want to be tested. And, if you don't want to be tested, there's obviously going to be a delay in hepatitis B diagnosis, which leads to continued transmission of hepatitis B from person-to-person. And, if you don't know you have the disease, then you can't really monitor and manage your disease well. And, there's a delay in treatment. And, as Joe said the first time you may even find out you have hepatitis B is when you have right upper quadrant pain. You do a sonogram, you may find out you have liver cancer. which obviously is what people usually die from, progression of the disease from liver cirrhosis to cancer. So, as a whole, we want to catch the disease early. We don't want to have these problems with mortality and cancer and cirrhosis.

Slide 28 Now, we can go back and say well, these are the patients. How about the people who provide the care? Are they up to par? This is a study done where surveys were mailed to Asian primary care doctors or healthcare providers who take care of more than 25 percent Asian patients. And, about 95 percent of the healthcare providers said they screen the patients for hepatitis B. But if you ask them if they're routinely screening all of their patients, only 20 percent does. And, if you ask them do you routinely screen all of the Asian patients, only 50 percent of the primary care doctors or healthcare providers say yes. And, you know, if you follow the CDC guideline, anything with a prevalence of greater than 2 percent needs to be screened. So, I'm going to guess that 50 percent is a little bit too low; it should be closer probably to 90 to even 99 percent. And, if you ask the question what's the reason for hepatitis B screening test in Asian patients, 26 percent said it was from elevated liver tests, and 21 percent said elevated liver tests plus a family

history of hepatitis B or liver disease. Again, when you have elevated LFTs and you're doing further testing, it's not screening anymore, really; you're trying to make a diagnosis. Screening means you're just testing all the at-risk population.18 percent of the doctors screen patients born outside of the United States, right? That should be maybe higher, as I said; if you have Asian patients who were born outside the United States, a lot more should be tested.

Slide 29 In terms of the most important reason for not ordering a screening test of Asian patients: Well, 23 percent said they're not considered to be an at-risk group for hepatitis B. 16 percent said they have no symptoms of hepatitis B… of liver disease. Again, they have their own misconception. Why would you not screen somebody, when they're an at-risk group, and only test people who have symptoms? The third thing is 15 percent said well, they've had their vaccination series. Well, in my practice, I always test the people with the vaccination series anyway because you want to know if they're immune. But, in certain countries, they just give vaccine without testing if you're a carrier or not, so sometimes people who are hepatitis B carriers are getting a vaccine, which aren't going to work anyway, so they should be tested. And, only 13 percent of the people said well, I'm not testing the Asian patients because they have no insurance. Well, as you know, these tests are pretty cheap. You can probably do a surface antigen antibody test for less than $30 with some of the commercial labs that you can make a deal with, so that shouldn't be an excuse. We really also need to educate our primary care doctors who care for our Asian patients so that a lot more patients are being tested. As my previous colleagues mentioned, a lot more people are left undiagnosed.

Slide 30 Now, if you happen to get the patients diagnosed and get them to the point where they're going to get treated, one of the biggest problems is non-adherence. I don't think non-adherence is really unique to just hepatitis B; I think it applies to diabetes, high blood pressure. People take their medicine, they stop the medicine, they skip a few days. Well, the problem with hepatitis B, is that if you do that, then there's always a risk of resistance. There's a survey of chronic hepatitis B on what is a barrier to treatment, about 300 patients, and they found out that medication is expensive in about close to 50 percent. 45 percent said forgetfulness. I always tell my patients to tie that hepatitis B medicine to the toothpaste, so when they brush their teeth, they can take one. There's a lot of concern of side effects, they're concerned about certain medication with kidneys and with bones and whatnot. But I think that goes along also with education. And, some people are nonadherent because they don't want other people to know. Slide 31 So, there's a lot of misconception, a lot of negative perceptions, and I think that comes from the fact because there's a gap in hepatitis B knowledge. Hepatitis B is not a national health priority issue like HIV. Because of that, there's a lack of education and funding, a lack of media coverage. You know, in certain Asian countries, a certain star has hepatitis B, they'll do a lot of public service announcements but we don't have that. A lot of the hepatitis B formal education is not integrated at school. I asked my daughter about hepatitis B and they don't have that in school. Only 14 states require hepatitis B vaccine before start of school, and only eight states mandate hepatitis B education. So, I think one of the biggest things we can do is that once a person is in front of you as a captive audience, I think the most important thing is not just give the medication and say take it, but I think you have to sit there and really try to understand what their understanding of hepatitis B is and try to help them understand a little bit better, and I think that goes a long way in helping them be more compliant with medication, and hopefully as this topic says, bring the Eastern philosophy closer to the Western perspectives in treatment. So, thank you very much.

Dr. Nguyen:
Thank you, Dr. Chu. And, I would like to thank again our faculty, Dr. Joseph Lim, Dr. Jian Zhang and Dr. Danny Chu for reviewing with us very important foundational differences in the Eastern and Western approaches. I also would like to thank our viewers, and we hope that the information we presented today will be helpful to you and your patients in your practice. As Dr. Chu pointed out, there is much to be done, both at the health policy level, as well as at the individual doctors and patient. So, we all can do more, one at a time. And, thank you again so much for joining us.