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Pfizer Also in DOJ Probe of Pharma Bribes Funding Iraqi Terrorists

Pfizer has joined three of its Big Pharma peers in a Department of Justice probe examining allegations that the companies paid bribes to a terrorist-run health ministry in Iraq.

https://www.fiercepharma.com/pharma/pfizer-discloses-department-justice-probe-into-iraq-terrorist-bribery-allegations

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India Apotex Plant Receives Third Warning Letter in 4 Years

Apotex, Canada's largest drugmaker, has again had a plant in India cited by the FDA in part because of testing methods that left doubt about the quality of products coming out of the manufacturing facility in Bangalore, India; citing it for many of the same issues uncovered in 2014 and 2015. In fact, the agency pointed out that it has found many of the same issues in a number of Apotex plants over the last five years, displaying its frustration that Apotex seems unable, or unwilling, to learn from past mistakes.

https://www.fiercepharma.com/manufacturing/apotex-plant-india-hit-third-warning-letter-four-years
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FDA Compounding Restrictions-Required Medications will Disappear-A Call for Intervention

Abstract

Drug compounding is undergoing a sea of change as the Food and Drug Administration (FDA) is imposing restrictions on what ingredients can be compounded and whether they may be held in the physician's office for multiple uses as well as limiting interstate shipments. The FDA has been subjecting ingredients that have historically been an important part of medical practice to a monograph style review, resulting in rejection of ingredients in favor of approved drugs, even those for which a *US Pharmacopeia* dietary supplement monograph exists. The article describes the encroachment by the FDA on the practice of medicine and efforts by the American Association of Naturopathic Physicians, the Integrative Medicine Consortium, and the International Academy of Compounding Pharmacists to address problems of access to needed medications.

Conclusion

The FDA's approach to compounding is a case study in a bureaucratic overreaction that threatens to do more harm than the original problem it was intended to solve. The FDA repeatedly cites the NECC tragedy as justification for its wholesale resetting of compounding practice, but there is no nexus between the criminal production of methylprednisolone acetate (MPA) and the removal of scores of needed ingredients from the market or prohibitions from office use. Ironically, pharmacies can still compound preservative-free MPA. Physicians are facing the loss of important drugs and nutraceuticals and the freedom to access them in their office. It is important to be aware of these changes, and to help educate the FDA about the value of these medications.

EVERY COMPOUNDING PHARMACIST SHOULD READ THIS DOCUMENT!!
http://www.imjournal.com/index.cfm/fuseaction/Content.Main/id/101
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Sci Rep 2018 Jul 17; 8:10812

Bacteriophages, the Microbiome, and Parkinson Disease: Possible Treatment Implications

Compared with healthy controls, patients with PD had reduced levels of Lactococcus *spp. in the gut and increased levels of lytic Lactococcus-specific bacteriophages.*

The microbiome's role in both the pathogenesis and treatment of Parkinson disease (PD) and of neurodegeneration in general has become a hot topic. To explore the idea that gut phagobiota (the combination of all bacteriophages) may be altered in PD, investigators used a published dataset to analyze bacteriophages and to determine the phage/bacteria ratio in early untreated PD patients and healthy controls.

Compared with controls, PD patients exhibited reductions in lactic acid producing bacteria implicated in dopamine production and in regulating intestinal permeability, particularly *Lactococcus* spp. However, the number of the corresponding bacteriophages was not decreased in PD patients. Moreover, the proportion of lytic-phase bacteriophages was increased in PD patients compared with controls. The authors speculate that phages present in dairy (lytic c2-like and 936-like phages) may have been responsible for the decreased numbers of *Lactococcus*.

COMMENT: This study was small and drew on a previous dataset from 31 PD patients. The human microbiome consists of bacteria, archaea, fungi, and viruses. Bacteriophages are viruses. These viruses are more numerous than many bacteria. Administration of bacteriophages can shift the microbiome and can influence intestinal permeability. The bacteriophage approach for treatment will depend on reduction of target bacteria. The recent epidemiologic finding of an association between dairy intake and the development of PD makes the current findings intriguing (Neurology 2017; 89:46). One can speculate that there is a link to bacteriophages. Whether the use of a bacteriophage or other approach to influence the microbiome will alter PD risk or result in a beneficial symptomatic effect for patients with PD remains unknown.

CITATION(S): Tetz G et al. Parkinson's disease and bacteriophages as its overlooked contributors. Sci Rep 2018 Jul 17; 8:10812. (https://doi.org/10.1038/s41598-018-29173-4)

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Ann Intern Med 2018 Jul 3; 169:36

Understanding Overdiagnosis as a Consequence of Cancer Screening

Helping clinicians, patients, insurers, and policymakers better understand and communicate about this screening outcome.

Overdiagnosis represents a central concern regarding the potential harms of cancer screening. In a Special Article funded by the Agency for Healthcare Research and Quality, the authors focus on defining, estimating, and communicating with patients about this important but elusive concept. Overdiagnosis — defined as detection of histologically confirmed cancer through screening that would not otherwise have been diagnosed during a person's lifetime had screening not happened — is not the only harm that can result from cancer screening. False-positive results, which occur when a screening test erroneously suggests cancer is present (e.g., positive breast imaging results leading to a negative biopsy) may be confused with overdiagnosis.

Because overdiagnosis cannot be directly measured (and cancer incidence varies widely with geographic region, race/ethnicity of the study population, and research methodology), estimates vary widely. Accordingly, reports estimating overdiagnosis should also note relevance to U.S. populations. Patients may best comprehend the concept of overdiagnosis when it is expressed as the number of overdiagnosed cancer cases per total number of persons screened. In the “excess-incidence” strategy, the number of cancers observed in a screened population is compared with that expected without screening; the difference represents the number of overdiagnosed cancers. Population-based randomized trials with long follow-up and minimal screening in the comparison groups provide the most reliable estimates of overdiagnosis.

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COMMENT: The U.S. public often finds it difficult to understand how cancer screening can generate harms; thus, it's challenging for clinicians to effectively communicate this concept to patients. Enthusiastic media-based support for screening, fears about cancer, low levels of health literacy, and financial incentives associated with fee-for-service healthcare combine to create formidable barriers to understanding and addressing overdiagnosis. For example, when national guidelines recently changed to advocate cervical cancer screening every 3 to 5 years instead of annually, I encountered numerous confused, angry patients. When discussing overdiagnosis, clinicians should consider their patients' values and priorities, keep the message simple, and discuss both the benefits and harms of screening.

CITATION(S): Davies L et al. Defining, estimating, and communicating overdiagnosis in cancer screening. Ann Intern Med 2018 Jul 3; 169:36. (https://doi.org/10.7326/M18-0694)

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Lancet 2018 Aug 4; 392:400

Combined Therapy of PPI and Aspirin Decreases Progression of Barrett Esophagus

A large, 8-year study supports high-dose proton-pump inhibitor plus daily full-dose aspirin use in patients with well-established Barrett esophagus.

In a phase III, prospective, industry-supported trial, investigators examined the safety and efficacy of treatment with a proton-pump inhibitor (PPI) plus aspirin to prevent progression of Barrett esophagus.

Over 2500 patients with Barrett esophagus were randomized to treatment with low-dose (20 mg once daily) or high-dose (40 mg twice daily) esomeprazole with or without full-dose, once-daily aspirin. The composite study endpoint was all-cause mortality or progression of Barrett esophagus to either high-grade dysplasia or cancer. Median follow-up was 9 years. Results were as follows:

- High-dose PPI was superior to low-dose PPI in delaying time to the composite endpoint.
- Aspirin use was superior to nonuse when NSAID users were censored from the analysis.
- The combination of high-dose PPI and daily aspirin had the strongest protective effect.
- Serious adverse events were rare (1%).

COMMENT: This is a very important study that should change practice. While both PPIs and aspirin have proven adverse side effects, their protective effects in this study population outweigh those risks and make it very reasonable to put patients with well-established Barrett esophagus on combined PPI and aspirin therapy. The need for a high-dose PPI could be greater in patients with longer segments of Barrett esophagus (due to poor esophageal motility and increased acid exposure), but that cannot be determined from this study. I will encourage my patients with Barrett esophagus to take this combination regimen but will also look forward to further studies that examine which subgroups might be managed with lower doses of PPI, aspirin, or both.

CITATION(S): Jankowski JAZ et al. Esomeprazole and aspirin in Barrett's oesophagus (AspECT): A randomised factorial trial. Lancet 2018 Aug 4; 392:400. (https://doi.org/10.1016/S0140-6736(18)31388-6)

Hvid-Jensen F and Drewes AM. Should aspirin and PPIs be recommended for patients with Barrett's oesophagus? Lancet 2018 Aug 4; 392:362. (https://doi.org/10.1016/S0140-6736(18)31618-0)

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Vaping: The FDA Weighing a Ban on Flavored E-cigarette Liquids

Teen vaping is reaching epidemic levels, and the FDA is considering regulation to curb it. One proposal would be banning flavoring of e-cigarette liquids. Companies "have introduced new products at an alarming pace in total defiance of law, with no apparent concern for FDA enforcement," the groups wrote. More than 2 million middle school, high school, and college teens use these battery-powered devices to heat liquid-based nicotine into an inhalable vapor.

https://www.usatoday.com/story/news/nation/2018/08/13/teen-vaping-fda-weighs-ban-flavored-e-cigarette-liquid/890218002/

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Gains Noted in Breastfeeding in U.S.

By Kelly Young, Edited by David G. Fairchild, MD, MPH, and Jaye Elizabeth Hefner, MD

Breastfeeding rates at 6 and 12 months increased from 2014 to 2015, but some areas are still falling short of Healthy People 2020 goals, according to the CDC's Breastfeeding Report Card.

Roughly 83% of women who gave birth in the U.S. in 2015 started breastfeeding. At 3 months, 47% were exclusively breastfeeding, but by 6 months this fell to 25%, just shy of the Healthy People 2020 target (25.5%). At 12 months, 36% of all infants were breastfeeding at least part of the time.

Of note, a quarter of infants are currently born at healthcare facilities that follow recommended practices for breastfeeding mothers and infants, while half of workplaces provide lactation support programs.

LINK(S): Breastfeeding Report Card (Free), Healthy People 2020 objectives (Free), Background: Physician's First Watch coverage of 2011 report card (Free)

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Int J Eat Disord 2018 Jul 22

Risk for Disordered Eating in Adolescents with Type 1 Diabetes

Overweight and obesity, lower physical activity level, high HgA_{1c} level, and missed insulin injections were risk factors for disordered eating behavior.

In a cross-sectional, population-based study in Italy, researchers examined the risk for disordered eating behaviors in adolescents with type 1 diabetes. Participants were screened with the Diabetes Eating Problem Survey-Revised (DEPS-R), a validated, 16-item, self-report screening tool.

Among 163 adolescents included in the analysis, the prevalence of screening positive for disordered eating behavior on the DEPS-R (i.e., score ≥20) was 42% (95% confidence interval, 31%–53%) in girls and 27% (95% CI, 17%–38%) in boys. A DEPS-R-positive profile was characterized by the following: overweight or obese, low physical activity level, low socioeconomic status, missing insulin injections, and poor metabolic control (i.e., hemoglobin A1c >7). In logistic regression analyses, overweight youth had a sixfold elevated risk for being DEPS-R-positive, and the probability of being DEPS-R-positive increased with rising HbA_{1c} level and number of insulin injections missed and decreased with each added hour of weekly physical activity.

COMMENT: These data underscore the need to screen adolescents with type 1 diabetes for disordered eating behaviors during both endocrinology and primary care visits. They also support the importance of multidisciplinary care, including mental health supports, in pediatric chronic disease management, as well as promotion of exercise. Although disordered eating was slightly more common in girls, over a quarter of the boys studied had a positive screen. This study is a “note to self” to remember to screen boys and not rule out an eating disorder just because the patient is not underweight.

CITATION(S): Cherubini V et al. Disordered eating behaviors in adolescents with type 1 diabetes: A cross-sectional population-based study in Italy. Int J Eat Disord 2018 Jul 22; [e-pub].
(https://doi.org/10.1002/eat.22889)

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Gastroenterology 2018 Aug 1; S0016-5085(18)34821-2

Serum Branched-Chain Amino Acid Level: A Possible Biomarker for Pancreatic Cancer Risk?

A large observational study in Japan shows a positive, dose-dependent association between total BCAA level and pancreatic cancer incidence.

Elevated serum levels of branched-chain amino acids (BCAAs), including leucine, isoleucine and valine, are shown to be biomarkers of elevated risks for diabetes, insulin resistance, and obesity. These conditions are also risk factors for the development of pancreatic cancer.

To determine the relationship between total serum BCAA level and pancreatic cancer risk, researchers performed a nested, case-control study among approximately 30,000 individuals aged 40 to 69 years enrolled

in a population-based, prospective cohort study in Japan. Patients gave blood samples for serum BCAA level assessment. Median follow-up was 16 years.

A dose-dependent association was observed between BCAA level and pancreatic cancer risk. The odds ratio for developing pancreatic cancer among patients in the highest quartile for BCAA level compared with those in the lowest quartile was 2.3 after adjustment for potential confounding factors. Serum BCAA level was significantly elevated in patients with cancer when blood samples were taken ≥10 years prior to diagnosis (odds ratio for highest vs. lowest quartile, 4.3; 95% confidence interval, 1.4–13.1) but not when they were taken <10 years before diagnosis (OR for highest vs. lowest quartile, 1.5; 95% CI, 0.6–4.1).

COMMENT: An easy-to-use, reliable, inexpensive biomarker is currently lacking for pancreatic cancer. These findings suggest that total serum BCAA level could be such a biomarker and if so, could be used as a screening test in asymptomatic individuals or potentially to gauge response to treatment in patients with pancreatic cancer. It is unknown if adjusting BCAA levels might lower the risk for pancreatic cancer. While this research is still in an early stage, BCAAs are likely to be a target of further study in the near future.

Note to readers: At the time we reviewed this paper, its publisher noted that it was not in final form and that subsequent changes might be made.

CITATION(S): Katagiri R et al. Increased levels of branched-chain amino acid associated with increased risk of pancreatic cancer in a prospective case–control study of a large cohort. Gastroenterology 2018 Aug 1; S0016-5085(18)34821-2; [e-pub]. (https://doi.org/10.1053/j.gastro.2018.07.033)
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Gastroenterology 2018 Jul 27

Safety and Efficacy of GS-0976 for Nonalcoholic Steatohepatitis

Is a drug for treating nonalcoholic fatty liver disease on the horizon?

Although nonalcoholic fatty liver disease (NAFLD) is one of the most common liver diseases, no specific drug therapies have yet been identified to treat it. Now, researchers report phase II safety and efficacy findings on the investigative drug GS-0976 for treatment of nonalcoholic steatohepatitis (NASH).

Investigators randomized 127 patients with NASH to receive GS-0976 20 mg, GS-0976 5 mg, or placebo daily for 12 weeks. NASH was defined by liver biopsy findings indicating NASH and stage 1–3 fibrosis, or by hepatic steatosis ≥8% on magnetic resonance imaging and liver stiffness ≥2.5 kPa on magnetic resonance enterography.

A hepatic steatosis reduction of ≥30% from baseline occurred significantly more frequently in the GS-0976 20-mg group (48%), but not the 5-mg group (23%), compared with the placebo group (15%). Liver stiffness based on magnetic resonance elastography did not differ among the groups, but GS-0976 20 mg was associated with a significant dose-dependent drop in the serum fibrosis marker TIMP1. Adverse events were similar across all groups, and of five serious adverse events reported, none were related to the study drug.

COMMENT: This candidate agent demonstrates a benefit of reduced hepatic steatosis in patients with NASH. Although hepatic fibrosis did not improve based on liver stiffness, this is likely due to the short study duration, and one serum fibrosis marker did improve, so longer-term studies might possibly show fibrosis improvement. Pending future phase III trial results, we may soon have a specific therapeutic option for our patients with NAFLD.

CITATION(S): Loomba R et al. GS-0976 reduces hepatic steatosis and fibrosis markers in patients with nonalcoholic fatty liver disease. Gastroenterology 2018 Jul 27; [e-pub]. (https://doi.org/10.1053/j.gastro.2018.07.027)

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Am J Gastroenterol 2018 Jul; 113:1045.

Are Antibiotics Necessary in Acute Uncomplicated Diverticulitis?

Perhaps surprisingly, antibiotic therapy did not improve outcomes in two randomized trials.

In the U.S., patients with acute diverticulitis almost always receive antibiotic therapy. However, in two recent randomized controlled trials from Sweden and the Netherlands, antibiotics did not improve outcomes in patients with uncomplicated diverticulitis during 6 to 12 months of follow-up (Br J Surg 2012; 99:532; Br J Surg 2017; 104:52). Now, the researchers from the Dutch trial — which involved 528 patients with first episodes of relatively mild, uncomplicated diverticulitis — report 2-year follow-up results.

Diverticulitis recurred in 15% of patients in both the antibiotic and no-antibiotic groups. During follow-up, incidences of complicated diverticulitis were not significantly different between groups (3.3% and 4.8%, *P*=0.403); sigmoid resection incidences also were similar (5% and 9%; *P*=0.085).

COMMENT: The authors and an editorialist note several caveats about this study; for example, about 10% of patients were lost to follow-up, and the difference in sigmoid resections approached statistical significance. But two randomized trials now have suggested that antibiotic therapy might be unnecessary for acute uncomplicated diverticulitis, and an American Gastroenterological Association guideline makes a conditional recommendation that "antibiotics should be used selectively, rather than routinely, in patients with acute uncomplicated diverticulitis" (Gastroenterology 2015; 149:1944). Nevertheless, I doubt that most U.S. clinicians will withhold antibiotic therapy in the foreseeable future. However, patients with mild diverticulitis sometimes present with symptoms that are spontaneously improving by the time they're seen in primary care; in such cases, it would be reasonable to observe without antibiotic therapy when patients are not ill-appearing and are staying well hydrated.

CITATION(S): van Dijk ST et al. Long-term effects of omitting antibiotics in uncomplicated acute diverticulitis. Am J Gastroenterol 2018 Jul; 113:1045. (https://doi.org/10.1038/s41395-018-0030-y)

Peery AF. It's actually a little complicated: Antibiotics for uncomplicated diverticulitis. Am J Gastroenterol 2018 Jul; 113:949. (https://doi.org/10.1038/s41395-018-0159-8)

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N Engl J Med 2018;379:701-703

https://www.nejm.org/doi/full/10.1056/NEJMp1807870?query=TOC

Tickborne Diseases — Confronting a Growing Threat

Catharine I. Paules, M.D., Hilary D. Marston, M.D., M.P.H., Marshall E. Bloom, M.D., and Anthony S. Fauci, M.D.

Every spring, public health officials prepare for an upsurge in vectorborne diseases. As mosquito-borne illnesses have notoriously surged in the Americas, the U.S. incidence of tickborne infections has risen insidiously, triggering heightened attention from clinicians and researchers.

According to the Centers for Disease Control and Prevention (CDC), the number of reported cases of tickborne disease has more than doubled over the past 13 years.[1] Bacteria cause most tickborne diseases in the United States, and Lyme disease accounts for 82% of reported cases, although other bacteria (including *Ehrlichia chaffeensis*, *Anaplasma phagocytophilum*, and *Rickettsia rickettsii*) and parasites (such as *Babesia microti*) also cause substantial morbidity and mortality. In 1982, a spirochete was identified as the causative organism of Lyme disease and was subsequently named *Borrelia burgdorferi*. *B. burgdorferi* (which causes disease in North America and Europe) and *B. afzelii* and *B. garinii* (found in Europe and Asia) are the most common agents of Lyme disease. The recently identified *B. mayonii* has been described as a cause of Lyme disease in the upper midwestern United States. Spirochetes that cause Lyme disease are carried by hard-bodied ticks (see graphic), notably *Ixodes scapularis* in the northeastern United States, *I. pacificus* in western states, *I. ricinus* in Europe, and *I. persulcatus* in eastern Europe and Asia. *B. miyamotoi*, a borrelia spirochete found in Europe, North America, and Asia, more closely related to the agents of tickborne relapsing fever, is also transmitted by *I. scapularis* and should be considered in the differential diagnosis of febrile illness occurring after a tick bite.

Patterns of spirochete enzootic transmission are geographically influenced and involve both small-mammal reservoir hosts, such as white-footed mice, and larger animals, such as white-tailed deer, which are critical for adult tick feeding. The rising incidence and expanding distribution of Lyme disease in the United States are probably multifactorial, but increased density and range of the tick vectors play a key role. The geographic range of *I. scapularis* is apparently increasing: by 2015, it had been detected in nearly 50% more U.S counties than in 1996.

Lyme disease's clinical manifestations range from relatively mild, nonspecific findings and classic erythema migrans rash in early disease to more severe manifestations, including neurologic disease and carditis (often with heart block) in early disseminated disease, and arthritis, which may occur many months after infection (late disease). Although most cases are successfully treated with antibiotics, 10 to 20% of patients report lingering symptoms after receiving appropriate therapy.[2] Despite more than four decades of research, gaps remain in our understanding of Lyme disease pathogenesis, particularly its role in these less well-defined, post-treatment symptoms.

Meanwhile, tickborne viral infections are also on the rise and could cause serious illness and death.[1]One example is Powassan virus (POWV), the only known North American tickborne encephalitis-causing flavivirus.[3] POWV was recognized as a human pathogen in 1958 after being isolated from the brain of a child who died of encephalitis in Powassan, Ontario. People infected with POWV often have a febrile illness that can be followed by progressive and severe neurologic manifestations, resulting in death in 10 to 15% of cases and long-term sequelae in 50 to 70% of survivors.[3] An antigenically similar virus, POWV lineage II, or deer tick virus, was discovered in New England in

1997. Both POWV subtypes are linked to human disease, but their distinct enzootic cycles may affect their likelihood of causing such disease. Lineage II seems to be maintained in an enzootic cycle between *I. scapularis* and white-footed mice — which may portend increased human transmission, because *I. scapularis* is the primary vector of other serious pathogens, including *B. burgdorferi.* Whereas only 20 U.S. cases of POWV infection were reported before 2006,[3] 99 were reported between 2006 and 2016. Other tickborne encephalitis flaviviruses cause thousands of cases of neuroinvasive illness in Europe and Asia each year, despite the availability of effective vaccines in those regions. The increase in POWV cases coupled with the apparent expansion of the *I. scapularis* range highlight the need for increased attention to this emerging virus.

The public health burden of tickborne pathogens is considerably underestimated. For example, the CDC reports approximately 30,000 cases of Lyme disease per year but estimates that the true incidence is 10 times that number.[1] Multiple factors contribute to this discrepancy, including limitations in surveillance and reporting systems and constraints imposed by available diagnostics, which rely heavily on serologic assays.[4] Diagnostic utility is affected by variability among laboratories, timing of specimen collection, suboptimal sensitivity during early infection, imperfect use of diagnostics (particularly in persons with low probability of disease), inability of a single test to identify coinfections in patients with acute infection, and the cumbersome nature of some assays. Current diagnostics also have difficulty distinguishing acute from past infection — a serious challenge in diseases characterized by nonspecific clinical findings. Moreover, tests may remain positive even after resolution of infection, leading to diagnostic uncertainty during subsequent unrelated illnesses. For less common tickborne pathogens such as POWV, serologic testing can be performed only in specialized laboratories, and currently available tests fail to identify novel tickborne organisms.

Such limitations have led researchers to explore new technologies. For example, one of the multiplex serologic platforms that have been developed can detect antibodies to more than 170,000 distinct epitopes, allowing researchers to distinguish eight tickborne pathogens.[4] In addition to its utility in screening simultaneously for multiple pathogens, this assay offers enhanced pathogen detection, particularly in specimens collected during early disease. Further studies are needed to determine such assays' applicability in clinical practice.

Nonserologic platform technologies may also improve diagnostic capabilities, particularly in identifying emerging pathogens. Two previously unknown tickborne RNA viruses, Heartland virus and Bourbon virus, were discovered by researchers using next-generation sequencing to help link organisms with sets of unexplained clinical symptoms. The development and widespread implementation of next-generation diagnostics will be critical to understanding the driving factors behind epidemiologic trends and the full clinical scope of tickborne disease. In addition, sensitive, specific and, where possible, point-of-care assays will facilitate appropriate clinical care for infected persons, guide long-term preventive efforts, and aid in testing of new therapeutics and vaccines.

In the United States, prevention and management of tickborne diseases include measures to reduce tick exposure, such as avoiding or controlling the vector itself, plus prompt, evidence-based treatment of infections. Although effective

therapies are available for common tickborne bacteria and parasites, there are none for tickborne viruses such as POWV.

The biggest gap, however, is in vaccines: there are no licensed vaccines for humans targeting any U.S. tickborne pathogen. One vaccine that was previously marketed to prevent Lyme disease, LYMErix, generated an immune response against the OspA lipoprotein of *B. burgdorferi*, and antibodies consumed by the tick during a blood meal targeted the spirochete in the vector.[5] Nonetheless, the manufacturer withdrew LYMErix from the market for a combination of reasons, including falling sales, liability concerns, and reports suggesting it might be linked to autoimmune arthritis, although studies supported the vaccine's safety. Similar concerns will probably affect development of other Lyme disease vaccines.[5]

Historically, infectious-disease vaccines have targeted specific pathogens, but another strategy would be to target the vector.[5] This approach could reduce transmission of multiple pathogens simultaneously by exploiting a common variable, such as vector salivary components. Phase 1 clinical trials are under way to evaluate mosquito salivary-protein–based vaccines in healthy volunteers living in areas where most mosquito-borne diseases are not endemic. Since tick saliva also contains proteins conserved among various tick species, this approach is being explored for multiple tickborne diseases.[5]

The burden of tickborne diseases seems likely to continue to grow substantially. Prevention and management are hampered by suboptimal diagnostics, lack of treatment options for emerging viruses, and a paucity of vaccines. If public health and biomedical research professionals accelerate their efforts to address this threat, we may be able to fill these gaps. Meanwhile, clinicians should advise patients to use insect repellent and wear long pants when walking in the woods or tending their gardens — and check themselves for ticks when they are done.