BIOMARKERS, CONCUSSIONS, AND THE DUTY OF CARE

Betsy J. Grey[*] *& Gary E. Marchant*[**]

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ABSTRACT

The United States is currently facing a "concussion epidemic." Concussions, also known as mild traumatic brain injuries, have increased in numerous settings, including transportation accidents, military combat, workplace injuries, domestic abuse, falls, and sports. The epidemic imposes huge costs on society. At the same time, our understanding of the injury remains limited. Currently, no proven way exists to physiologically detect concussion risk or damage. Determining whether a concussion has occurred and been resolved remains largely a clinical diagnosis, relying mostly on self-reported symptoms. Our knowledge of long-term implications of repetitive concussions is also limited. Science is racing to develop objective measures, or biomarkers, of concussive injury that will tell us who is more likely than not to be susceptible to harm and the extent of harm they may have already suffered. The availability of biomarkers will lead to a deeper understanding of changes to the brain that occur in a concussion and enable us to trace back earlier into what we think of as a diseased state.

These scientific developments will have enormous implications for questions of risk and loss distribution in society. In particular, they portend a major reexamination of fundamental tort issues of duty, breach, causation, and fault allocation. Applying the developing research to the legal landscape will shed light on duties, as well as causal issues, and may help substantiate latent injury claims. This Article examines those questions in the context of youth

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* Professor of Law and Alan A. Matheson Fellow, Sandra Day O'Connor College of Law at Arizona State University. We thank Michael Saks, Bob Dauber, Joel Nomkin, Zachary Kramer, and the participants at the ASU 2015 Interdisciplinary Workshop on Concussive Injury and Biomarkers for their insights and suggestions. Ashleigh Pearlstein, Ken Ralston, and Brian Richardson provided excellent research assistance.

** Regents Professor and Lincoln Professor of Emerging Technologies, Law & Ethics, Center for Law, Science & Innovation, Sandra Day O'Connor College of Law at Arizona State University.

sports. The development of biomarkers will modify responsibilities for mitigating risks, screening, and monitoring players. It will affect the ability of the player to assume risks and will also implicate certain privacy interests. In general, the development of these biomarkers will shift responsibilities in the diagnosis and management of concussions, as well as long-term injuries, to those most directly involved in the player's participation.

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INTRODUCTION

Our nation is facing an epidemic of concussive brain injuries, usually referred to in the medical world as mild traumatic brain

injuries (mTBI).[1] This epidemic of mTBI imposes enormous human and economic costs on society. A major impediment to preventing, diagnosing, and treating such brain injuries is the lack of objective and feasible medical tests to detect such injuries. Over the past few years, scientific research has begun to develop accurate, objective diagnostic measures of the injury—especially concussive injury. The advances from this explosion of research will upend assumptions that underlie current medical and policy approaches to mTBI, and will create a myriad of new legal applications, opportunities, and challenges. In particular, the potential development of objective diagnostic tests of concussive injury through biomarkers, as well as potential tests of susceptibility, requires us to reexamine fundamental issues of risk, duty, causation, and allocation of fault.

A few cases illustrate the nature of the TBI problem. Curtis Parker was an amateur wrestler who went to a local gym to improve his wrestling.[2] His trainer instructed him to leave the ring due to his complaints of a headache; Curtis returned six days later and, after falling to the mat, went into a seizure.[3] He died nine days later.[4] Curtis's parents brought a wrongful death action against the club and the trainer, alleging that they "failed to exercise reasonable care in not requiring Curtis to obtain medical clearance before allowing him to resume his [] lessons."[5] The plaintiffs' expert testified that Curtis's subdural hemorrhage resulted from second-impact syndrome, in which individuals who suffer a second concussion before fully recovering from a prior concussion are more susceptible to serious brain injury.[6] On cross-examination, the expert acknowledged that

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1. Kimberly G. Harmon et al., *American Medical Society for Sports Medicine Position Statement: Concussion in Sport*, 47 BRIT. J. SPORTS MED. 15, 16-17 (2013). A note on terminology: most lay people, policymakers, athletes, and coaches use the term "concussion" to refer to a constellation of neurological symptoms, such as dizziness, clouded thinking, and even unconsciousness, that can result from a head trauma. However, the term concussion is not a medically precise or defined term. Rather, specialists refer to mild traumatic brain injury, with the word "mild" distinguishing concussive injuries from more severe brain injuries resulting from major traumas, such as a bullet, explosion, or car accident that permanently disfigures the brain. While all concussions are considered mTBIs, not all mTBIs are concussions. More background on this terminology and definitions is provided in *infra* Section I.A.

2. Parker v. S. Broadway Athletic Club, 230 S.W.3d 642, 643 (Mo. Ct. App. 2007).

3. *Id.* at 644.

4. *Id.*

5. *Id.*

6. *Id.* at 644-45; *see infra* note 80 and accompanying text.

many kinds of headaches occur, not all of which stem from a concussion, and that other symptoms of concussions exist, none of which Curtis complained of.[7] The trial court held that the plaintiffs did not establish that the club knew or should have known that Curtis had sustained a concussion at the earlier lesson and entered judgment in favor of defendants, which was affirmed on appeal.[8]

Chris Benoit, nicknamed "The Canadian Crippler," was a champion professional wrestler with World Wrestling Entertainment.[9] In 2007, after having twenty-two years of experience in the ring, he murdered his wife and seven-year-old son and then hanged himself.[10] Although there was much speculation about the cause of this shocking event—ranging from steroids usage to a failing marriage—Dr. Julian Bailes, Jr., then the Chair of Neurosurgery at West Virginia University, and his colleagues suspected brain damage from repeated concussive injury and received permission to examine slices of Benoit's brain.[11] They discovered that Benoit's brain was severely damaged and, like an Alzheimer's patient, his brain was riddled with aggregates of a neural protein called tau.[12] These tangled deposits were consistent with severe chronic traumatic encephalopathy (CTE), a progressive degenerative neurological disease found in individuals who have been subjected to multiple concussions and other forms of head injuries.[13] Currently, this form of brain damage can be confirmed

7. *Parker*, 230 S.W.3d at 645.

8. *Id.*

9. Brenda Goodman, *Wrestler Killed Wife and Son, Then Himself*, N.Y. TIMES, June 27, 2007, at A15.

10. Stephanie Cajigal, NEUROLOGY TODAY, Sept. 18, 2007, at 1, 16, http://journals.lww.com/neurotodayonline/Fulltext/2007/09180/Brain_Damage_May_Have_Contributed_to_Former.1.aspx; RICHARD BERGER, A FOOL FOR OLD SCHOOL . . . WRESTLING, THAT IS 79 (2009).

11. *Id.*

12. *Benoit's Brain Showed Severe Damage from Multiple Concussions, Doctor and Dad Say*, GOOD MORNING AM., http://abcnews.go.com/GMA/story?id=3560015 (last visited Feb. 13, 2016); *see also* Bennet I. Omalu et al., *Chronic Traumatic Encephalopathy, Suicides and Parasuicides in Professional American Athletes: The Role of the Forensic Pathologist*, 31 AM. J. FORENSIC MED. PATHOLOGY 130, 130-32 (2010) [hereinafter Omalu et al., *Suicides and Parasuicides*].

13. *Wrestler Chris Benoit Brain's Forensic Exam Consistent with Numerous Brain Injuries*, SCI. DAILY (Sept. 6, 2007), http://www.sciencedaily.com/releases/2007/09/070905224343.htm [hereinafter Sports Legacy Institute]; Bennet I. Omalu et al., *Chronic Traumatic Encephalopathy in a Professional American Wrestler,* 6 J. FORENSIC NURSING. 130, 130-36 (2010) [hereinafter Omalu et al., *American Wrestler*].

only by autopsy.[14] Symptoms of the disease, which include memory loss, depression, suicidal thoughts, and aggressive behavior,[15] also have been noted in ice hockey players, soccer players, boxers, and professional football players.[16]

San Francisco 49ers linebacker Chris Borland, twenty-four and fresh off his first season of playing in the NFL, announced his retirement from football because of his concerns about the long-term effects of repetitive head trauma.[17] As he explained, "I just honestly want to do what's best for my health. . . . From what I've researched and what I've experienced, I don't think it's worth the risk."[18] He was explicit about his apprehension about brain injuries,[19] stating, "I don't want to have any neurological diseases or die younger than I would otherwise."[20]

These three examples illustrate the types of challenges presented by this enormous public health problem facing our nation today, which include the difficulty of accurately diagnosing concussions and determining who is qualified to do so, the search for other diagnostic measures, and the growing medical and public awareness of the long-term effects of concussions. Experts at the

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14. Sports Legacy Institute, *supra* note 13; Omalu et al., *American Wrestler*, *supra* note 13, at 135.

15. Helen Ling, John Hardy & Henrik Zetterburg, *Neurological Consequences of Traumatic Brain Injuries in Sports*, 66 MOLECULAR & CELLULAR NEUROSCIENCE 114, 119-20 (2015) (reviewing these symptoms and other consequences of TBI across a range of contact sports).

16. *Id.* at 118-19; *see also* Jeffrey G. Caron & Gordon A. Bloom, *Ethical Issues Surrounding Concussions and Player Safety in Professional Ice Hockey*, 8 NEUROETHICS 5, 6 (2015) (reviewing data on concussion incidence rates in ice hockey); Chadwick Hales et al., *Late-Stage CTE Pathology in a Retired Soccer Player with Dementia*, 83 NEUROLOGY 2307, 2307 (2014); Paul McCrory, Tsharni Zazryn & Peter Cameron, *The Evidence for Chronic Traumatic Encephalopathy in Boxing*, 37 SPORTS MED. 467, 467 (2007).

17. Ashley Fantz & Steve Almasy, *Chris Borland, 24, to Retire from NFL, Cites Fear of Concussions*, CNN (Mar. 17, 2015, 8:37 PM), http://www.cnn.com/2015/03/17/football/chris-borland-retirement-nfl-concussions/index.html.

18. *Id.*

19. Ken Belson, *Chris Borland, Fearing for Health, Retires from 49ers. At 24.*, N.Y. TIMES, Mar. 18, 2015, at A1.

20. Mark Fainaru-Wada & Steve Fainaru, *SF's Borland Quits over Safety Issues*, ESPN (Mar. 17, 2015), http://espn.go.com/espn/otl/story/_/id/12496480/san-francisco-49ers-linebacker-chris-borland-retires-head-injury-concerns. He explained that "when you read about Mike Webster and Dave Duerson and Ray Easterling, you read all these stories, and to be the type of player I want to be in football, I think I'd have to take on some risks that, as a person, I don't want to take on." *Id.* He was referring to prominent NFL players who were diagnosed with CTE after their deaths. *Id.* "Duerson and Easterling committed suicide." *Id.*

Centers for Disease Control and Prevention (CDC) estimate that 2.5 million people sustain a traumatic brain injury (TBI) every year in the United States, many in contact sports, such as football, hockey, and soccer, but also as a result of military combat, workplace injuries, domestic abuse, vehicle crashes, falls, head injuries during seizures, and other accidents.[21] Resulting brain damage can have short-term effects in learning and memory, as well as long-term effects.[22] The CDC report estimates that the total costs to society as a result of these injuries exceed $76 billion per year.[23]

Society has begun to respond to this TBI epidemic, from policy making at the front end to litigation at the back end. At the front end, policymakers at the federal, state, and local levels all have acknowledged the national health problem. The Department of Defense and the Department of Veterans Affairs have expanded their funding for research in brain injury.[24] States have addressed concussion management in high school sports through legislation and regulations.[25] Local school districts and sports programs have changed their rules for participation in those programs.[26]

On the litigation front, professional and collegiate athletes have brought lawsuits against their leagues. More than 5,000 former players in the National Football League (NFL) sued the NFL, claiming it failed to take reasonable steps to protect them from concussive brain injuries, while at the same time concealing the

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21. *See* CTR. FOR DISEASE CONTROL AND PREVENTION, TRAUMATIC BRAIN INJURY IN THE UNITED STATES: EPIDEMIOLOGY AND REHABILITATION 2 (2014), http://www.cdc.gov/traumaticbraininjury/pdf/TBI_Report_to_Congress_Epi_and_Rehab-a.pdf [hereinafter CDC, *Addressing Critical Gaps*] (citing MARK FAUL ET AL., TRAUMATIC BRAIN INJURY IN THE UNITED STATES: EMERGENCY DEPARTMENT VISITS, HOSPITALIZATIONS AND DEATHS 2002–2006 (2010), http://www.cdc.gov/traumaticbraininjury/pdf/blue_book.pdf). TBI remains a leading cause of injury and death of adults, along with general trauma. *See* Michael DeCuypere & Paul Klimo Jr., *Spectrum of Traumatic Brain Injury from Mild to Severe*, 92 SURGICAL CLINICS N. AM., 939, 940 (2012).

22. CDC, *Addressing Critical Gaps*, *supra* note 21, at 3.

23. *Severe TBI*, CDC, http://www.cdc.gov/TraumaticBrainInjury/severe.html (last visited Mar. 4, 2016).

24. Press Release, Dept. of Veterans Affairs, *VA and DoD to Fund $100 Million PTSD and TBI Study* (Sept. 19, 2012), http://www.va.gov/opa/pressrel/pressrelease.cfm?id=2386; *see* Barry Meier & Danielle Ivory, *Concussion Inc.*, N.Y. TIMES, July 5, 2015, at BU1.

25. *See infra* Subsection II.A.1.a.

26. *See, e.g.*, Trisha Volpe, *Focus on Concussions Transforms High School Football in Minnesota*, MPR NEWS (Sept. 30, 2014), http://www.mprnews.org/story/2014/09/30/high-school-concussions-transform-high-school-football-in-minnesota.

long-term risks associated with concussion.[27] The settlement of that class action lawsuit covers all retired former professional football players and provides individual payments of up to $5 million for certain neurological disorders and medical monitoring of all players.[28]

The National Collegiate Athletic Association (NCAA),[29] the National Hockey League,[30] soccer's Federation Internationale de Football Association (FIFA),[31] and World Wrestling Entertainment[32] are all currently embroiled in lawsuits involving athletes' head injuries. These claims are reaching the high school level as well.[33] The reverberations of these legal clashes are changing how head injuries are handled in football and other sports, across all ages. Professional sports organizations,[34] high school programs,[35] and

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27. Plaintiff's Master Administrative Long-Form Complaint, *In re* Nat'l Football League Players' Concussion Injury Litig., 307 F.R.D. 351 (E.D. Pa. 2015) (No. 2:12-md-02323-AB, MDL No. 2323).

28. *In re* Nat'l Football Players' Concussion Injury Litig., 307 F.R.D. at 366. The neurological conditions include different levels of neurocognitive impairment, Alzheimer's disease, Parkinson's disease, Amyotrophic Lateral Sclerosis, and death with CTE. *Id.* The settlement also includes $10 million for education about concussions. *Id.* at 368-69. A $75 million fund provides eligible retired players with baseline assessment examinations of their neurological functioning and cognitive decline. *Id.* at 368. About 200 players have opted out of the settlement. *Id.* at 369.

29. *In re* NCAA Student-Athlete Concussion Injury Litig., No. 13-C-9116, MDL No. 2492, 2014 U.S. Dist. LEXIS 174334, at *6 (N.D. Ill. Dec. 17, 2014).

30. *In re* Nat'l Hockey League Players' Concussion Injury Litig., MDL No. 14-2551, 2015 BL 82307, at *2 (D. Minn. Mar. 25, 2015).

31. Class Action Complaint, Mehr v. Fédération Internationale de Football Ass'n, No. 14-cv-3879, 2015 WL 4366044 (N.D. Cal. July 16, 2015).

32. Haynes v. World Wrestling Entm't Inc., No. 3:14-cv-01689-ST, 2015 BL 203505, at *1-2 (D. Or. June 25, 2015).

33. *See* Class Action Complaint, Bukal v. Illinois High School Ass'n, No. 2014-CH-19131 (Cook Cty. Cir. Ct., Ill., Dec. 1, 2014) (alleging that the association did not do enough to protect players from concussions). These claims are likely to grow. *See* Michael Tarm, *High School Head Injury Lawsuit Filed*, HUFFINGTON POST (Dec. 18, 2014), http://www.huffingtonpost.com/2014/11/30/high-school-head-injury-l_n_6245374.html. The attorney who filed the class action lawsuit against the NCAA says that his "goal is to bring the fight to the high school level." Sara Ganim, *Class-Action Lawsuit Filed over High School Football*, CNN (Dec. 2, 2014), http://www.cnn.com/2014/12/01/us/concussion-lawsuit-high-school-football.

34. Adam Caplan, *NFL Levies Huge Fines for Hits to Head*, FOX SPORTS (June 2, 2014, 1:48 PM), http://www.foxsports.com/nfl/story/helmet-fines-James-Harrison-Dunta-Robinson-Brandon-Meriweather-101910 [http://http://web.archive.org/web/20150526193403/http://www.foxsports.com/nfl/story/helmet-fines-James-Harrison-Dunta-Robinson-Brandon-Meriweather-101910?].

35. *See supra* note 33.

youth football organizations[36] have already introduced new policies on concussions and increased the penalties for helmet-to-helmet hits.

Recognizing the epidemic of acquired brain injury is just part of the problem; understanding and diagnosing the injury itself presents enormous challenges. Unlike the readily apparent nature of certain injuries like broken bones or torn skin, brain injury is subtle and generally not obvious to an untrained observer. The human brain can be injured in many ways,[37] and the type of brain injury that results from hits to the head, or acquired brain injury, can occur in numerous ways as well—from a single major impact (such as a car accident or wartime blast) or from lesser but frequent impacts (such as football tackles).[38]

Diagnosing an mTBI is particularly difficult.[39] Although there are some objective measures to assist in the diagnosis of mTBIs, in the end, it remains currently a clinical diagnosis based mainly on self-reported symptoms.[40] The symptoms vary among individuals and may manifest at different times.[41] The ability to diagnose CTE is limited as well; we do not yet have an objectively verifiable neurocognitive measurement for diagnosis and prognosis of CTE with an established link to acquired brain injury. Epidemiological studies have associated repetitive head injuries to Alzheimer's, Parkinson's, and Amyotrophic Lateral Sclerosis (ALS) diseases as well as CTE,[42] but that does not definitively answer whether an individual suffers from those diseases as a result of head injuries or other risk factors.

The methodology for diagnosis of mTBIs and CTE is changing, however, as scientists are starting to discover and develop tools to

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36. *Rule Changes Regarding Practice & Concussion Prevention*, POP WARNER (June 13, 2012), http://www.popwarner.com/About_Us/Pop_Warner_News/Rule_Changes_Regarding_Practice___Concussion_Prevention_s1_p3977.htm.

37. Brain damage can occur from *in utero* to the end of life and can result from strokes, infections, tumors, and toxins, among other things. *See* Christina Kwasnica et al., *Congenital and Acquired Brain Injury. 3. Spectrum of the Acquired Brain Injury Population*, 89 Supplement 1 ARCHIVES PHYSICAL MED. REHABILITATION S15-20 (2008).

38. *Id.* at S17-18.

39. *See* Raquel C. Gardner & Kristine Yaffe, *Epidemiology of Mild Traumatic Brain Injury and Neurodegenerative Disease*, 66 MOLECULAR & CELLULAR NEUROSCIENCE 75, 76 (2015) (reviewing diagnostic criteria for mTBI).

40. *Id.*

41. *See* L. Syd M. Johnson, *Sport-Related Neurotrauma and Neuroprotection: Are Return-to-Play Protocols Justified by Paternalism?*, 8 NEUROETHICS 15, 19 (2015).

42. *See* Gardner & Yaffe, *supra* note 39, at 78.

detect the subtle damage that occurs when individual molecules are disturbed by brain injury.[43] Scientists expect this research to lead to objective measures—biological markers or "biomarkers"—of these acquired brain injuries in the living brain.[44] They seek to identify biomarkers of effect and susceptibility. For biomarkers of effect, scientists hope to develop novel techniques to understand exactly how the brain is damaged and how it might be repaired.[45] The aim is that these biomarkers will not only signal the presence of a concussion, but also the extent of it. The objective is also to detect the continued presence of the concussion even when outward symptoms have disappeared.[46] Similarly, the goal is that biomarkers can be used to detect long-term effects such as CTE, rather than waiting for the definitive test from an autopsy.[47] For biomarkers of susceptibility, scientists hope to determine whether certain people are more susceptible to suffering concussions and CTE.[48] The difficulties that inhere in the current approach to diagnosis of concussive injury, as well as the advances in biomarker research that may change that approach, are discussed in Part I.

Developing biomarkers of effect and susceptibility for concussive injury will have enormous legal and policy implications. This is the focus of Part II. The scientific developments will challenge courts and policymakers to rethink when civil liability should be imposed, how brain injury cases are litigated, and when and how governments should regulate social activity in efforts to reduce the incidence and harms of brain injury. These questions are examined in the context of youth sports.

Part II specifically examines how development of biomarkers of effect will transform the duty of care of those involved in youth sports, including schools, private leagues, trainers, coaches, parents, and the players themselves, leading to an overall increase of concussive management duties. The change will be implemented on two levels—both through common law duties as well as in legislation aimed at concussive management. Not only will expectations regarding timely and accurate diagnosis of concussive

43. Linda Papa et al., *Systematic Review of Clinical Studies Examining Biomarkers of Brain Injury in Athletes After Sports-Related Concussion*, 32 J. NEUROTRAUMA 661, 669 (2015).

44. *Id.*

45. *Id.*

46. *See infra* Subsection II.A.1.c.

47. *See infra* Subsection I.C.2.

48. *See infra* Subsection I.C.3.

injury increase, but a commensurate increase in the duties to both avoid and mitigate risks, including an increase in screening and monitoring duties, will occur as well. Availability of biomarkers of effect will fundamentally change the way the elements of causation and injury are proved and may be used by both plaintiffs and defendants as objective evidence to prove or disprove those elements. These biomarkers will give us greater understanding of disease progression and may also lead to recognition of earlier claims for subclinical injuries revealed by those biomarkers. Biomarkers of anticipated long-term effects, such as CTE, will raise the specter of latent injury claims, which are based on the premise that a plaintiff has incurred an injury that puts him or her at increased risk of future disease. These types of claims often seek recovery for medical monitoring or emotional harm, but remain controversial because of their speculative nature and the fear of limitless liability. Biomarkers will make these claims less speculative.

Part II also considers how development of biomarkers of susceptibility will have an impact on the duties owed to players, as well as the duty the player owes to himself or herself. The development of these biomarkers will likely generate a duty for schools and other sports sponsors to screen and possibly to exclude those individuals with susceptibility biomarkers from participating in those sports. At a minimum, it will likely engender duties to monitor them more closely, provide accommodations, and implement additional preventive measures. Screening will also raise significant privacy issues, since releasing results of susceptibility screening to third parties—such as parents, insurance companies, and employers—can have a broad, long-term impact. The duty to inform of risks, as well as the ability to accept those risks in play, will also be transformed.

Part III concludes that the development of biomarkers of effect and susceptibility will transform the legal landscape of concussive injury, both from a public policy and a litigation perspective. Examination of these issues requires both a deep understanding of the science involved and an explication of the theoretical basis and purpose of tort claims and recovery. Given the anticipated increased accuracy in diagnosis, prognosis, and cessation of injury, as well as susceptibility to injury, the availability of biomarkers should lead to a more accurate and just result in litigation. At the same time, development of biomarkers may open the door to requiring more demanding evidence in court. At the meta-level, the combination of the medical and legal applications of mTBI biomarkers will

hopefully lead to fewer injuries and safer practices in sports and elsewhere, but it is sure to cause significant disruption and risk exposure to sports teams, employers, the military, and product manufacturers.

I. CONCUSSIVE INJURY

A. Defining and Diagnosing Brain Injuries

Traumatic brain injury occurs when an external force, such as impact or rapid acceleration or deceleration, causes damage to the brain.[49] Although research on acquired brain injury continues to advance, a single, universal definition of TBI has yet to be determined. Aside from being caused by an external source, the definition can encompass various scenarios. The damage can be focal (occurring at the local site of impact with neurological effects specific to the area affected) or diffuse (often delayed and widespread).[50] It can be based on a direct or indirect blow to the head, with a sudden acceleration to the brain.[51] It can be a closed head injury or penetrating head injury (when an object pierces the skull).[52] It can be from a single blow or a series of smaller repeated impacts. Scientists seek to develop a consensus in diagnosing and treating TBI as awareness of the injury increases in both the public as well as the medical field.

To understand acquired brain injury, a brief overview of the biomechanics involved is useful. The brain is made of soft tissue and is cushioned by spinal fluid and encased in the protective shell of the skull.[53] The brain tissue is often described as a "Jell-O-like" substance.[54] When an individual sustains trauma, the impact to the head can jolt the brain and cause it to move around within the skull and even make contact with it. These shocks to the brain can result in

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49. *See* Sarah Malanowski & Nicholas Baima, *On Treating Athletes with Banned Substances: The Relationship Between Mild Traumatic Brain Injury, Hypopituitarism, and Hormone Replacement Therapy*, 8 NEUROETHICS 27, 28 (2015).

50. Decuypere & Klimo, *supra* note 21, at 941-42.

51. *Id.*

52. *Id.* at 941.

53. *See* Y. King Liu, *Biomechanics of "Low-Velocity Impact" Head Injury*, *in* THE EVALUATION AND TREATMENT OF MILD TRAUMATIC BRAIN INJURY 49, 58 (Nils R. Varney & Richard J. Roberts eds., 1st ed. 1999).

54. *See, e.g.*, *id.*

chemical changes in nerve cells, mechanical disruption of axons, changes in brain blood flow, and neuro inflammation.[55]

Fundamentally, the brain uses neurons (or nerve cells) to communicate with different systems of the brain. All neurons have three main parts: (1) the cell body; (2) the axon; and (3) the dendrites.[56] Much of the recent research on brain trauma focuses on axons.[57] Axons, which exit the cell body, are used to communicate with other neurons through nerve impulses.[58] Axons extend across the different layers of brain tissue—from gray matter (cerebral cortex) to white matter (subcortical area)—to connect the neurons in both areas.[59] When there is trauma to the brain, the different layers of the brain slide across each other, which causes unnatural stresses on the axons.[60] Research reveals that stretching or tearing an axon causes the nerve impulse not to transmit or to transmit less efficiently.[61] Common cognitive deficits caused by the damaged axons are attention and concentration difficulties, fatigue, and impaired short-term memory.[62]

The terms "concussion" and "mTBI" are often used interchangeably,[63] although mTBI is considered by some to be a broader term than concussion.[64] Medical diagnosis of acquired brain trauma usually distinguishes between severe and mild TBIs.[65] This

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55. Douglas H. Smith & David F. Meaney, *Axonal Damage in Traumatic Brain Injury*, 6 NEUROSCIENTIST 483, 484-87 (2000); Esteban Toledo et al., *The Young Brain and Concussion: Imaging as a Biomarker for Diagnosis and Prognosis*, 36 NEUROSCIENCE & BIOBEHAVIORAL REVS. 1510, 1513-14 (2012).

56. *See* HARVEY LODISH ET AL., MOLECULAR CELL BIOLOGY § 21.1 (4th ed. 2000).

57. *See* Douglas H. Smith, Ramona Hicks & John T. Povlishock, *Therapy Development for Diffuse Axonal Injury*, 30 J. NEUROTRAUMA 307, 307 (2013).

58. *See* MICHAEL S. GAZZANIGA, RICHARD B. IVRY & GEORGE R. MANGUN, COGNITIVE NEUROSCIENCE: THE BIOLOGY OF THE MIND 24-28, 60 (2d ed. 2002).

59. *See id.* at 64-66.

60. Smith & Meaney, *supra* note 55, at 484-87.

61. *See id.*

62. *See* Fumihiko Yasuno et al., *Decision-Making Deficit of a Patient with Axonal Damage After Traumatic Brain Injury*, 84 BRAIN & COGNITION 63, 63 (2014).

63. The terms "concussion" and "mTBI" are used interchangeably in the literature and are often treated as synonymous. *See* Paul McCrory et al., *Consensus Statement on Concussion in Sport: The 4th International Conference on Concussion in Sport Held in Zurich, November 2012*, 47 BRIT. J. SPORTS MED. 250, 250 (2013).

64. *See* Harmon et al., *supra* note 1, at 16-17 ("[A]ll concussions are MTBIs, not all MTBIs are concussions.").

65. Approximately 20% of the TBIs diagnosed each year are classified as moderate or severe, and 80% are classified as mild. *See* Malanowski & Baima,

distinction, although widely accepted, is inexact; TBI is considered a spectrum, and the precise distinction between the two levels of brain injury lacks consensus in both medicine and law. By definition, "mild" or "minor" traumatic brain injury will not cause the injured survivor to die, but beyond that, the terminology "mild" or "minor" can be misleading;[66] even a "minor" TBI can cause significant damage.[67] Some definitions distinguish a TBI from mTBI by how long a person loses consciousness.[68] Yet a person can incur a concussive injury and potentially serious long-term consequences even without losing consciousness, so consciousness is not a requirement for diagnosing an mTBI.

There is no agreed-upon definition of mTBI or concussion, because there is no consensus on objective criteria for defining and diagnosing this type of injury.[69] Rather, mTBI currently remains a subjective clinical diagnosis based primarily on patient history and observable behavioral symptoms.[70] These symptoms can include confusion, lightheadedness, blurred vision, dizziness, ringing in the ears, fatigue, nausea, and trouble with memory.[71] The person may feel dazed and have a vacant stare.[72] Sometimes, but not always, there is loss of consciousness.[73] The symptoms often resolve within

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supra note 49, at 128. Scientists further break down this dichotomy into four categories—mild, moderate, severe, and vegetative state. *See infra* notes 114-17 and accompanying text; *Glasgow Coma Scale*, TRAUMATIC BRAIN INJ., http://www.traumaticbraininjury.com/symptoms-of-tbi/glasgow-coma-scale (last visited Feb. 13, 2016); *Traumatic Brain Injury: Hope Through Research*, NAT'L INST. NEUROLOGICAL DISORDERS & STROKE, http://www.ninds.nih.gov/disorders/tbi/detail_tbi.htm#266623218 (last visited Feb. 13, 2016).

66. Semyon Slobounov et al., *Sports-Related Concussion: Ongoing Debate*, 48 BRITISH. J. SPORTS MED. 75, 75 (2014) ("[T]here is nothing mild about mTBI at the cellular level." (emphasis omitted)).

67. Smith, Hicks & Povlishock, *supra* note 57, at 313.

68. *See, e.g.*, CDC, *Addressing Critical Gaps*, *supra* note 21, at 17 (defining loss of consciousness of thirty minutes or less as "mild," thirty minutes to twenty-four hours as "moderate," and greater than twenty-four hours as "severe").

69. *See* Toledo et al., *supra* note 55, at 1511; Richard P. Dutton et al., *Diagnosing Mild Traumatic Brain Injury: Where Are We Now?*, 70 J. TRAUMA 554, 554 (2011). The International Conference on Concussion in Sport periodically publishes a consensus statement revising its definition of concussion. *See* McCrory et al., *supra* note 63, at 250.

70. Dutton et al., *supra* note 69, at 554.

71. *Id.* at 554; Jonathan C. Edwards & Jeffrey D. Bodle, *Causes and Consequences of Sports Concussion*, 42 J.L. MED. ETHICS 128, 128 (2014).

72. Edwards & Bodle, *supra* note 71, at 128.

73. *Id.*

minutes to days[74] after a concussion, but in some cases there are more enduring symptoms such as persistent headaches, sleep disturbance, poor attention and concentration, irritability, and depression that can last for several weeks or longer.[75] It is not surprising that this spectrum of symptoms exists, considering the diverse ways in which a brain injury can happen, as well as the different brain structures that could be affected by the external trauma.

Mild TBIs do not show up on standard imaging studies, such as a CT scan or MRI, since the injuries are typically not structural injuries to the brain, but rather, are functional problems caused by swelling or bruising.[76] Sometimes the injured person can appear "normal." Moreover, some symptoms are evident immediately; others surface days or even weeks later,[77] and it has become clear that some head injuries occur that have no immediate cognizable symptoms, which are now classified as subconcussions.[78] As noted earlier, there is no universally accepted definition of concussion.[79]

The accuracy of identifying mTBIs and determining whether an individual is fully recovered is critical. Most significantly, the risk of severe injury can increase with repeated concussions, producing a rare, and sometimes disputed, phenomenon referred to as the Second

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74. Harmon et al., *supra* note 1, at 17 (noting that 80%-90% of athletes have symptom resolution within seven days of injury).

75. *Id.* at 24.

76. McCrory et al., *supra* note 63, at 250-51 ("Concussion may result in neuropathological changes, but the acute clinical symptoms largely reflect a functional disturbance rather than a structural injury and, as such, no abnormality is seen on standard structural neuroimaging studies."); *see also* Erica D. Bruce et al., *Neuroimaging and Traumatic Brain Injury: State of the Field and Voids in Translational Knowledge*, 66 MOLECULAR & CELLULAR NEUROSCIENCE 103, 104 (2015) (presenting evidence that CT imaging is not generally effective for mTBI, but may be effective in identifying severe cases of TBI).

77. *See* Omalu et al., *American Wrestler*, *supra* note 13, at 132 (discussing an autopsy report stating that visual examination of the brain showed no sign of trauma, and trauma was only visible under microscopic examination).

78. Thomas W. McAllister et al., *Effect of Head Impacts on Diffusivity Measures in a Cohort of Collegiate Contact Sport Athletes*, 82 NEUROLOGY 63, 66 (2014) (finding a relationship between magnitude and timing of head impacts and effects on white matter in brains of athletes who had no reported concussions).

79. *See* Annette Greenhow & Jocelyn East, *Custodians of the Game: Ethical Considerations for Football Governing Bodies in Regulating Concussion Management*, 8 NEUROETHICS 65, 69 (2015) (listing differences in approaches, such as whether it is a "head injury" or a "brain injury"; whether it is a functional issue or structural injury; whether it is an mTBI; and the extent of the association between head trauma and long-term cognitive issues).

Impact Syndrome.[80] Furthermore, therapy for brain repair is controversial; the type of care the individual should receive during recuperation is not agreed upon.[81] Some doctors prescribe brain silence (no reading, no math, no computers), while others say some brain stimulation is therapeutic.[82] Some researchers suggest that treatment may depend on what part of the brain received the trauma.[83] And even harder is determining whether chronic brain damage has occurred (and its cause) or whether certain individuals might be more susceptible, as discussed below.

B. Defining CTE

CTE is a progressive chronic neurodegenerative disease associated with a person sustaining repeated blows to the head[84] with

80. *See* Tareg Bey & Brian Ostick, *Second Impact Syndrome*, 10 W. J. EMERGENCY MED., 6, 6-7 (2009). Because of the difficulties inherent in collecting data on this type of injury, some scientists challenge the diagnosis of Second Impact Syndrome. *See, e.g.*, Paul R. McCrory & Samuel F. Berkovic, *Second Impact Syndrome*, 50 NEUROLOGY 677, 679-83 (1998) (challenging the clinical support as insufficient to establish Second Impact Syndrome as a risk factor for cerebral swelling). However, most scientists agree that risk of exacerbated injury increases with subsequent impact before one is fully recovered. *See* Matthew P. MacFarlane & Thomas C. Glenn, *Neurochemical Cascade of Concussion*, 29 BRAIN INJ. 139, 147-49 (2015) (acknowledging the potential controversy, but nonetheless supporting that successive injuries have shown cumulative effect, and cautioning about the risk of Second Impact Syndrome, particularly among the younger population).

81. *See* Meier & Ivory, *supra* note 24.

82. *See* Lester Mayers, *Return-to-Play Criteria After Athletic Concussion: A Need for Revision*, 65 ARCHIVES NEUROLOGY 1158, 1158, 1160-61 (2008).

83. *Id.* at 1160 (outlining that some studies have identified portions of the brain that showed abnormalities thirty days post-injury, suggesting a need to consider location of injury in recovery timing).

84. *What is CTE?*, BU CTE CTR., http://www.bu.edu/cste/about/what-is-cte (last visited Feb. 13, 2016). Scientists of the BU Center, through dozens of case studies involving deceased athletes whose brains exhibit the distinct tau pattern of CTE, have concluded that there is a "clear environmental etiology" and that "repetitive mild traumatic brain injury" may cause CTE. *See, e.g.*, Johnson, *supra* note 41, at 16. Not everyone agrees: The 2013 Zurich consensus statement on concussion in sport finds such a conclusion speculative and states that the causal link between concussive injury and CTE "remains unproven." *See* McCrory et al., *supra* note 63, at 254. Critics point to the lack of epidemiological studies and evidence that deals with the roles of other factors, such as genetic vulnerability, alcohol, drug use, and risky behaviors outside of sports. Brad Partridge & Wayne Hall, *Repeated Head Injuries in Australia's Collision Sports Highlight Ethical and Evidential Gaps in Concussion Management Policies*, 8 NEUROETHICS 39, 41 (2015). The link between CTE and concussion injury is still being debated. *See*

a group of symptoms that include memory loss; movement disorders, including Parkinson's disease; and mood disorders, aggressive or violent behaviors, depression, suicidality, substance abuse, and cognitive decline.[85] Most athletes who have suffered concussions go on to live normal, apparently healthy lives, so it is not clear why some individuals develop CTE and others do not.[86] Repeated head trauma seems to be a key risk factor, as the condition was originally known by the name of "punch drunk syndrome" and associated with boxers,[87] but has now been found in others with a history of repeated brain trauma.[88] Although it is not yet clear whether CTE is a signature disease that is specific to repetitive head injuries, autopsy research on CTE suggests this possibility.[89] CTE manifests symptoms similar to those found in Alzheimer's[90] and can take years or even decades after the brain trauma has occurred to manifest.[91] Researchers suggest that CTE results in progressive cognitive decline and aberrant behavior in affected individuals. As one researcher noted, "[t]he progression of neurological impairment seen in athletes diagnosed post-mortem with CTE suggests that it is

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Frédéric Gilbert, *State of the Concussion Debate: From Sceptical to Alarmist Claims*, 8 NEUROETHICS 47, 47 (2015).

85. *What is CTE?*, *supra* note 84 (defining CTE as a "progressive degenerative disease of the brain found in athletes (and others) with a history of repetitive brain trauma, including symptomatic concussions as well as asymptomatic subconcussive hits to the head").

86. Edwards & Bodle, *supra* note 71, at 132.

87. Harrison S. Martland, *Punch Drunk*, 91 JAMA 1103, 1103-05 (1928).

88. Gilbert, *supra* note 84, at 47 (acknowledging that symptoms of this disorder have been observed across multiple sports platforms where participants are at risk for repeated head injury and exploring how that risk is interpreted); Bennet I. Omalu et al., *Chronic Traumatic Encephalopathy in a National Football League Player: Part II*, 59 NEUROSURGERY 1086, 1087 (2006); Bennet I. Omalu et al., *Chronic Traumatic Encephalopathy in a National Football League Player*, 57 NEUROSURGERY 128, 129 (2005) [hereinafter Omalu et al., *National Football League Part I*].

89. Assuming that a causal relationship is established, the injury threshold—the number and types of trauma to the brain—will also need to be determined. *See, e.g.*, Ann C. McKee et al., *The Spectrum of Disease in Chronic Traumatic Encephalopathy*, 136 BRAIN 43, 61-62 (2013).

90. *Id.* at 60.

91. Some recent research suggests that CTE can also develop over only a few years. Christine Baugh et al., *Chronic Traumatic Encephalopathy: Neurodegeneration Following Repetitive Concussive and Subconcussive Brain Trauma*, 6 BRAIN IMAGING BEHAV. 244, 252 (2012); *see also* Benoit C. Mouzon et al., *Chronic Neuropathological and Neurobehavioral Changes in a Repetitive Mild Traumatic Brain Injury Model*, 75 ANNALS NEUROLOGY 241, 250-51 (2014) (describing mouse study of neurobiological deficits in months following a TBI).

inevitable that the capacity for autonomous decision making will eventually be impaired in athletes with CTE."[92]

CTE can be diagnosed definitively only through autopsy; there is currently no available way of diagnosing it in the living brain.[93] Although the studies of CTE are not nearly as advanced as those of Alzheimer's disease,[94] scientists have discovered that CTE is marked by the abnormal buildup of a protein called tau in the brain, a protein also associated with Alzheimer's.[95] Importantly, recent research suggests that the threshold for developing CTE may be lower than previously thought. Subconcussive impacts, ones that do not manifest symptoms identified with concussions, may be sufficient to develop CTE.[96] This is a significant change in the medical field's understanding of brain trauma.[97] Risk factors for CTE, beyond brain trauma, remain unknown.[98]

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92. *See* Johnson, *supra* note 41, at 17. At this point, it may not be possible to determine exactly when that autonomy has been impaired or disappears completely. *Id.*

93. Omalu et al., *National Football League Part I*, *supra* note 88, at 129.

94. *See* Robert C. Cantu, *Chronic Traumatic Encephalopathy in the National Football League*, 61 NEUROSURGERY 223, 223-24 (2007) (describing the history of CTE research; acknowledging that the prevalence of the problem is unknown and "[o]nly an immediate prospective study will determine the true incidence of this problem"); Christopher Randolph, Stella Karantzoulis & Kevin Guskiewicz, *Prevalence and Characterization of Mild Cognitive Impairment in Retired National Football League Players*, 19 J. INT'L NEUROPSYCHOLOGICAL SOC'Y 873, 873 (2013) (noting that the "first attempt to systematically explore late-life cognitive impairments in retired NFL players" occurred in 2005).

95. *What is CTE?*, *supra* note 84 (explaining that CTE "triggers progressive degeneration of the brain tissue, including the build-up of an abnormal protein called tau").

96. Baugh et al., *supra* note 91, at 245; Brandon E. Gavett, Robert A. Stern & Ann C. McKee, *Chronic Traumatic Encephalopathy: A Potential Late Effect of Sport-Related Concussive and Subconcussive Head Trauma*, 30 CLINICS SPORTS MED. 179, 184 (2011).

97. *See* McKee et al., *supra* note 89, at 62 ("[F]or some athletes and war fighters, there may be severe and devastating long-term consequences of repetitive brain trauma that has traditionally been considered only mild."); Gilbert, *supra* note 84, at 51-52 (calling for a precautionary approach to addressing policy change despite uncertainty of CTE causation); *see also* Ray W. Daniel, Steven Rowson & Stefan M. Duma, *Head Impact Exposure in Youth Football*, 40 ANNALS BIOMEDICAL ENGINEERING 976, 976 (2012) (demonstrating that even sub-concussive impacts in youth football practice can produce the same kinds of forces as concussive impacts).

98. Philip H Montenigro et al., *Clinical Subtypes of Chronic Traumatic Encephalopathy: Literature Review and Proposed Research Diagnostic Criteria for Traumatic Encephalopathy Syndrome*, 6 ALZHEIMER'S RES. & THERAPY 68, 69 (2014); McCrory et al., *supra* note 63, at 257 ("[T]he speculation that repeated

C. Advances in Biomarker Research

There is a growing recognition that the current approach for the diagnosis and prognosis of mTBI, based on a graded-symptoms checklist, is ineffective and needs to be replaced by more objective biomarkers.[99] A "biomarker" is an objective physiological indicator of a biological disease, injury state, or disease predisposition.[100] Biomarkers may be developed from a blood test, saliva, spinal fluid, brain scans, eye tracking, or urine. These biomarkers may measure a genetic variant, ribonucleic acid (RNA) levels, a protein, a metabolite, an image, or any other subclinical marker of disease predisposition, status, or progression. Because diagnoses of both mTBI and CTE are based largely on self-reported clinical symptoms, scientists have been searching for biomarkers associated with those injured brain states to allow medicine to move beyond a subjective clinical diagnosis.

Many things can turn up as "markers," but to be effective, measurements of brain injury must demonstrate acceptable levels of certainty to warrant sufficient confidence in the test and establish scientific validity.[101] Biomarkers are likely to be probabilistic rather than determinative.[102] It is also likely that they will work in conjunction with other measures, such as clinical features and patient history.[103] Biomarkers of effect may interact with biomarkers of

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concussion or subconcussive impacts cause CTE remains unproven."). In addition to athletes, CTE has been "found in non-athletes who have experienced repetitive head impacts, including epileptics, developmentally disabled individuals who head-bang," "victims of physical abuse," and military members who have served in combat. Montenigro et al., *supra*, at 68. CTE may have a high incidence of comorbidity with other diseases, including Parkinson's and Alzheimer's. *See* McKee et al., *supra* note 89, at 61.

99. Slobounov et al., *supra* note 66, at 76.

100. *See NCI Dictionary of Cancer Terms*, NAT'L CANCER INST., http://www.cancer.gov/dictionary?CdrID=45618 (last visited Feb. 13, 2016). The National Cancer Institute defines a biomarker as a "biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition." *Id.*

101. *See* Linda Papa, Damyan Edwards & Michelle Ramia, *Exploring Serum Biomarkers for Mild Traumatic Brain Injury*, *in* BRAIN NEUROTRAUMA: MOLECULAR, NEUROPSYCHOLOGICAL, AND REHABILITATION ASPECTS 301, 301 (Firas H. Kobeissy ed., 2015).

102. *See id.* at 301-02.

103. *See id.* at 302, 305.

susceptibility such as genetics and previous brain injuries, as well as confounding factors such as sex, age, and ethnicity.

Two fundamental types of error can occur in determining the validity of a test involving its accuracy and reliability. The first, called a Type I error, or false positive, occurs when the effect that is being studied is identified when in fact the effect does not exist.[104] The second, called a Type II error, or false negative, occurs when a true effect is not detected.[105] Establishing acceptable levels of Type I and Type II errors is important to determine the validity of a test. These levels are related to the sensitivity and specificity of a test. Sensitivity is a measure of the proportion of true positives that are correctly identified; the fewer the false negatives, the higher the sensitivity of the test.[106] Specificity measures the proportion of negatives that are correctly identified; the fewer false positives the test produces, the higher the specificity of the test.[107]

Setting the levels of acceptable errors is a critical issue in the search for biomarkers in concussive injury. Many things can be potential "markers" for head trauma, but they are generally not very sensitive or specific tests.[108] Other limitations exist as well.[109] Studies of biomarkers tend to be small, with selected subjects, which brings selection bias into question.[110] And with regard to CTE in particular, the subjects may also have other potential risk factors for long-term cognitive impairment, which may be hard to separate out.[111]

Yet even with these limitations in mind, the advances in research are real and developing rapidly.[112] The search for

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104. *Type I and II Errors and Significance Levels*, COMMON ~~MISTEAKS~~ MISTAKES IN USING STATISTICS: SPOTTING AND AVOIDING THEM (May 12, 2011), http://www.ma.utexas.edu/users/mks/statmistakes/errortypes.html.

105. *Id.*

106. Tze-Wey Loong, *Understanding Sensitivity and Specificity with the Right Side of the Brain*, 327 BMJ 716, 716-17 (2003).

107. *Type I and II Errors*, *supra* note 104.

108. Linda Papa et al., *Protein Biomarkers for Mild Traumatic Brain Injury*, *in* BIOMARKERS OF BRAIN INJURY AND NEUROLOGICAL DISORDERS 221, 222 (Kevin K.W. Wang, Zhiqun Zhang & Firas H. Kobeissy eds., 2015).

109. Imaging such as CT and MRI can find damage when it exists, but these tests are typically used to confirm an already strong clinical suspicion or localize the problem to a specific brain region. *Id.* Additionally, CT scanning generally has a low sensitivity to detect diffuse injury, and while MRI technology can detect diffuse injury, it is often cost-prohibitive for widespread use. *Id.*

110. *See* McKee et al., *supra* note 89, at 44, 61.

111. *Id.* at 61.

112. Enormous funding has been designated for research into concussive injury biomarkers. *See, e.g.*, *The Head Health Initiative Overview*, HEAD HEALTH

biomarkers falls into two main types: (1) biomarkers of effect, which indicate if an individual has suffered a concussion and whether it has been resolved; and (2) biomarkers of susceptibility, which indicate that an individual is at increased risk of suffering from concussive injury. Biomarkers of effect are not stable over time, so the timing of the test is critical.[113] Set forth below are examples of recent research on biomarkers of effect that may be used for diagnosis and prognosis of concussive injury, including biomarkers of CTE and biomarkers of susceptibility to concussive injury. All of these different types of biomarkers will have a direct impact on the legal landscape of concussive injury.

1. *Biomarkers of Effect*

Biomarkers of effect have the potential to detect mTBIs and determine whether the concussion has been resolved. They also have the potential to detect CTE and the progression of the disease, which will be discussed in the next Subsection. This Subsection reviews some recent developments in the biomarker of effect research generally.

As discussed above, TBI is a spectrum. More specifically, it is generally considered in four categories: mild, moderate, severe, and vegetative state.[114] Mild and moderate TBI typically result in concussion,[115] whereas severe TBI typically results in coma or death.[116] Researchers have found biomarkers to be accurate in

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INITIATIVE, https://ninesights.ninesigma.com/web/head-health/head-health (last visited Feb. 13, 2016) (announcing a $22 million investment in biomarker research for concussive injury); *Department of Defense to Fund $5.5 Million Concussion Study*, MED. C. WIS., (Dec. 15, 2014), http://www.mcw.edu/MCW-News-Center/College-News/Department-of-Defense-to-fund-5.5-million-concussion-study.htm [http://web.archive.org/web/20150910000858/http://www.mcw.edu/MCW-News-Center/College-News/Department-of-Defense-to-fund-5.5-million-concussion-study.htm] (announcing the start of a biomarkers study funded by the Department of Defense).

113. Gary E. Marchant, *Genetics and Toxic Torts*, 31 SETON HALL L. REV. 949, 970 (2001) (referring to genetic biomarkers) [hereinafter Marchant, *Genetics and Toxic Torts*].

114. *See Glasgow Coma Scale*, *supra* note 65.

115. Sharon M. Valente & Diane Fisher, *Traumatic Brain Injury*, 7 J. FOR NURSE PRAC. 863, 863 (2011).

116. *See Glasgow Coma Scale*, *supra* note 65. The traditional clinical diagnostic for distinguishing between mild, moderate, and severe TBI is the Glasgow Coma Scale (GCS). *Id.* GCS scores below 9 indicate more serious injury, while 9–12 are considered moderate and 13–15 are considered mild (mTBI). *Id.*

identifying severe TBI, including serum-based markers[117] as well as brain scanning tools, such as computed tomography (CT) and magnetic resonance imaging (MRI). Biomarkers that can indicate mild injury are especially needed as CT and MRI scans have more difficulty detecting these injuries.[118]

While validated biomarkers of mTBI are not currently available, scientists have made rapid progress in recent years in developing a number of possible biomarkers.[119] Those developments

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117. *See* Emine Meric et al., *The Prognostic Value of Neuron-Specific Enolase in Head Trauma Patients*, 38 J. EMERGENCY MED. 297, 300 (2010) (finding increased levels of Neuron-Specific Enolase (NSE) coincide with more severe trauma, specifically for lower Glasgow scores indicating severe trauma); Yoshinori Yamazaki et al., *Diagnostic Significance of Serum Neuron-Specific Enolase and Myelin Basic Protein Assay in Patients with Acute Head Injury*, 43 SURGICAL NEUROLOGY 267, 271 (1995) (finding that Myelin Basic Protein (MDP) in serum was an accurate marker for severe trauma); Stefania Mondello et al., *AII-Spectrin Breakdown Products (SBDPs): Diagnosis and Outcome in Severe Traumatic Brain Injury Patients*, 27 J. NEUROTRAUMA 1203, 1206 (2010) (finding SBD145 provided detection as early as six hours after injury, while SBDP120 was comparable to SBDP145 after seven days from injury).

118. Jonathan T. Finnoff, Elena J. Jelsing & Jay Smith, *Biomarkers, Genetics, and Risk Factors for Concussion*, 3 PM&R 452, 453 (2011).

119. One problem with these studies is that the biomarker results are tested by reference to conventional measures. The biomarkers being developed do not yet answer the question whether an individual has suffered a concussion or has CTE; the researcher must look to other indicia. Most of the biomarker studies thus far have only been validated when compared to controls (without trauma) and those with trauma verified by neuropsychological or other conventional testing, which is based on clinical observations (whether drawing from subjective reports of the patient, observations of neurological symptoms, or results of other tests). *See* Ali Alawieh et al., *Neuro-Proteomics and Neuro-Systems Biology in the Quest of TBI Biomarker Discovery*, *in* BIOMARKERS OF BRAIN INJURY AND NEUROLOGICAL DISORDERS, *supra* note 108, at 21-22 (describing problems with validation in biomarker research); Papa et al., *supra* note 43, at 661 (stating no consensus has yet been reached for how to validate biomarkers). While some approaches compare biomarkers with the current clinical and observational diagnostic methods, others seek to also validate fluid biomarkers against other, non-invasive tests, such as MRI data. *E.g.*, Matthew T. McCarthy & Barry E. Kosofsky, *Clinical Features and Biomarkers of Concussion and Mild Traumatic Brain Injury in Pediatric Patients*, 1345 ANNALS N.Y. ACAD. SCI. 89, 93 (2015).

In other words, we validate our new tools with our old tools. We have not yet reached the point at which these variables are an independent (and presumably more dependable) measure. This is new research, and we need further longitudinal studies to tie validity to longer term outcomes. Another problem is that we have begun to measure physiological changes that have no (or not yet any) manifestation in cognition or behavior. Uzma Samadani et al., *Sensitivity and Specificity of an Eye Movement Tracking-Based Biomarker for Concussion*, CONCUSSION 7, 17 (2015) (stating that biomarker and imaging testing appear to

are the focus of this Article, given that these injuries are more prevalent than severe TBI among athletes and the military, as well as the general population.[120] We outline below a few of the more prevalent biomarkers that are currently under study.

S100B, a calcium binding protein that regulates cell development and degradation, has some potential as a blood-based biomarker of concussive injury.[121] It is well documented that elevated levels of the S100B protein are present in the blood after brain injury.[122] In one study, researchers found that S100B levels in serum correlated with the severity of TBI and were consistent with the results of CT scans,[123] but found that S100B levels were less sensitive indicators of injury in cases of mTBI.[124] In contrast, another study suggested that measurement of S100B in serum could accurately predict recovery from mTBI.[125] Finding some middle ground, a 2013

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detect "subclinical" injury, even though the patient continues to have cognitive function levels that pass neurocognitive testing procedures). And there is always a danger that juries or policy-makers will prefer the evidence of biomarkers over other forms of evidence, given our cultural addiction to faith in what is "physical," although other studies suggest otherwise. *See* Nicholas J. Schweitzer et al., *Neuroimages as Evidence in a Mens Rea Defense: No Impact*, 17 PSYCHOL., PUB. POL'Y, & L. 357, 366 (2011) (finding no evidence that neuroimaging unduly influences juries over verbal, neuroscience-based evidence; neuroscience evidence was more effective than clinical psychological evidence but that effect did not translate into differences in juries). But while these limitations may be fodder for evidentiary challenges or cross-examination, they do not justify an absolute bar to using biomarkers in legal or policy decisions.

120. *See* Geoffrey T. Manley & Andrew I. R. Maas, *Traumatic Brain Injury: An International Knowledge-Based Approach*, 310 JAMA 473, 473 (2013).

121. More specifically, S100B is a calcium binding protein that regulates protein phosphorylation and degradation, cell growth, and differentiation. *See* Valentina Di Pietro et al., *S100B and Glial Fibrillary Acidic Protein as Indexes to Monitor Damage Severity in an In Vitro Model of Traumatic Brain Injury*, 40 NEUROCHEMICAL RES. 991, 997 (2015).

122. Stephen M. Bloomfield et al., *Reliability of S100B in Predicting Severity of Central Nervous System Injury*, 6 NEUROCRITICAL CARE 121, 124 (2007). Higher levels of S100B indicate significant injury, while slightly elevated levels may be present from activity such as jogging. *Id.* at 125. Although it may be difficult to determine at what level S100B presence indicates injury, at high levels it is highly correlative with injury. *Id.*

123. Lynn Babcock et al., *Ability of S100B to Predict Severity and Cranial CT Results in Children with TBI*, 26 BRAIN INJ. 1372, 1378 (2012).

124. *Id.* at 1379. In those cases, additional symptoms, such as nausea, were useful in determining the severity of the injury prior to a CT scan. *Id.* at 1378.

125. WJ Townsend et al., *Head Injury Outcome Prediction in the Emergency Department: A Role for Protein S-100B?*, 73 J. NEUROLOGY NEUROSURGERY PSYCHIATRY 542, 544 (2002). The authors found that levels of S100B could accurately predict patient outcomes at one month from injury. *Id.* at 542.

study compared S100B accuracy with traditional prognosis techniques and found that while S100B was not as accurate in determining the severity of injury, the use of S100B along with these other prognostic tools created a more effective test than the traditional prognostics alone.[126]

Scientists are studying glial fibrillary acidic protein (GFAP), another protein released upon TBI, as a potential biomarker of effect.[127] Presence of GFAP in serum may indicate intracranial hemorrhage and damage to the blood-brain barrier (BBB).[128] In a 2012 study, researchers took serum samples of individuals hospitalized for TBI and measured the GFAP levels in the serum.[129] The study found that the amount of GFAP in the serum increased with the severity of TBI and correlated with more significant injury discovered by CT scans.[130] The researchers also found that GFAP levels were elevated within an hour after injury.[131]

The human brain can be injured in many ways, and the type of injury that results from hits to the head (acquired brain injury) can occur in many ways as well—from a lone but powerful impact (such as a transportation accident or battlefield injury) or from less powerful but more frequent impacts (such as shaken baby syndrome

126. Mehdi Moazzez Lesko et al., *Comparison of Several Prognostic Tools in Traumatic Brain Injury Including S100B*, 28 BRAIN INJ. 987, 991 (2014). Traditional prognostic tests include CT scans, pupillary reactivity, and Glasgow. *Id.* at 987.

127. *See* Di Pietro et al., *supra* note 121, at 996.

128. Zhifeng Kou et al., *Combining Biochemical and Imaging Markers to Improve Diagnosis and Characterization of Mild Traumatic Brain Injury in the Acute Setting: Results from a Pilot Study*, 8 PLOS ONE 1, 10 (2013); Praveen Ballabh, Alex Braun & Maiken Nedergaard, *The Blood-Brain Barrier: An Overview: Structure, Regulation, and Clinical Implications*, 16 NEUROBIOLOGY DISEASE 1, 1 (2004) ("The blood-brain barrier (BBB) is a diffusion barrier, which impedes influx of most compounds from blood to brain."). Dysfunction of the BBB may result in stroke, neuroinflammatory disorders, and other neurologic diseases. *See id.* Authors of a 2013 study measured serum GFAP levels of nine patients with mTBI injury and compared these levels with the results of MRIs. *Id.* at 3. The authors found that certain levels of GFAP in serum may indicate bleeding across the BBB at small levels beyond MRI detection. *Id.* at 10.

129. Linda Papa et al., *Elevated Levels of Serum Glial Fibrillary Acidic Protein Breakdown Products in Mild and Moderate Traumatic Brain Injury Are Associated with Intracranial Lesions and Neurosurgical Intervention*, 59 ANNALS EMERGENCY MED. 471, 471 (2012) (studying 108 individuals).

130. *Id.* at 476.

131. *Id.*

or football tackles).[132] One study of patients suffering TBI found that UCH-L1 levels were significantly increased in serum six to twenty-four hours after injury and through the next seven days.[133] Another study found that UCH-L1 is an accurate marker in mTBI as well.[134] Authors of a 2012 study measured levels of UCH-L1 in patients who suffered mild and moderate TBI.[135] The study found significantly higher levels of UCH-L1 compared to the control group, even in those with mTBI.[136] A separate study found that measuring both UCH-L1 and GFAP levels could lead to a highly effective biomarker test.[137]

Total tau (T-tau), a protein secreted by the axons of unmyelinated nerve cells when they are injured,[138] is another potential biomarker of concussion. A study by Dr. Pashtun Shahim suggested that the blood levels of T-tau could be used to gauge the

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132. Stefania Mondello et al., *Clinical Utility of Serum Levels of Ubiquitin C-Terminal Hydrolase as a Biomarker for Severe Traumatic Brain Injury*, 70 NEUROSURGERY 666, 666 (2012) [hereinafter Mondello (2012)]; Stefania Mondello et al., *Neuronal and Glial Markers Are Differently Associated with Computed Tomography Findings and Outcome in Patients with Severe Traumatic Brain Injury: A Case Control Study*, 15 CRITICAL CARE 156, 165 (2011) [hereinafter Mondello (2011)]; Linda Papa et al., *Serum Levels of Ubiquitin C-Terminal Hydrolase Distinguish Mild Traumatic Brain Injury from Trauma Controls and Are Elevated in Mild and Moderate Traumatic Brain Injury Patients with Intracranial Lesions and Neurosurgical Intervention*, 72 J. TRAUMA ACUTE CARE SURGERY 1335, 1343 (2012).

133. Mondello (2012), *supra* note 132, at 668-69 (studying ninety-five patients). The authors also found the levels of UCH-L1 could be predictive of patient survival. *Id.* at 670 (finding UCH-L1 may predict survival in patients even as soon as six hours from injury).

134. Papa et al., *supra* note 132, at 1339.

135. *Id.* at 1336. They sampled eighty-six patients with mild TBI and ten with moderate TBI. *Id.* at 1337.

136. *Id.* at 1338 (finding that levels of UCH-L1 could differentiate between control and very mild cases of TBI, including patients with a GCS of 15).

137. Mondello (2011), *supra* note 132, at 156. In the 2010 study, researchers measured both UCH-L1 and GFAP levels in eighty-one patients with GCS scores of 8 and lower (severe TBI). *Id.* They found both biomarkers to be much higher in those patients than in the control group. *Id.* at 158. Interestingly, UCH-L1 levels were higher in diffuse injury than mass legion, whereas GFAP levels were higher in mass legion than diffuse injury. *Id.* at 161. While the study did not include patients with mTBI, it still leads to the conclusion that the two biomarkers are released on different biochemical pathways and suggests that the combination of both could result in a highly effective biomarker test. *Id.* at 164.

138. John Q. Trojanowski et al., *Distribution of Tau Proteins in the Normal Human Central and Peripheral Nervous System*, 37 J. HISTOCHEMISTRY CYTOCHEMISTRY 209, 209 (1989).

severity of concussions in athletes and to assess when it is safe to return to play.[139] Measuring blood levels of T-tau to determine brain injury is a new concept; Dr. Shahim noted that studies show that T-tau is usually found only in the cerebrospinal fluid but may get into the blood at detectable levels after concussion with axonal injury.[140]

Dr. Shahim's study involved 288 professional ice hockey players in Sweden.[141] The researchers measured serum levels of three potential biomarkers, all of which have been previously associated with brain injury: neuron-specific enolase (NSE), S100B, and T-tau.[142] To create a baseline, the researchers took blood tests from the athletes for the three biomarkers at the start of the season.[143] Half of these players were tested again after a friendly game, in which there were no concussions, to assess the effect of exercise.[144] Results showed that the levels of two of the biomarkers—S100B and NSE—increased after the friendly match, but there was no change in T-tau levels.[145]

Researchers then measured the T-tau level of players who sustained concussions during the season at different times.[146] The plasma levels of T-tau increased in the concussed hockey players, with the highest concentrations immediately after the injury, with a second peak between twelve and thirty-six hours later.[147] Significantly, the T-tau concentrations at one hour after concussion

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139. Pashtun Shahim et al., *Blood Biomarkers for Brain Injury in Concussed Professional Ice Hockey Players*, 71 JAMA NEUROLOGY 684, 684 (2014).

140. *Id.* at 690; *see* Jeffrey Randall et al., *Tau Proteins in Serum Predict Neurological Outcome After Hypoxic Brain Injury from Cardiac Arrest: Results of a Pilot Study*, 84 RESUSCITATION 351, 352 (2013).

141. Shahim et al., *supra* note 139, at 686.

142. *See* M.R. Graham et al., *Direct Hits to the Head During Amateur Boxing Is Associated with a Rise in Serum Biomarkers for Brain Injury*, 24 INT'L J. IMMUNOPATHOLOGY PHARMACOLOGY 119, 119 (2011); Sanna Neselius et al., *Olympic Boxing Is Associated with Elevated Levels of the Neuronal Protein Tau in Plasma*, 27 BRAIN INJ. 425, 426 (2013); Henrik Zetterberg et al., *Sustained Release of Neuron-Specific Enolase to Serum in Amateur Boxers*, 23 BRAIN INJ. 723, 723-24 (2009).

143. *See* Shahim et al., *supra* note 139, at 685.

144. *Id.*

145. *Id.* at 686. This result casts doubts on the usefulness of NSE and S100B as biomarkers for mTBI. That the levels of both were elevated after a friendly match that did not result in a concussion (which was presumably a consequence of exertion and bruising of muscles and peripheral tissue) suggests a lack of specificity for brain injury. *Id.* at 690.

146. *Id.* at 685. The players' tau levels were measured at one hour, twelve hours, thirty-six hours, six days, and when the athlete returned to play. *Id.*

147. *Id.* at 686-87, 689.

predicted the number of days it took for the concussion symptoms to resolve.[148] T-tau measurements remained significantly elevated in players who had suffered a concussion compared with preseason levels at all time-points measured in this study, even when the concussion symptoms resolved and players were safe to return to play.[149]

These results suggest that serum levels of T-tau may prove to be a useful biomarker to diagnose and predict the outcomes of concussions among athletes.[150] Further studies may show how long it takes for plasma T-tau levels to normalize and whether persistently elevated levels of plasma T-tau can identify athletes who have sustained multiple concussion.[151]

Scientists from the University of Pennsylvania used the same Swedish ice hockey players' study to investigate a different biomarker for potential diagnostic use.[152] They found that a blood protein called SNTF,[153] a protein that is present at undetectable levels in healthy human brains but is produced under conditions where nerve cells are traumatized and begin to die,[154] surged and stayed elevated in the professional hockey players with persistent concussion symptoms, but not in players whose symptoms subsided within a few days.[155] The increased levels of SNTF were strongly correlated with diffuse axonal injury and long-term cognitive dysfunction.[156] Other results showed that when used in conjunction with the biomarker T-tau, the diagnostic accuracy was improved and was more effective than tau alone.[157]

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148. *Id.* at 687, 689.

149. *Id.* at 686.

150. *Id.* at 689-91.

151. T-tau levels may also be able to identify individuals who are at risk for developing CTE. *See infra* notes 166-78 and accompanying text.

152. Robert Siman et al., *Serum SNTF Increases in Concussed Professional Ice Hockey Players and Relates to the Severity of Postconcussion Symptoms*, 32 J. NEUROTRAUMA 1294, 1294-95 (2015).

153. Calpain-cleaved alpha-ll-spectrin N-Terminal fragment, or SNTF, is a brain-enriched protein. Robert Siman et al., *Evidence that the Blood Biomarker SNTF Predicts Brain Imaging Changes and Persistent Cognitive Dysfunction in MildTBI Patients*, 4 FRONTIERS NEUROLOGY 1, 1 (2013).

154. Siman et al., *supra* note 152, at 1295.

155. *Id.* at 1298.

156. *Id.* Researchers concluded that concussions that lead to long-term brain dysfunction cause SNTF to accumulate in the axon tracts of the brain, and that elevated blood levels of SNTF are a measure of this diffuse axonal injury. *Id.*

157. *Id.* at 1299.

Blood serum is not the only area of focus.[158] Research in ophthalmology also has promising results. Researchers at NYU have developed new technology to assess the location and impact of brain injury by tracking the eye movements of patients as they watch music videos for less than four minutes.[159] In the neurologically healthy subjects, the ratios of how the eye moved vertically and horizontally were close to one to one.[160] But in the participants with damage in the nerves that move the eyes or with brain swelling adjacent to those nerves, all showed abnormal eye movement ratios correlating to the nerve that was affected.[161] In every case where the abnormal eye movement was due to swelling in the brain, surgery to correct the brain problem also restored the eye movements to normal range.[162]

There has also been important progress in applying new brain scan technologies for detecting mTBI, which as discussed above is usually not detected by conventional CT or MRI scans.[163] Magnetoencephalography (MEG) is a functional brain imaging technique that measures the neuronal current in the grey areas of the

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158. Scientists are increasingly seeking to develop minimally invasive or non-invasive means of reliably detecting both the presence and severity of concussive injury that still rely on biological systems and are considered types of biomarkers. Measuring a subject's movement and balance is one recent development that shows potential. *See* Jasper O. Chang et al., *An Alternative to the Balance Error Scoring System: Using a Low-Cost Balance Board to Improve the Validity/Reliability of Sports-Related Concussion Balance Testing*, 24 CLINICAL J. SPORT MED. 256, 261 (2014).

159. Uzma Samadani et al., *Detection of Third and Sixth Cranial Nerve Palsies with a Novel Method for Eye Tracking While Watching a Short Film Clip*, 122 J. NEUROSUGERY 707, 708-09 (2015).

160. *Id.* at 709.

161. *Id.* at 709-15.

162. *Id.* at 707, 709-17. In a subsequent study, researchers tracked eye movement of seventy-five trauma subjects and sixty-nine non-injured control subjects. Uzma Samadani et al., *Eye Tracking Detects Disconjugate Eye Movements Associated with Structural Traumatic Brain Injury and Concussion*, 32 J. NEUROTRAUMA 548, 549 (2015). As in the previous study, subjects with abnormal results gradually returned to baseline values during the follow-up period with recovery. *Id.* at 551. Results indicated that measures of horizontal disconjugacy were significantly increased in the trauma patients relative to the control group. *Id.* at 550-51. These findings suggest that methods such as eye tracking may prove to be consistently more sensitive to detecting brain injury than the currently employed methods of CT scan or observation by simple finger or pen-light tracking administered by a physician.

163. *See* Bruce et al., *supra* note 76, at 103-04; Erin D. Bigler, *Neuroimaging Biomarkers in Mild Traumatic Brain Injury (mTBI)*, 23 NEUROPSYCHOLOGY REV. 169, 170 (2013).

brain that in one study was able to accurately diagnose over 80% of mTBI patients, compared to less than 10% for MRI scanning for the same patients.[164] Several other neuroimaging modalities are also being investigated for providing biomarkers of mTBI.[165]

2. *Biomarkers of CTE*

Researchers have focused on a number of potential biomarkers for CTE.[166] In particular, they have focused on the abnormal tangles of neural protein tau that accumulate in neurons of brains of individuals with CTE and with Alzheimer's, and which can be measured using brain-imaging technologies in living patients.[167] A recent study involved fourteen retired NFL football players, all of whom had sustained at least one concussion, and with various degrees of suspected CTE.[168] Their results were compared with participants with healthy brains and participants who met the standard diagnostic criteria for Alzheimer's.[169]

The researchers scanned the brains of participants using Positron Emission Tomography (PET)[170] after injecting them with a specially developed radioactive tracer called [F-18] FDDNP, which binds to deposits of the tau.[171] Using these PET scans, the researchers were able to pinpoint where in the brain these abnormal proteins accumulated. They found that the imaging pattern in people with suspected CTE differs significantly from healthy volunteers and

164. Ming-Xiong Humang et al., *Single-Subject-Based Whole-Brain MEG Slow-Wave Imaging Approach for Detecting Abnormality in Patients with Mild Traumatic Brain Injury*, 5 NEUROIMAGE: CLINICAL 109, 115 (2014).

165. Bigler, *supra* note 163, at 171-74; Toledo et al., *supra* note 55, at 1519-23.

166. Montenigro et al., *supra* note 98, at 2.

167. Jorge R. Barrio et al., *In Vivo Characterization of Chronic Traumatic Encephalopathy Using [F-18]FDDNP PET Brain Imaging*, 112 PROC. NAT'L ACAD. SCI. E2039, E2039, E2044 (2015). This research built on preliminary work published in 2013. Gary W. Small et al., *PET Scanning of Brain Tau in Retired National Football League Players: Preliminary Findings*, 21 AM. J. GERIATRIC PSYCHIATRY 138 (2013).

168. Barrio et al., *supra* note 167, at E2040.

169. *Id.* at E2041.

170. PET is an imaging technique, similar to MRI or CT, that "allows the non-invasive detection and quantification of proteins linked to disease." David T. Chien et al., *Early Clinical PET Imaging Results with the Novel PHF-Tau Radioligand [F18]-T808*, 38 J. ALZHEIMER'S DISEASE 171, 171 (2014).

171. Barrio et al., *supra* note 167, at E2040.

those with Alzheimer's.[172] The researchers identified four distinctive patterns of tau tangles in the brains of the former football players that did not appear in the normal brains of the controls in the study. In particular, they found that the former athletes had higher levels of FDDNP in the amygdala and subcortical regions of the brain.[173] The researchers suggested that these patterns mimic the damage that occurs from a concussion, starting in the midbrain, moving toward the subcortical areas and amygdala, and then advancing to the cerebral cortex.[174] In contrast, the tau tangles in the brains of the Alzheimer's-diagnosed participants appeared to start in the cerebral cortex.[175]

The study was small and not without controversy.[176] There have been a small number of other studies using PET or other brain imaging technologies that have differentiated CTE from Alzheimer's in living, at-risk individuals.[177] These findings indicate a promising

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172. *Id.* at E2044.

173. *Id.* at E2043-44.

174. *Id.* at E2045-46.

175. *Id.* at E2044. Researchers intend to expand the study to determine whether there is a "blast variant" version of CTE. *Id.* at E2045-46.

176. A panel of experts convened by the National Institute of Neurological Disorders and Stroke concluded that the pathological signature of CTE is found in the cerebral cortex. *Report from the First NIH Consensus Conference to Define the Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy*, NAT'L INST. HEALTH, http://www.ninds.nih.gov/research/tbi/ReportFirstNIHConsensusConference.htm (last updated Mar. 31, 2015). Furthermore, some of the lead scientists on the study charged several former NFL players with suspected CTE a fee to get a PET scan with their FDDNP tracer, which led to a warning from the FDA because FDDNP has not been approved for clinical use. Ken Belson, *Researchers Seeking to Find a Brain Disease in Living Patients Are Under F.D.A. Scrutiny*, N.Y. TIMES, Apr. 12, 2015, at SP4. The PET scans cost about $10,000 to administer. *Id.*

177. Christine M. Baugh et al., *Current Understanding of Chronic Traumatic Encephalopathy*, 16 CURRENT TREATMENT OPTIONS NEUROLOGY 306, 313 (2014). [F18]-T808 is another tau-specific ligand biomarker researchers have found that may be detected with PET imaging. *Id.* at 314. While this study used [F18]-T808 detection as an indicator of Alzheimer's disease, it could be useful in detecting other tauopathy neurodegenerative diseases, including CTE. Chien et al., *supra* note 170, at 171; Baugh et al., *supra* note 91, at 251.

Diffusion tensor imaging (DTI) is another imaging technique that may prove useful. Michael H. Chappell et al., *Distribution of Microstructural Damage in the Brains of Professional Boxers: A Diffusion MRI Study*, 24 J. MAGNETIC RESONANCE IMAGING 537, 537 (2006). DTI differs from MRI or CT imaging because it is sensitive to diffusion (molecules traveling across areas of differing concentrations), making it sensitive to microstructural changes. *Id.* Detecting these microstructural changes may give insight to brain injury that other imaging

way to diagnose CTE in the living brain, but more validation is needed before they can be used to diagnose CTE reliably in living patients.[178] This may require long-term, longitudinal epidemiological studies.[179]

While there are fewer studies regarding in vivo biomarkers for CTE than TBI, research of bodily fluid biomarkers in TBI and mTBI may also prove useful in diagnosing CTE.[180] Researchers have found that various biomarkers are expressed for differing periods of time after injury. In a 2012 study, researchers found that levels of neurofilament light protein and GFAP were elevated in the cerebral spinal fluid of amateur boxers two weeks after a bout.[181] In another study, the investigators measured the NSE levels in serum of amateur boxers who spent two months without boxing[182] and found those boxers still had higher levels of NSE compared to controls.[183] These biomarkers that are still expressed weeks and months after injury (and may be prolonged in those with prior injury) have potential for diagnosing CTE in the living brain.[184] Thus, repeat measurements of markers that have previously been used to diagnose mTBI and TBI may be useful in identifying individuals at higher risk for developing

techniques cannot. *Id.* In a study of eighty-one professional boxers, researchers found certain abnormalities in the brain shown by DTI indicated damage due to the boxer's history. *Id.* at 538. These abnormalities were present even if the subject had no history of major trauma, suggesting that DTI may be useful in detecting CTE in a patient without a history of TBI. *Id.* at 538, 540.

178. *See In re* Nat'l Football Players' Concussion Injury Litig., 307 F.R.D. 351, 399 (E.D. Pa. 2015) (describing limitations of studies of abnormal tau protein in living brains of individuals with histories of repetitive mTBI, including the small size of the studies, the bias in the selection of the subjects, and the failure to control for other potential risk factors, such as higher weight, lifestyle changes, age, or substance abuse).

179. *Id.*

180. Jesse Mez, Robert A. Stern & Ann C. McKee, *Chronic Traumatic Encephalopathy: Where Are We and Where Are We Going?*, 13 CURRENT NEUROLOGY & NEUROSCIENCE REP. 407, 415 (2013).

181. Sanna Neselius et al., *CSF-Biomarkers in Olympic Boxing: Diagnosis and Effects of Repetitive Head Trauma*, 7 PLOS ONE 1, 3 (2012).

182. Zetterberg et al., *supra* note 142, at 724.

183. *Id.* The study noted that the half-life of NSE is only forty-eight hours. *Id.* at 725. The same research group found in an earlier study that neurofilament light protein levels were elevated in the cerebral spinal fluid even after three months resting time. Henrik Zetterberg et al., *Neurochemical Aftermath of Amateur Boxing*, 63 ARCHIVES NEUROLOGY 1277, 1279 (2006).

184. Ryan C. Turner et al., *Repetitive Traumatic Brain Injury and Development of Chronic Traumatic Encephalopathy: A Potential Role for Biomarkers in Diagnosis, Prognosis, and Treatment?*, 3 FRONTIERS NEUROLOGY 1, 7 (2013).

CTE.[185] Since those with a concussive history have almost a six-times greater risk of future concussive injury, mTBI and TBI biomarkers and repeated measurement after injury could help predict and diagnose CTE.[186]

3. *Biomarkers of Susceptibility*

Some people may have a genetic or other predisposition to concussion and CTE. Although several genetic biomarkers potentially may be connected with an increased risk of concussion,[187] most of the research has focused on the apolipoprotein E (APOE) gene because of its association with Alzheimer's.[188] More specifically, research has focused on the ϵ4 allele of the APOE gene, which may impose greater concussion risks on carriers of the allele.[189] Other studies have indicated that the APOE ϵ4 allele may contribute to genetic susceptibility of CTE.[190]

The APOE gene regulates apolipoprotein (Apo E) production. Apo E helps lipid transportation in the brain, maintains neural structural integrity, and promotes recovery after neural injury.[191] Scientists believe that the normal ϵ3 allele promotes neural recovery, while ϵ4 inhibits neural growth.[192] Some studies have suggested that the ϵ4 allele inhibits recovery from TBI and results in a poorer patient outcome.[193] In one study, those with the ϵ4 allele were found to have a worse recovery six months after injury, and those who were ϵ4 homozygotes had a significantly higher chance of death resulting from their injuries.[194] Another study surveyed the results of seventy children who suffered TBI and found that the possession of the ϵ4 allele resulted in worse recovery than children with the ϵ3 / ϵ3 and

185. *Id.*

186. Mez, Stern & McKee, *supra* note 180, at 412.

187. Cameron B. Jeter et al., *Biomarkers for the Diagnosis and Prognosis of Mild Traumatic Brain Injury/Concussion*, 30 J. NEUROTRAUMA 657, 659 (2013).

188. *Id.* at 666; Baugh et al., *supra* note 91, at 249.

189. Jeter et al., *supra* note 187, at 666.

190. *See* Mez, Stern & McKee, *supra* note 180, at 413.

191. Finnoff, Jelsing & Smith, *supra* note 118, at 454.

192. *Id.*; Graham M. Teasdale et al., *Association of Apolipoprotein E Polymorphism with Outcome After Head Injury*, 350 LANCET 1069, 1070 (1997).

193. Finnoff, Jelsing & Smith, *supra* note 118, at 454; Teasdale et al., *supra* note 192, at 1071; Thomas Roland Terrell et al., *APOE, APOE Promoter, and Tau Genotypes and Risk for Concussion in College Athletes*, 18 CLINICAL J. SPORT MED. 10, 10-11 (2008).

194. Teasdale et al., *supra* note 192, at 1070.

ϵ3 / ϵ2 genotypes.[195] Other studies have suggested, however, that there is no connection between the ϵ4 allele and the frequency of mTBI.[196] Given these conflicting results, no consensus exists at this time on whether Apo ϵ4 is a useful susceptibility biomarker of mTBI risk.[197] While the evidence suggests that Apo ϵ4 does not increase the incidence of mTBI, it may increase the severity of or delay recovery from mTBI, at least in adults.[198] However, most researchers believe additional research is needed before the Apo ϵ4 allele can be used as a biomarker of concussion susceptibility.[199]

For CTE, a study of sixty-eight CTE cases noted that CTE occurred with no greater frequency in APOE ϵ4 carriers compared to the normal U.S. population.[200] In contrast, another review of CTE injuries found that in the ten cases of CTE where the APOE genotype was reported, five individuals carried at least one APO ϵ4 allele.[201] Other studies have found that older football players who carry the APOE ϵ4 allele scored lower on cognitive tests than similarly aged players without the allele or less experienced players

195. Eva Brichtová & Libor Kozák, *Apolipoprotein E Genotype and Traumatic Brain Injury in Children—Association with Neurological Outcome*, 24 CHILD'S NERVOUS SYS. 349, 355 (2008).

196. Terrell et al., *supra* note 193, at 14; Vicki L. Kristman et al., *Does the Apolipoprotein ϵ4 Allele Predispose Varsity Athletes to Concussion? A Prospective Cohort Study*, 18 CLINICAL J. SPORT MED. 322, 327 (2008).

197. Sam Gandy & Steven T. DeKosky, *APOE ε4 Status and Traumatic Brain Injury on the Gridiron or the Battlefield*, 4 SCI. TRANSLATIONAL MED. 1, 1 (2012) (finding, through informal poll, that two-thirds of TBI experts are opposed to using APOE status at this time to screen for participation in high school or college sports).

198. David W. Lawrence et al., *The Role of Apolipoprotein E Epsilon (ε)-4 Allele on Outcome Following Traumatic Brain Injury: A Systematic Review*, 29 BRAIN INJ. 1018, 1027 (2015); Lisa M. Moran et al., *Apolipoprotein E4 as a Predictor of Outcomes in Pediatric Mild Traumatic Brain Injury*, 26 J. NEUROTRAUMA 1489, 1490 (2009).

199. Michael Makdissi et al., *Revisting the Modifers: How Should the Evaluation and Management of Acute Concussions Differ in Specific Groups?*, 47 BRIT. J. SPORTS MED. 314, 317-18 (2013); Jeffrey S. Kutcher & James T. Eckner, *At-Risk Populations in Sports-Related Concussion*, 9 CURRENT SPORTS MED. REP. 16, 18 (2010).

200. Mez, Stern & McKee, *supra* note 180, at 416. The study found, however, that those who were ϵ4 homozygotes were overrepresented compared to the U.S. population. *Id.* Because the study's results were ambiguous, the researchers concluded that further research is needed to determine whether there is a link between the ϵ4 allele and CTE. *Id.*

201. Ann C. McKee et al., *Chronic Traumatic Encephalopathy in Athletes: Progressive Tauopathy After Repetitive Head Injury*, 68 J. NEUROPATHOLOGY EXPERIMENTAL NEUROLOGY 709, 732 (2009).

of any genotype, suggesting that the combination of APOE ϵ4 and repeated impacts may contribute to long-term cognitive effects.[202] These results indicate that the ϵ4 allele may be a genetic risk factor for CTE,[203] but more studies are needed to determine whether the ϵ4 allele is actually a genetic risk factor in CTE.

A more promising genetic marker for mTBI susceptibility may be the rare type APOE promoter allele G-219T. The G-219T promoter allele (specifically the T/T genotype) is associated with lower transcriptional activity (the first step of gene expression in which a segment of DNA is copied onto RNA), reducing the amount of Apo E expressed.[204] In a 2008 study, scientists took genetic samples from student–athletes and sequenced their genomes.[205] The authors found that the presence of the T/T genotype resulted in a three-fold higher risk of concussion compared to the normal G/G genotype.[206] Authors of another study found further evidence of the T allele's genetic susceptibility.[207] They surveyed 196 college athletes, taking saliva samples to determine their APOE genotype, and found that individuals with the rare T allele have more than eight times greater chance of concussion.[208]

The search to identify biomarkers is diverse, widespread, and advancing rapidly. Scientists are testing different serum-based markers to give us new tools to understanding whether an individual's brain has been injured, how extensive the injury is, whether it has been resolved, and whether certain people are more susceptible to suffering concussions and CTE. Identifying and measuring the presence of biomarkers such as the T-tau protein or

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202. Kenneth C. Kutner et al., *Lower Cognitive Performance of Older Football Players Possessing Apolipoprotein E ϵ4*, 47 NEUROSURGERY 651, 655 (2000).

203. *Id.* at 655-56.

204. Ryan T. Tierney et al., *Apolipoprotein E Genotype and Concussion in College Athletes*, 20 CLINICAL J. SPORTS MED. 464, 466 (2010). The G-219T allele alters transcription, changing the amount of Apo E expressed, which may influence concussion susceptibility in some cases. *Id.* at 466-67.

205. Terrell et al., *supra* note 193, at 11.

206. *Id.* at 13. The authors also found those with the G/T genotype did not have a statistically higher risk of concussion compared to the G/G normal genotype. *Id.*

207. Tierney et al., *supra* note 204, at 466.

208. *Id.* at 465-66. Those with the rare promoter allele, and the two rare APOE alleles (ϵ2, and ϵ4) were found to be at a ten times higher risk factor. *Id.* at 464, 466. This suggests that the rare-type allele in the promoter region may be a better indicator of concussive susceptibility than just the ϵ4 allele alone, but the ϵ4 allele may still be a significant genetic factor in concussive susceptibility.

the APOE gene look particularly promising. Use of these biomarkers will undoubtedly begin to seep into the legal landscape and change how we evaluate risk and responsibility in law.

II. TRANSFORMING THE LEGAL LANDSCAPE

The development of reliable biomarkers of effect and susceptibility will significantly inform courts and policy makers as they wrestle with the complex questions regarding the nature of concussive injury, the need for regulation in the area, and the allocation of fault and duties with regard to head injuries. In the litigation context, biomarker evidence will be judged against admissibility standards as embedded in the *Daubert* principles.[209] These admissibility tests may be difficult to meet, but even so, they may delay but ultimately not forestall the effect of biomarkers seeping into the legal landscape. And as biomarker evidence enters the courtroom, the consequences for tort analysis are likely to be dramatic.

A. Legal Implications of Biomarkers of Effect

The ability to detect biomarkers of effect of concussive injury long before clinical symptoms appear may have an impact on each element of tort liability. As every first year law student knows, the required elements for recovery of damages in tort are: (1) duty; (2) breach of duty; (3) causation; and (4) damages.[210] Although the development of biomarkers will affect these elements in torts involving acquired head injury in all settings,[211] this Article focuses these issues in the context of torts involving youth sports and

209. *See* Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579 (1993). The tests include whether the technique can be tested, whether it has been subjected to peer review and publication, whether the potential or known error rate of the technique has been determined, and whether the technique has gained general acceptance within the scientific community. *Id.* at 593-94.

210. DAN B. DOBBS, THE LAW OF TORTS 270-73 (2000).

211. *See, e.g.*, N.J. Div. of Youth and Family Servs. v. L.G.C., 2010 WL 1426879 (N.J. Super. Ct. App. Div. 2010) (domestic relations); Garrison v. Shineski, No. 10-3614, 2011 WL 6005212 (Vet. App. 2011); Maselter v. Astrue, No. 07-2921 (RHK/JSM), 2008 WL 4527828 (D. Minn. 2008) (social security disability benefits); Weeks Marine, Inc. v. Am. S.S. Owners Mut. Prot. & Indem. Ass'n, No. 08 Civ. 9878(NRB), 2011 WL 3796331 (S.D.N.Y. 2011) (whether insurance coverage for "brain injury" of employees includes concussion); U.S. v. Reilly, 662 F.3d 754 (6th Cir. 2011) (sentencing variance for veteran).

concussive injury.[212] Sports present unique challenges in torts because the sanctioned athletic activity (such as tackling in football or body checking in hockey) would be considered tortious conduct under other circumstances. In addition, state legislative action has modified standards of care and legal duties in the school sports area.

1. *Duty and Breach*

Duty in the youth-sports area stems from the general common law obligation to provide a relatively safe environment to engage in the activity.[213] Concussive management on the playing field is the first area of concern. This may include the duty of sports sponsors to inform players about the risks of concussions, provide equipment, implement both rules and a playing environment that do not impose unreasonable risks of injury, accurately diagnose concussions, and remove players from play and not to allow them to return until their concussions have resolved.

Legal duties for concussive injury prevention and management trace to a mixture of legislation and common law principles. This Subsection examines both, including examination of return-to-play legislation under state law, as well as the rise of the use of athletic trainers as the front line for concussive management. These approaches to concussion management only address management of "acute" concussion and do not address the long-term issues associated with concussion,[214] except in a general sense.

Significant challenges exist to concussive management. Concussive management depends on the cooperation of the player and candor in reporting symptoms.[215] Some players simply may not

212. It is generally accepted that two populations are at a heightened risk for concussion and mTBI: athletes and military combat personnel. L. Syd M. Johnson, Brad Partridge & Frédéric Gilbert, *Framing the Debate: Concussion and Mild Traumatic Brain Injury*, 8 NEUROETHICS 1, 2 (2015) [hereinafter Johnson, *Framing the Debate*]. This Article focuses on legal duties for concussive management with regard to athletes. Legal duties involved in combat personnel are dominated by sovereign immunity issues. Jonathan Turley, *Pax Militaris: The Feres Doctrine and the Retention of Sovereign Immunity in the Military System of Governance*, 71 GEO. WASH. L. REV. 1, 1-2 (2003). Furthermore, diagnosis and treatment of mTBI for combat victims are complicated by the similarity of symptoms with PTSD. Johnson, *Framing the Debate*, *supra.*

213. *See, e.g.*, Searles v. Trs. of Saint Joseph's Coll., 695 A.2d 1206, 1209 (Me. 1997).

214. Long-term issues will be discussed *infra* at Subsection II.A.2.

215. Johnson, *supra* note 41, at 19.

recognize the symptoms of a concussion.[216] In addition, there are powerful, coercive social and economic pressures to underreport symptoms.[217] The resistance to reporting concussion symptoms exists at all levels of sports,[218] including high school.[219]

A further challenge to concussive management is the lack of consensus regarding the definition, diagnosis, and treatment for concussions.[220] The current approach generally only addresses clinically evident concussions.[221]

a. Return-to-Play Determinations Under State Law

States have been at the forefront in regulating concussive injury in the youth-sports area.[222] All fifty states and the District of Columbia now have legislation to prevent concussions and to limit further injury to student–athletes who sustain concussions.[223] States

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216. Andrew W. Breck, Note, *Keeping Your Head on Straight: Protecting Indiana Youth Athletes from Traumatic Brain Injuries Through "Return-to-Play" Legislation*, 9 IND. HEALTH L. REV. 215, 221 (2012).

217. Johnson, *supra* note 41, at 20.

218. John Keim, *Most Would Play SB with Concussion*, ESPN (Jan. 28, 2014), http://espn.go.com/nfl/story/_/id/10358874/majority-nfl-players-play-super-bowl-concussion-espn-survey (reporting that 85% of players surveyed would play in the Super Bowl with a concussion); *NFL Concussion Poll: 56 Percent of Players Would Hide Symptoms to Stay on Field*, SPORTING NEWS (Nov. 12, 2012), http://www.sportingnews.com/nfl/story/2012-11-11/nfl-concussions-hide-symptoms-sporting-news-midseason-players-poll (reporting that 56% of NFL players surveyed would try to hide concussion symptoms).

219. Johnson, *supra* note 41, at 19; *see also* Frederick P. Rivara et al., *The Effect of Coach Education on Reporting of Concussions Among High School Athletes After Passage of a Concussion Law*, 42 AM. J. SPORTS MED. 1197, 1197 (2014) (discussing a study of Washington State, the first state to adopt return-to-play legislation, which found that over two-thirds of high school athletes who suffered mTBI reported playing with symptoms); Emily Kroshus et al., *Concussion Under-Reporting and Pressure from Coaches, Teammates, Fans and Parents*, 134 SOC. SCI. & MED. 66, 66 (2015) (quantifying, in study of 328 players at four colleges in seven sports, the pressure from coaches, teammates, parents, and fans to continue to play after head impact).

220. Johnson, Partridge & Gilbert, *supra* note 212, at 2.

221. Johnson, *supra* note 41, at 15-16.

222. Various concussion management protocols have also been voluntarily adopted by sports teams and leagues. Critics argue that these protocols are vague, "wide open to interpretation by trainers and medical staffs," and not empirically validated. Johnson, *supra* note 41, at 19.

223. *See* CTRS. FOR DISEASE CONTROL, GET A HEADS UP ON CONCUSSION IN SPORTS POLICIES INFORMATION FOR PARENTS, COACHES, AND SCHOOL & SPORTS PROFESSIONALS 1, 4 (n.d.), http://www.cdc.gov/headsup/pdfs/policy/headsuponconcussioninsportspolicies-a.pdf

have dominated legislative action in this area, since there is no federal law that regulates youth athletic concussions, nor is there a central governing body to promulgate health and safety standards.

The goal of return-to-play legislation is to ensure that student–athletes recover from concussions and do not play with an injured brain.[224] The legislation is generally focused on managing single instances of concussion and is based on the assumption that preventing concussed players from returning to play before their symptoms have resolved will lower the risk of developing long-term cognitive impairment.[225] Most state statutes have three major components: (1) removal from play, (2) medical clearance for return to play, and (3) education. Generally, the statutes charge the school districts, the state department of health or board of education, or the athletic association to implement the statutes.[226] Although these statutes have much in common, their most noteworthy characteristic is their lack of uniformity.

The vast majority of these laws mandate that student–athletes who experience a concussion be removed from play and obtain a specified individual's permission before returning to play.[227] The statutes vary on who can grant that permission, although most statutes require a health care provider trained in the evaluation and management of concussions to make the determination.[228] States differ on whether the health care provider is required to be "licensed" or a neutral decision maker.[229] In other words, some states allow

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224. Breck, *supra* note 216, at 218.

225. *See* Steven P. Broglio et al., *National Athletic Trainers' Association Position Statement: Management of Sport Concussion*, 49 J. ATHLETIC TRAINING 245, 249-51 (2014).

226. *See, e.g.*, N.M. STAT. ANN. § 22-13-31(D) (West 2015) (charging school districts with development and implementation responsibilities); OKLA. STAT. ANN. tit. 70, § 24-155(A) (West 2015) (charging school districts and athletic associations with implementation responsibilities).

227. CHILDREN'S SAFETY NETWORK, LEGISLATION ON SPORTS-RELATED CONCUSSIONS 1 (Sept. 2013), http://www.childrenssafetynetwork.org/sites/childrenssafetynetwork.org/files/CSN_SportsConcussion_Legislation2013.pdf. Wyoming does not specifically require medical evaluation or clearance before a youth athlete is permitted to return to play. *See* WYO. STAT. ANN. § 21-3-110 (West 2015).

228. Some states allow medical clearance by any health care provider. *See, e.g.*, ARIZ. REV. STAT. § 15-341(24)(b) (2015).

229. For example, Arizona's definition of a health care provider includes physicians, athletic trainers, nurse practitioners, and physician's assistants who have been trained in the evaluation and management of concussions and head injuries. *See* § 15-341(24)(b). Alabama and Texas require a licensed physician to make the

anyone who has been trained to be an evaluator, and even a coach may suffice.[230]

Although most states require training in head injuries, the states vary on who is responsible for developing the training protocols and who is required to receive the training.[231] The majority of states simply delegate education initiatives to the state's school districts with no further instruction.[232] Although most of the statutes require distribution of information to coaches and students regarding concussions, only some of them require in-depth training for coaches.[233] Many states do not require students to complete training, even though diagnosis currently depends heavily on the player recognizing internal symptoms.[234]

Most states do not mandate a waiting period before returning to play.[235] Only a few states require the schools to collect concussion data, and significantly, not a single statute requires baseline testing of student–athletes before the season.[236]

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return-to-play determination. ALA. CODE § 22-11E-2(d) (2015); TEX. EDUC. CODE ANN. § 38.157(a)(1) (West 2015). California requires a licensed health care provider, meaning a health care provider who is trained in the management of concussion. CAL. EDUC. CODE § 49475 (West 2015).

230. A few states do not address who will make the determination. *See, e.g.*, 2011 ILL. LAWS 97-0078.

231. Many states do not require the participation of a medical or public health entity in the development of their education initiatives. *See, e.g.*, IDAHO CODE ANN. § 33-1625(1) (West 2015); N.J. STAT. ANN. § 18A:40-41.3(b) (West 2015).

232. *See, e.g.*, COLO. REV. STAT. ANN. § 25-43-103(1)(a) (West 2015) (charging each public school with responsibility of educating coaches annually regarding concussions); TENN. CODE ANN. § 68-55-502(b)(1)(A)-(B) (West 2015) (stating that public schools should create guidelines regarding treatment of concussions and that coaches should be trained annually on that treatment).

233. *See, e.g.*, OR. REV. STAT. ANN. § 336.485(2)(a) (West 2015). Those states that require training vary on how often training should take place. *See* Kevin Brandwein, *Goals and Obstacles in Legislating Concussion Management in Youth Sports*, 10 WILLAMETTE SPORTS L.J. 28, 46 (2013).

234. Most of the statutes require distribution of information to parents, and most—but not all—of the statutes require students and parents to sign a form confirming the receipt of concussion information. Brandwein, *supra* note 233, at 46; *see, e.g.*, WIS. STAT. ANN. § 118.293(3)(a) (West 2015) (requiring only a parent's signature prior to preseason under Wisconsin law).

235. California has the longest (seven day) mandatory waiting period. CAL. EDUC. CODE § 49475(a)(1) (West 2015). In contrast, Arizona allows a student to return to play the next day if the trained health care provider clears the player. ARIZ. REV. STAT. § 15-341(24)(b) (2015).

236. *See* Hosea H. Harvey, *Reducing Traumatic Brain Injuries in Youth Sports: Youth Sports Traumatic Brain Injury State Laws, January 2009–December 2012*, 103 AM. J. PUB. HEALTH 1249, 1249-54 (2013).

This diversity of approaches reflects the lack of consensus on the best approach to concussive management.[237] Some commentators question the efficacy of these types of concussive management legislation altogether, especially when the risks and mechanics of mTBI injuries are not fully understood.[238] Furthermore, current laws and regulations do not specify how to determine the presence of a concussion, leaving it to the discretion of the evaluator, who may or may not be a licensed health care provider.

Development of biomarkers of effect will reshape this legislative landscape. It will lead the way toward establishing evidence-based guidelines for making return-to-play decisions after concussions and in reducing the problems created by the dependence on self-reporting by the player. As use of biomarkers becomes standard medical procedure, regulatory bodies are likely to incorporate these tests into their requirements, which should lead to greater standardization, particularly in the requirements for removal from play, medical clearance, and education. Legislation or regulations may specify the use of biomarkers for the return-to-play determination, as well as require evaluators who are trained in the use of biomarkers and qualified to interpret them. Furthermore, statutes may require the creation of baselines for each athlete, once a biomarker gives us something to measure.[239] In this way, when there is evidence of a potential concussion, trained personnel can compare the levels of the biomarkers post-injury to those baseline measurements.[240]

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237. Johnson, *supra* note 41, at 24 ("To be effectively neuroprotective . . . it is likely RTP protocols would have to be significantly more conservative and restrictive, and require a much longer period of rest and recovery.").

238. *See* Johnson, Partridge & Gilbert, *supra* note 212, at 2-3. Critics point out that the statutes do not require changes to how the sport itself is played. Johnson, *supra* note 41, at 24.

239. Some leagues have begun to use neuropsychological testing to create baselines. Christopher Randolph, *Baseline Neuropsychological Testing in Managing Sport-Related Concussion: Does It Modify Risk?*, 10 CURRENT SPORTS MED. REP. 21, 21 (2011). These are subject to "sandbagging," or intentional manipulation by the players, to avoid later detection of concussions. For example, Peyton Manning admitted to deliberately sandbagging the baseline test. *See* Rick Reilly, *Talking Football with Archie, Peyton, Eli*, ESPN (Apr. 27, 2011, 9:32 AM), http://sports.espn.go.com/espn/news/story?id=6430211.

240. As mentioned above, no statute currently requires baseline testing of student–athletes. Some athletic programs have adopted a form of baseline testing through cognitive testing programs. Some programs, such as imPACT, implement baseline testing, but this test is adopted solely on a voluntary basis. *See About ImPACT*, IMPACT, https://www.impacttest.com/about/ (last visited Feb. 13, 2016).

Similarly, collection of concussion data, both pre- and post-season, will likely become standard through legislation, regulation, or protocol. The data will allow schools and sports leagues to identify individual, at-risk players as well as to discern overall group patterns that may have an impact on policies on concussive management, such as how long a waiting period appears most effective. The availability of such data will help shape future public health measures as well.

At the same time, the development and validation of biomarkers will create their own set of new complexities and questions. With so many different types of biomarkers in different stages of development, there will be issues as to which biomarkers should be used and when. It is likely that there will be frequent changes in best practices with regard to the choice and application of biomarkers as the science in this area rapidly changes. Who should specify which biomarkers are the state of the art and should be used? If it is the legislature, there may be problems keeping the statutes up to date with constantly shifting science. If that responsibility is delegated, there may be problems with consistency and accountability. Another set of issues is how much reliance should be placed on rapid, real-time "on the sidelines" biomarker assays, such as a blood screen, versus more expensive and rigorous tests—involving brain scans or other technologies—that can only be conducted away from the playing field.

On a broader scale, with the identification of biomarkers, there may be more calls for uniform federal legislation, regulations, or creation of a uniform model code for the states to follow. This alignment could lead to a minimum standard of concussion prevention, care, and management and could incorporate—either directly or indirectly—the use of biomarkers. Standardization would likely include requiring baseline testing at the beginning of each season and requiring schools and teams to report concussion incidents to a registry. Such legislation could potentially include civil liability or penalties for noncompliance.

b. Private Law Remedies

Individuals will continue to seek private law remedies against the sponsors of sports activities and those involved in managing players. These claims will be made in professional malpractice lawsuits or in negligence claims against the entity sponsoring the athletic event.

The standard of care is typically determined by the conduct of a reasonable person of ordinary abilities under the same circumstances, but this duty is generally enhanced when the defendant possesses special knowledge, skill, training, or experience that is superior to the ordinary person.[241] Accordingly, coaches, trainers, and other professionals may be held to this higher standard of care. Practicality and costs of using biomarkers will enter into the equation of whether a given duty exists and whether the failure to use them might constitute the breach of duty to provide a safe environment.[242] An important dynamic in addressing these questions is: "What are other teams and leagues doing?" Thus, if one or two college-based or high school teams start baseline biomarker testing of their players, will that set a standard of care that may create liability risks for similar teams or leagues? Will this potential to create new standards of liability act as a deterrent to prevent teams or leagues from adopting new biomarker tests and baseline testing?

The duty and breach issues that could arise in these lawsuits include the failure to create a baseline, the failure to timely screen for a concussion, the misdiagnosis of a concussion, and the misdiagnosis of treatment and cessation of a concussion, including allowing a student athlete to return to play with the continued presence of concussion biomarkers. These claims may arise even if the state statute does not address these issues; but if the legislation does address them, plaintiffs will argue that the statute creates a minimum standard of care. Some of these claims are discussed below in the context of athletic trainers, whose use is on the rise.[243]

Athletic trainers are certified health care professionals who work closely with physicians to "provide preventative services,

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241. DOBBS, *supra* note 210, at 288-90; *see* Cerny v. Cedar Bluffs Junior/Senior Pub. Sch., 628 N.W.2d 697, 706 (Neb. 2001) (finding the standard of care regarding diagnosis of concussive injury owed by members of coaching staff to be that of a reasonably prudent person holding a state teaching certificate with coaching endorsement; dismissing complaint seeking to recover injuries allegedly resulting from negligence of coaches who allowed concussed player to reenter game).

242. *See* United States v. Carroll Towing Co., 159 F.2d 169, 173 (2d Cir. 1947) (discussing the "Learned Hand formula" of duty; balancing the magnitude of the loss if an accident occurs, the probability of the accident's occurring, and the burden of taking precautions that would avoid it).

243. Colin Poitras, *Pressing Need for Full-Time Athletic Trainers in High Schools*, UCONN TODAY (Mar. 27, 2015), http://today.uconn.edu/2015/03/pressing-need-for-full-time-athletic-trainers-in-high-schools (reporting that the use of athletic trainers has doubled in the last two decades and that about 70% of public high schools have athletic trainers).

emergency care, clinical diagnosis, therapeutic intervention and rehabilitation of injuries and medical conditions."[244] Generally, athletic trainers work continuously with players and usually are the first-responding health care providers when injury strikes.[245] As first responders on the playing field, the diagnosis and treatment of concussions are often solely shouldered by athletic trainers. The exact responsibilities given to athletic trainers, however, vary depending on the state, school, and skill levels of the trainers.

Athletic trainers are often given specialized duties with regard to concussive injury management.[246] Trainers initially diagnose concussions, evaluate the player and determine when it is safe to return to play, and oversee the rehabilitation and treatment of the concussion.[247] While trainers are encouraged to send the injured athlete to a physician, they often manage the injury themselves.[248] The largest accrediting organization, the National Athletic Trainer's Association (NATA), provides continuing education, which can include concussive injury management.[249]

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244. *Athletic Training*, NAT'L ATHLETIC TRAINERS' ASS'N, http://www.nata.org/athletic-training (last visited Feb. 13, 2016). Athletic trainers work under various job titles such as occupational health manager, physician extender, or rehabilitation specialist. *Id.* To become an athletic trainer, students must complete a collegiate academic major and then be certified by the national organization, National Athletic Trainer's Association (NATA). *Id.* The Commission on Accreditation of Athletic Training Education accredits the college program. Students who finish their baccalaureate degree then must pass the NATA Board of Certification (BOC) examination to be nationally certified. NAT'L ATHLETIC TRAINERS' ASS'N, ATHLETIC TRAINING EDUCATION OVERVIEW 1, http://www.nata.org/sites/default/files/AT-EducationOverview.pdf (last visited Feb. 13, 2016). Forty-seven states require this certification to practice athletic training. *Id.* at 2.

245. Schools, training facilities, clinics, physicians' offices, and sporting venues employ athletic trainers to help athletes condition and perform. *Athletic Training*, *supra* note 244. At the secondary school level, schools generally hire the trainers as independent contractors. *Id.*

246. Alexandra Svokos, *A Majority of High Schools Lack Full-Time Athletic Trainers to Keep Kids Safe*, HUFFINGTON POST (Nov. 18, 2014, 6:29 AM), http://www.huffingtonpost.com/2014/11/18/high-school-athletic-trainers_n_6146672.html.

247. Broglio et al., *supra* note 225, at 245.

248. *Id.*

249. *See, e.g.*, *Concussion Wise for Athletic Trainers*, CONCUSSIONWISE, http://www.concussionwise.com/concussion-wise-athletic-trainers (last visited Feb. 13, 2016). However, continuing education units are not specified. *See Certification Maintenance Requirements*, BOARD CERTIFICATION FOR ATHLETIC TRAINER, http://www.bocatc.org/ats/maintain-certification/continuing-education (last visited Feb. 13, 2016) (listing available units).

Some states specify the use of athletic trainers as qualified health care professionals under return-to-play legislation,[250] but many schools, especially at the high school level, do not hire them due to lack of funding, small school size, rural location, or a belief that coaches will suffice.[251] Despite the inevitable risks of not having a physician present throughout the stages of a concussive injury, some studies suggest that use of athletic trainers helps student–athletes more than it hurts them.[252] The studies indicate that high schools that employ athletic trainers have lower overall injury rates, and concussions are more likely to be properly diagnosed.[253]

At the same time, the effectiveness of using athletic trainers in concussive management may be undermined by conflict-of-interest pressures. In an informal 2013 survey of athletic trainers working for college football programs, nearly half of the trainers responded that they have felt pressure from the coaches to return the injured player to play before the players were medically approved to do so.[254] This problem is exacerbated by the fact that athletes, who also feel pressure to return to play, may misreport their symptoms to the trainer.[255]

Trainers may be subject to tort liability for failing to adhere to recognized practices for concussive management.[256] Determining the

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250. *See, e.g.*, ARIZ. REV. STAT. ANN. § 15-341(24)(b) (2015).

251. Svokos, *supra* note 246.

252. Press Release, Am. Acad. Pediatrics, High Schools with Athletic Trainers Have More Diagnosed Concussions, Fewer Overall Injuries (Oct. 22, 2012), https://www.aap.org/en-us/about-the-aap/aap-press-room/pages/High-Schools-with-Athletic-Trainers-have-More-Diagnosed-Concussions-Fewer-Overall-Injuries.aspx.

253. *Id.*

254. Brad Wolverton, *Coach Makes the Call: Athletic Trainers Who Butt Heads with Coaches over Concussion Treatment Take Career Hits*, CHRON. HIGHER EDUC. (Sept. 2, 2013), http://chronicle.com/article/Trainers-Butt-Heads-With/141333. Of the 101 trainers surveyed, thirty-two reported that the coaching staff had hiring and firing power over their position, fifty-three reported they felt pressure to return a student to play faster than they feel they should have, and forty-two said they felt pressure to return a student to the field even after he experienced a concussion. Jerry Hinnen, *Survey: 42 Percent of Trainers Pressured to OK Concussed Players*, CBS SPORTS (Sept. 4, 2013, 1:28 PM), http://www.cbssports.com/collegefootball/eye-on-college-football/23476122/survey-42-percent-of-trainers-pressured-to-ok-concussed-players.

255. *Id.*; *see supra* note 213-19 and accompanying text.

256. Barbara Osborne, *Principles of Liability for Athletic Trainers: Managing Sport-Related Concussion*, 36 J. ATHLETIC TRAINING 316, 316, 318-19 (2001). *But see* Morris v. Adm'rs of Tulane Ed. Fund, 891 So.2d 57, 61 (La. Ct. App. 2004) (holding that athletic trainers are not "health care providers" under the state medical malpractice act and thus do not automatically qualify for protection

legal standard of care is difficult, however, if there is no universally accepted standard for concussion diagnosis and treatment by athletic trainers.[257] While courts generally take into account NATA's guidelines, these guidelines are not determinative.[258] Courts have already recognized that athletic trainers owe players a duty of care in concussive management.[259] For example, the plaintiff in *Pinson v. State*[260] suffered a blow to the head during football practice, walked to the sideline, and then collapsed unconscious.[261]

The school's athletic trainer sent him in an ambulance to the hospital[262] but failed to properly inform the physician of Pinson's symptoms and the time he lost consciousness.[263] After his release, Pinson repeatedly complained of headaches and nausea to the trainer, but the trainer nonetheless cleared him to return to play.[264] When he collapsed at another practice, Pinson remained in a coma for several weeks and suffered severe, permanent neurological damage.[265] After Pinson brought suit, the court held that the athletic trainer did not exercise the required standard of care and breached his duty when he failed to report Pinson's headaches to the physician.[266] The court found that the athletic trainer was responsible for 30% of the plaintiff's damages.[267]

As the use of athletic trainers continues to rise, the duty of care imposed on them almost certainly will encompass biomarker testing

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under the statute). Trainers may keep professional liability insurance. *See, e.g.*, *Athletic Trainers*, PROLIABILITY, http://www.proliability.com/professional-liability-insurance/athletic-trainers (last visited Feb. 13, 2016).

257. Osborne, *supra* note 256, at 317.

258. Marie-France Wilson, *Young Athletes at Risk: Preventing and Managing Consequences of Sports Concussions in Young Athletes and the Related Legal Issues*, 21 MARQ. SPORTS L. REV. 241, 281-82 (2010).

259. If a team does not have a medical trainer, the coach will likely be identified as the responsible party and be subject to potential liability. The absence of an athletic trainer could be a source of culpability for the team or league if the judge or jury finds that the standard of care requires a properly trained athletic trainer to be on the sidelines.

260. Pinson v. State, No. 02A01-9409-BC-00210, 1995 WL 739820, at *4 (Tenn. Ct. App. 1995).

261. *Id.* at *1.

262. *Id.* The athletic trainer found palsy on the left side of Pinson's face, noting that he had no control of the left side of his body and no response to pain, sound, or movement. *Id.*

263. *Id.*

264. *Id.* at *1-2.

265. *Id.* at *2.

266. *Id.* at *7.

267. *Id.* at *3.

once it can be practically employed on or near the playing field. Availability of such tests will encourage schools to employ athletic trainers to administer them. NATA may require training and use of the biomarkers in concussive management, but regardless, the tests' availability will raise and perhaps clarify the professional standard of care of athletic trainers.[268] The availability of objective measures may also serve to protect athletic trainers from liability, since they currently rely mostly on subjective measures. Moreover, the use of such tests will make it easier for trainers to consistently adhere to proper procedures, as well as enhance their ability to resist conflict-of-interest pressures. At the same time, increasing the exposure to liability for concussive management may have the unintended consequence of discouraging organized sports in schools.

c. Duty to Screen and Monitor

The availability of biomarkers of effect may expand the concussive management duties of schools or other sponsors of youth sports teams to include periodic testing of their players for biomarker indications of concussive injury. These duties may include testing players before play, during the season, and after the season. Pre-play screening will establish an individual player's baseline, while monitoring will help determine whether the player has suffered concussive injury and whether the concussion is resolved, making it safe to return to play. This duty may arise even if a player does not manifest outward symptoms of brain injury.

Pre-season and periodic screening for mTBI with biomarkers will pose many challenges. The high incidence of concussive injury[269] may engender a greater duty to screen and monitor youth athletes. However, what constitutes this duty may change based on the type of testing available. The cost of a serum assay (to determine the amount of a particular biomarker in blood) is estimated to be

268. Again, the issue of which biomarkers are the current state of the art will complicate decisions on which biomarkers to use and the relevant standard of care.

269. For example, the rate of concussive injury in NCAA football was 3.1/1,000 athletic exposures in the 2004 to 2009 season. NCAA, GUIDELINE 2I: CONCUSSION OR MILD TRAUMATIC BRAIN INJURY (MTBI) IN THE ATHLETE 1 (2010), http://www.muhlenberg.edu/pdf/main/athletics/athletic_training/2010-11ncaaconcussions_mtbi.pdf. An athletic exposure includes both games and practices. Although the statistics between SCD and concussion incident rate are not the same measure, it is readily apparent that concussive injury is much more frequent.

around $20 to $25.[270] Although this cost is not large on an individual basis, it may become a large burden with widespread implementation. Regardless, this cost is much lower than the cost of a CT or MRI scan.[271] Additionally, the cost also depends on when the duty to screen arises—only pre-season, regularly throughout the season, or only after injury. While there is clearly a duty for teams to check their athletes for injury as part of their reasonable duty of care,[272] the extent of this duty is undetermined.[273] What particular advantage or benefit would screening athletes prior to a season and during a season provide?[274] Should all athletes be screened, and how

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270. The cost of a S100B assay was estimated to be from $15 to $25. Shuolun Ruan, Katia Noyes & Jeffrey J. Bazarian, *The Economic Impact of S-100B as a Pre-Head CT Screening Test on Emergency Department Management of Adult Patients with Mild Traumatic Brain Injury*, 26 J. NEUROTRAUMA 1655, 1658 (2009).

271. *See id.* Outside of a biomarker assay, an athletic association could also submit a questionnaire to athletes regarding previous concussive injury and current symptoms and also evaluate them using the Glasgow Coma Score throughout and before the season. These questionnaires and self-reporting methods would be low-cost, but are less objective than a biomarker assay or imaging scan, as they rely on self-reporting symptoms as opposed to an objective measure.

272. *See* Searles v. Trs. of Saint Joseph's Coll., 695 A.2d 1206, 1209 (Me. 1997) (holding that coaches and athletic trainers have a duty to exercise reasonable care for the health and safety of athletes that may include monitoring a knee injury during the season and overturning defendant's motion for summary judgment).

273. For example, would a regular test require only self-reporting symptoms and determination of a Glasgow Coma Score, or would it require assays of serum for biomarkers or comprehensive imaging tests? Settlement negotiations from a recent lawsuit against the NCAA may give insight into how the duty may be analyzed. The proposed settlement requires that

> [f]irst, the NCAA will institute a policy requiring all student-athletes to undergo pre-season baseline testing for each sport they play prior to beginning practice or competition. Second, the NCAA will revise its return-to-play guidelines to provide that "[s]tudents with a diagnosed concussion will be prohibited from returning to play or participation in any practice or game on that same day and must be cleared by a physician before being permitted to return to play in practice or competition." Third, medical personnel, who are trained in the diagnosis, treatment, and management of concussions, will be present at all games of Contact Sports—defined as football, lacrosse, wrestling, ice hockey, field hockey, soccer, and basketball—and be available during all Contact Sports practices.

In re NCAA Student-Athlete Concussion Injury Litig., 2014 U.S. Dist. LEXIS 174334, at *16-17 (N.D. Ill. Dec. 17, 2014) (citations omitted). The proposed settlement also requires reporting of a concussion and providing concussion education to athletes and faculty. *Id.* at *18.

274. Hopefully, injuries would be prevented by tracking down those already symptomatic of concussive injury and preventing them from returning to play.

often should the screening occur? What is the duty to a student who starts late in the season? Questions like these will have to be addressed to determine screening and monitoring duties and consequent liability risks. Furthermore, this duty may also depend on the development of other new devices to detect concussive injury and determine severity on the sidelines, potentially used in conjunction with biomarkers.[275]

2. *Medical Monitoring and Increased Risk Claims*

Although advances in biomarker research will directly affect concussive management duties on the playing field, these advances also implicate other, less obvious, concussive management duties. Biomarkers will give us a deeper understanding of the disease process and trace back earlier into what we think of as the diseased state. In this way, successive concussive injuries implicate a potential latent risk for CTE, since CTE is a progressive condition associated with repetitive brain injury that may take years to develop.

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275. Kara E. Schmid & Frank C. Tortella, *The Diagnosis of Traumatic Brain Injury on the Battlefield*, 3 FRONTIERS NEUROLOGY 1, 2 (2012). A variety of tests are being developed. Currently, one may take ELISAs (enzyme-linked immunosorbent assays) to measure the amount of a biomarker in serum. *Id.* at 3. An ELISA is a laboratory technique in which samples are plated onto a tray, and the concentration of a marker in the sample is calculated. *See An Introduction to ELISA*, ABD SEROTEC, https://www.abdserotec.com/an-introduction-to-elisa.html (last visited Feb. 13, 2016). However, ELISAs can take four to twenty-four hours to complete. Schmid & Tortella, *supra*, at 3. A cartridge for an I-STAT (a handheld blood reader) is in development that may detect concussions using UCH-L1 and GFAP biomarkers (mentioned above), which are present as soon as fifteen minutes after injury. Michele D. Sullivan, *Biomarker Test May Allow Immediate Diagnosis of Concussion*, CLINICAL NEUROLOGY NEWS (Aug. 28, 2014), http://www.clinicalneurologynews.com/index.php?id=9868&tx_ttnews%5Btt_news%5D=294465&cHash=b99dda1fa2164b3a2190d785a83e45f7. Should these devices become available to the public, athletic organizations may have a duty to carry them in sports competitions to quickly and efficiently determine if concussive injury occurred. These devices may be deployed in the military as early as 2016. *Id.* However, due to the high cost of an I-STAT, requiring such a device at all games and practices may be too burdensome. *See I-STAT Portable Clinical Analyzer*, ALLIVET, http://www.allivet.com/p-2452-i-stat-portable-clinical-analyzer.aspx?gclid=CjwKEAjwxMetBRDJx6Sz2p7DsQ0SJADJHAqN1mFPG6aQAjRQlKygks4dCaTlLPo98lSnY2nz2r9PJxoC21Dw_wcB (last visited Feb. 13, 2016). Another portable device that may be able to detect concussions is a portable functional near-infrared spectroscopy device. *Researchers Find Portable, Low-Cost Optical Imaging Tool Useful in Concussion Evaluation*, SCIENCEDAILY (June 26, 2014), http://www.sciencedaily.com/releases/2014/06/140626022036.htm. The device accurately indicated concussive injury and would be low cost. *Id.*

Latent injury claims confront the fundamental tort principle that the plaintiff must demonstrate "harm" (typically a physical harm) before being allowed to recover damages.[276] In addition, the time gap between exposure and disease creates significant practical hurdles in recovery, such as statutes of limitations and proof problems from dated evidence. Despite these jurisprudential and practical problems, courts have recognized in latent injury toxic tort cases a set of compensatory damages during the latency period that may exist between exposure and disease.[277] These latent injury torts reflect the view that certain injuries follow a continuum between an initial event, such as exposure, and a medically diagnosable disease.

Latent injury claims permit a claimant to receive compensation before a serious disease has been manifested. Proponents argue that the claims promote the public health interest in fostering access to medical testing, stressing the value of early diagnosis and treatment for many types of diseases.[278] Similarly, by mitigating serious future illnesses, the claims can reduce the overall costs to the responsible parties as well as to society.[279] Moreover, the claims can enhance deterrence for risk creation.[280] Finally, they reflect basic societal notions of fairness and elemental justice by allowing the individual who has been wrongfully exposed to a likely future injury to receive compensation for the fear of getting the future injury, as well as avoid bearing the expense of medical monitoring.[281] Other supporters suggest that, by allowing recovery for the latent risk itself rather than waiting for the serious disease manifestation, the claims address practical problems such as access to proof.[282]

Critics argue that latent injury claims are brought by individuals who, despite exposure to a hazard, have not yet been significantly injured and, therefore, are not yet entitled to

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276. *See* Jamie A. Grodsky, *Genomics and Toxic Torts: Dismantling the Risk-Injury Divide*, 59 STAN. L. REV. 1671, 1673 (2007).

277. The latent injury claims emerged out of asbestos claims, among others. *See id.* at 1682-83.

278. Gary E. Marchant, *Genetic Susceptibility and Biomarkers in Toxic Injury Litigation*, 41 JURIMETRICS J. 67, 84 (2000) [hereinafter Marchant, *Genetic Susceptibility*].

279. Anita J. Patel, *Medical Monitoring: Missouri's Welcomed Acceptance*, 73 MO. L. REV. 611, 623 (2008).

280. Marchant, *Genetic Susceptibility*, *supra* note 278, at 85.

281. James Pizzirusso, *Increased Risk, Fear of Disease and Medical Monitoring: Are Novel Damage Claims Enough to Overcome Causation Difficulties in Toxic Torts?*, 7 ENVTL. LAW. 183, 202 (2000).

282. Marchant, *Genetic Susceptibility*, *supra* note 278, at 85.

compensation.[283] They contend that this claim should not be recognized too readily for fear of flooding the courts with frivolous claims and disproportionately burdening defendants.[284] A major concern is limited resources, so that if money is allocated now for these damages, sufficient money may not be available later for recovery by those who actually suffer from the disease in question.[285]

Three types of claims generally arise in the latent risk area. Claimants may seek recovery for: (1) the increased risk of a disease; (2) the fear of developing future disease; and (3) medical monitoring costs.[286] All of these claims are based on the premise that the plaintiff has either incurred some injury or has been exposed to a hazard and, as a result, is now at an increased risk of future disease. These claims all require that the increased risk be significant.[287] Aside from these commonalities, these are distinctive claims, however. The first, increased risk, seeks compensation for the fact of the increased risk itself, assigning a value to the increased risk without any certainty that the disease will later manifest; the second, fear of future injury, is an emotional harm claim for the fear and anxiety of getting the more serious disease; and the third, medical monitoring, is seeking payment for the cost of monitoring the at-risk, exposed plaintiff to detect and prevent the onset of disease.[288]

Medical monitoring is the most widely used of these claims, although no consensus exists regarding the elements of the claim.[289]

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283. *Id.*

284. *Id.*

285. *Id.*

286. Marchant, *Genetics and Toxic Torts*, *supra* note 113, at 976.

287. In *Donovan v. Philip Morris USA, Inc.*, the plaintiffs alleged that Marlboro cigarette smoke, with excessively high levels of carcinogen, caused physiological changes and lung tissue damage that led to significantly increased risk of lung cancer in the future. 914 N.E.2d 891, 899 (Mass. 2009). The court recognized subcellular injury as a present physical injury. *Id.* at 901. The court stated that "[w]e must adapt to the growing recognition that exposure to toxic substances and radiation may cause substantial injury which should be compensable even if the full effects are not immediately apparent." *Id.*; *see also* Werlein v. United States, 746 F. Supp. 887, 901 (D. Minn. 1990), *vacated in part on other grounds*, 793 F. Supp. 898 (D. Minn. 1992) (denying the defendant's motion for summary judgment because "[b]ased on the record before it, this Court cannot rule as a matter of law that plaintiffs' alleged injuries are not 'real' simply because they are subcellular").

288. Pizzirusso, *supra* note 281, at 198-204.

289. Generally, plaintiffs are required to prove: (1) exposure greater than normal; (2) to a proven hazardous substance; (3) due to defendant's negligence; (4) plaintiff has a significantly increased risk of contracting a serious latent disease as a proximate result of the exposure; (5) a medical monitoring procedure exists that

An early case that influenced the development of the doctrine involved potential brain injury. In *Friends for All Children, Inc. v. Lockheed Aircraft Corp.*,[290] the court examined a claim brought on behalf of 150 Vietnamese orphans who survived a military transport plane crash.[291] The plaintiffs sought injunctive relief to require the plane's manufacturer to fund a medical surveillance program to determine whether depressurization of the plane's cabin caused the children to suffer brain injury.[292] The court agreed that the manufacturer should compensate the children for the monitoring costs, reasoning that such compensation was no different from an ordinary tort damage award:

> [E]ven in the absence of physical injury [the plaintiff] ought to be able to recover the cost for the various diagnostic examinations proximately caused by [the defendant's] negligent action. . . . The cause of action . . . accords with commonly shared intuitions of normative justice which underlie the common law of tort. . . . [I]n this case, the crash exposed the plaintiffs to the risk of serious brain damage . . . [and] comprehensive diagnostic examinations are needed to determine whether and to what extent treatment may be necessary.[293]

Courts and commentators used the language in the case to suggest that it opened the door to a new claim of medical monitoring.[294] The claim was more firmly established by the New Jersey Supreme Court in *Ayers v. Township of Jackson*.[295] There, the New Jersey Supreme Court upheld a jury's decision to award medical monitoring costs for plaintiffs who were exposed to toxic

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makes early detection of the disease possible; and (6) the monitoring regime is reasonably necessary according to accepted scientific principles. *See* Redland Soccer Club, Inc. v. Dep't of Army, 696 A.2d 137, 145-46 (Pa. 1997). States generally require expert testimony to support the claim with proof that the monitoring is reasonable and necessary. They also allow traditional defenses to the claim, such as assumption of risk and contributory negligence. The relief ordered may vary: Some courts will order court-supervised programs; others will order defendants to pay plaintiffs certain sums of money; and others will require defendants to pay plaintiffs' medical expenses directly. *See generally* Jonathan I. Handler et al., *A Growing Number of States Recognize Medical Monitoring Claims*, 25 BNA INSIGHTS 222 (2010).

290. 746 F.2d 816 (D.C. Cir. 1984).

291. *Id.* at 819.

292. *Id.* at 822.

293. *Id.* at 825.

294. D. Scott Aberson, Note, *A Fifty-State Survey of Medical Monitoring and the Approach the Minnesota Supreme Court Should Take When Confronted with the Issue*, 32 WM. MITCHELL L. REV. 1095, 1099 (2006).

295. 525 A.2d 287, 312 (N.J. 1987).

pollutants from a landfill that had leached into residential drinking water:

> [W]e hold that the cost of medical surveillance is a compensable item of damages where the proofs demonstrate, through reliable expert testimony predicated upon the significance and extent of exposure to chemicals, the toxicity of the chemicals, the seriousness of the diseases for which individuals are at risk, the relative increase in the chance of onset of disease in those exposed, and the value of early diagnosis, that such surveillance to monitor the effect of exposure to toxic chemicals is reasonable and necessary.[296]

A number of courts followed suit, using the *Ayers* court's factors to permit post-exposure, pre-symptom medical monitoring damages.[297] The United States Supreme Court reached a different conclusion in a case arising under a federal statute. In *Metro-North Commuter Railroad Co. v. Buckley*,[298] the Court construed the Federal Employers' Liability Act (FELA) to require a showing of physical symptoms before medical monitoring costs can be awarded.[299] The Court did not want to create "a new, full-blown, tort cause of action" for a variety of policy reasons, in particular to protect the interests of potential future plaintiffs not before the court.[300]

Although *Buckley* is not binding on the states, a number of states have followed the Supreme Court's lead, requiring a showing of physical injury before allowing a medical monitoring claim or a claim for emotional distress for increased risk to go forward.[301] For

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296. *Id.*

297. *See, e.g.*, *In re* Paoli R.R. Yard PCB Litig., 35 F.3d 717, 787 (3d Cir. 1994); Burns v. Jaquays Mining Corp., 752 P.2d 28, 33-34 (Ariz. Ct. App. 1987); Potter v. Firestone Tire & Rubber Co., 863 P.2d 795, 821-25 (Cal. 1993); Redland Soccer Club, Inc. v. Dep't of Army, 696 A.2d 137, 144-45 (Pa. 1997); Hansen v. Mountain Fuel Supply Co., 858 P.2d 970, 979-81 (Utah 1993). In contrast, Nevada has held that medical monitoring claims could proceed even in the absence of physical injury. *See* Sadler v. PacifiCare of Nev., Inc., 340 P.3d 1264, 1264 (Nev. 2014).

298. Metro-N. Commuter R.R. Co. v. Buckley, 521 U.S. 424 (1997).

299. *Id.* at 440 (interpreting FELA, 45 U.S.C. §§ 51-50 (1997)).

300. *Id.* at 443. The Court found that mere exposure to a substance is insufficient, in light of concerns of a "'flood' of less important cases (potentially absorbing resources better left available to those more seriously harmed) and the systemic harms that can accompany 'unlimited and unpredictable liability' (for example, vast testing liability adversely affecting the allocation of scarce medical resources)." *Id.* at 442.

301. *See, e.g.*, Genereux v. Raytheon Co., 754 F.3d 51, 56 (1st Cir. 2014) (denying claim for medical monitoring for beryllium-related diseases because plaintiffs did not demonstrate subcellular change). The court distinguished risk and

states that require a showing of physical injury, some (but not all) states allow plaintiffs to satisfy the requirement by demonstrating asymptomatic subcellular changes to indicate exposure and increased risk of future disease.[302]

Under either view—requiring physical symptoms or not—development of biomarkers of effect, both of concussive injury in general and CTE in particular, may make a medical monitoring claim more viable in the youth sports area. Like the plaintiffs in *Friends for All Children*, claimants can show exposure by physical impact. For those states that require physical symptoms stemming from exposure, the plaintiff may be able to demonstrate through biomarker evidence that these repeated blows resulted in objectively measurable concussive or even (asymptomatic) subconcussive

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harm and found that plaintiffs' expert "disclaimed any ability to state that any one plaintiff . . . had already suffered harm (that is, subcellular or other physiological change)." *Id.*; Paz v. Brush Engineered Materials, Inc., 949 So. 2d 1, 5-6 (Miss. 2007) (rejecting claim "for mere exposure to a harmful substance without proof of current physical or emotional injury from that exposure"); Sinclair v. Merck & Co., 948 A.2d 587, 595-96 (N.J. 2008) (rejecting claim in pharmaceutical products case); Lowe v. Philip Morris USA, Inc., 183 P.3d 181, 187 (Or. 2008) (rejecting claim in absence of current physical injury). A subsequent Supreme Court case, *Norfolk & Western Railway Co. v. Ayers*, suggested that workers suffering from asbestosis, a non-malignant respiratory disease that arises from exposure to asbestos, would be sufficient to satisfy the physical injury requirement for latent injury claims. 538 U.S. 135, 148 (2003).

302. In *Donovan v. Philip Morris USA, Inc.*, the plaintiffs alleged that Marlboro cigarette smoke, with excessively high levels of carcinogen, caused physiological changes and lung tissue damage that led to significantly increased risk of lung cancer in the future. 914 N.E.2d 891, 895 (Mass. 2009). The Court recognized subcellular injury as a present physical injury. *Id.* at 898. The Court explained, "We must adapt to the growing recognition that exposure to toxic substances and radiation may cause substantial injury which should be compensable even if the full effects are not immediately apparent." *Id.* at 901; *see also* Werlein v. United States, 746 F. Supp. 887, 901 (D. Minn. 1990), *vacated in part on other grounds*, 793 F. Supp. 898, 901 (D. Minn. 1992) (denying the defendant's summary judgment because "[b]ased on the record before it, this Court cannot rule as a matter of law that plaintiffs' alleged injuries are not 'real' simply because they are subcellular"). A federal district court, in approving the recent NFL settlement, refused to recognize a claim for subclinical injury compensation. *In re* Nat'l Football Players' Concussion Injury Litig., 307 F.R.D. 351, 409 (E.D. Pa. 2015). Although objectors to the settlement argued that retired football players should receive compensation for CTE before death, the district court denied the claim. *Id.* at 399. The court found that, even assuming a biomarker of abnormal tau protein during life will be available in the next decade, the presence of a marker alone does not indicate that the individual has or will develop symptoms of CTE. *Id.* at 402. ("The Settlement compensates symptoms that cause Retired Players to suffer, not the presence of abnormal tau protein (or any other irregular brain structure) alone.").

injuries. If biomarkers of CTE are developed, then that will strengthen the latent injury claims even more.

From a broader perspective, development of biomarkers will challenge what we mean by a showing of physical symptoms of disease connected to the exposure in latent injury claims.[303] Professor Jamie Grodsky has argued, for example, that courts generally need to rethink the concept of "physical injury" as advances in genetic science make it easier to detect the consequences of toxic exposure before the manifestation of clinical symptoms of disease.[304] The same challenge will be presented here.

Biomarker evidence will also be used to fulfill another element—demonstrating a significant increased risk of disease. Availability of this evidence could be a double-edged sword, however, making a latent injury claim even harder to prove if the biomarkers are not present in an exposed plaintiff. For example, in *Sheridan v. NGK Metals Corp.*,[305] plaintiffs claimed that exposure to beryllium dust and particulates increased their risk of developing chronic beryllium disease (CBD) and asked the court to establish a fund to have beryllium manufacturers and suppliers pay for the costs of medical surveillance.[306] The Third Circuit upheld the lower court's dismissal of the claim, holding that the plaintiffs failed to provide medical tests demonstrating that they had immunological markers showing a predisposition to developing CBD after exposure to beryllium. Comparing the case to a prior case (*Pohl*),[307] the court explained:

> Because the plaintiffs in *Pohl* were not beryllium sensitized and had not otherwise made a plausible showing that they faced a 'significantly increased risk' of developing CBD, the [*Pohl* court] held that these plaintiffs had failed to make a prima facie showing of their medical monitoring claim under [the increased risk test].[308]

The injury threshold for CTE—the severity and number of injuries that is required to trigger brain changes that lead to CTE—is still not known.[309] Not everyone who has been subjected to repetitive concussive injury develops CTE; other risk factors, such as genetic

303. *See* Grodsky, *supra* note 276, at 1712-14; Marchant, *Genetics and Toxic Torts*, *supra* note 113, at 950.

304. Grodsky, *supra* note 276, at 1712-14.

305. 609 F.3d 239 (3d Cir. 2010).

306. *Id.* at 247.

307. Pohl v. NGK Metals Corp., 936 A.2d 43 (Pa. Super. Ct. 2007).

308. *Sheridan*, 609 F.3d at 248.

309. *See* Johnson, Partridge & Gilbert, *supra* note 212, at 16.

background, age, sex, or substance abuse, may come into play as causal factors.[310] Like the court in *Sheridan*, a court may require a showing that the plaintiff has a detectable predisposition to develop a particular disease after exposure. We may reach agreement on general causation—that repeated blows to the head can lead to CTE. It may be still be difficult, however, to show specific causation—the specific, increased risk to the individual—without demonstrating that the individual has biomarkers to indicate individual susceptibility.[311] Existing biomarkers for CTE may or may not address this individual increased risk; the detection of abnormal tau tangles in the living brain may not necessarily indicate the development in the future of CTE. Long-term longitudinal studies may be needed to demonstrate this higher risk among the "exposed" population.

Relatedly, plaintiffs who seek damages for emotional harm will need to demonstrate that they have a genuine fear of developing the future disease, which is objectively reasonable.[312] Although plaintiffs may be able to demonstrate the individual subjective fear through traditional proof, such as sleeplessness and other indications of anxiety, this may not be sufficient to meet the objective element of the claim. The objective criterion requires proof on the likely increased risk for an individual developing CTE.[313] When biomarkers of CTE, in conjunction with epidemiological studies, enhance our knowledge of the increased risk, this may indicate the "reasonableness" of the fear of harm. In contrast, the absence of a biomarker may indicate that the fear is unreasonable and bar recovery for the emotional-harm claim.

The paramount challenge is to determine whether a biomarker is sufficiently predictive to qualify for any type of latent injury claim. In other words, we need to separate valid from speculative claims, dividing those who are "injured" from those who are merely

310. *Id.*

311. *See* DOBBS, *supra* note 210, at 535-36 (explaining general and specific causation).

312. *See* Andrew R. Klein, *Fear of Disease and the Puzzle of Futures Cases in Tort*, 35 U.C. DAVIS L. REV. 965, 974-79 (2012) (discussing cases). *But see* RESTATEMENT (THIRD) OF TORTS: PHYSICAL & EMOTIONAL HARM § 46 cmt (h) (AM. LAW INST. 2012) (distinguishing "cancerphobia" claims from other emotional distress claims).

313. *See* Potter v. Firestone Tire & Rubber Co., 863 P.2d 795, 811 (Cal. 1993) (requiring a showing of significant increased risk of contracting future injury to support an emotional harm claim).

at some "risk."[314] As science can get us closer to a more accurate predictive measure, the recognition of these claims should be commensurate. This approach would comport with the policy reasons behind the claims—to detect disease at an early stage and to allow for medical intervention to reduce or eliminate the impact of the disease, ultimately reducing overall health care costs, as well as to serve social policy.

Of course, the development of biomarkers to detect early signs of CTE does not address the effectiveness of early intervention. At this stage, medicine does not have a way to arrest the development of CTE, other than ceasing additional impacts. The lack of proven treatments challenges—at least partially—the objective behind awarding damages for post-exposure but pre-clinical symptom claims, since the plaintiff may not be able to demonstrate a need for special testing or medical intervention. Presumably, advances in discovering biomarkers will also spark development in subcellular interventions.

Even with these reservations, development of biomarkers of effect should serve to address the jurisprudential and practical concerns of the courts in this area. They should help identify who is likely to develop certain diseases among those exposed to risk.[315] This will serve the values of deterrence as well as the utilitarian concern of adequate resources.

3. *Causal Proof*

In proving the causal element of a tort claim, plaintiff bears the burden of showing that an injury can be caused by defendant's negligence (general causation) as well as showing that the defendant's negligence did cause plaintiff's harm (specific causation).[316] Biomarkers of effect can provide powerful evidence of both elements of causation. The lack of such biomarkers can be used by the defendant to argue against causation.

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314. This was an area of significant dispute in the settlement between players and the NFL. *See In re* Nat'l Football Players' Concussion Injury Litig., 307 F.R.D. 351, 365-66, 396-423 (E.D. Pa. 2015).

315. While this Article does not address class action litigation per se, the advances in biomarker research should help to individualize claims rather than require remedies based on exposures and general averages.

316. DOBBS, *supra* note 210, at 535-36 (2000). Sometimes we do not need to separate out these two questions, since it is obvious that the action can and did cause the injury, such as a broken limb stemming from a car accident.

Proving causation of injury is a major hurdle in bringing a lawsuit to recover for concussive injuries.[317] The first issue is whether the plaintiff has actually incurred a concussion. Using self-reported symptoms to show causation of concussive injury is naturally subject to attack as self-interested testimony.[318] As an objective measure, biomarkers will help to demonstrate whether an actual concussive injury has occurred, leaving less room for challenge.[319]

Next, plaintiffs must prove their symptoms were caused by an activity associated with the defendant. In the simple case of a concussion that immediately results from a single impact, the nexus between exposure and effect will be straightforward. However, proving causation of long-term injuries like CTE presents more difficult challenges. Most concussions do not result in long-term effects.[320] For those concussions that do result in cognitive and other effects, these results may take a long time to manifest, which makes proof of causation and injury even more challenging. Long latency periods open the door to problems of multiple causal factors. Moreover, the passage of time between the initial "exposure" and the manifestation of the full-blown disease may erode the plaintiff's ability to prove the amount and length of exposure to concussive injury. Furthermore, we do not yet know precisely the amount of repetitive concussive injuries required to produce CTE or how long CTE takes to manifest. The latency period for CTE is likely to vary from individual to individual. This indeterminacy adds to causal problems.

Development of biomarkers for CTE may address some of these challenges. It may turn out that CTE is a signature disease—only stemming from repetitive head trauma—with a signature

317. Douglas K.W. Landau, *Proving Damages in Child Concussion Cases*, TRIAL, Sept. 2014, at 40-41.

318. Stockard R. Hickey III, *Defending Questionable Mild Traumatic Brain Injury Claims*, FOR DEF., June 2014, at 14, 17.

319. *See* Rael T. Lange et al., *Diffusion Tensor Imaging Findings and Postconcussion Symptom Reporting Six Weeks Following Mild Traumatic Brain Injury*, 30 ARCHIVES CLINICAL NEUROPSYCHOLOGY 7, 7-8, 22 (2015) (finding that mere involvement in personal injury litigation, among other facts, tends to increase self-reported symptoms).

320. Michael McCrea et al., *Acute Effects and Recovery Time Following Concussion in Collegiate Football Players: The NCAA Concussion Study*, 290 JAMA 2556, 2556, 2560 (2003); *Can Concussions Impact Memory or Intelligence?*, UPMC HEALTH BEAT (Dec. 4, 2014), http://share.upmc.com/ 2014/12/can-concussions-impact-memory-intelligence.

abnormal pattern of the tau protein. Even more significant, the development of biomarkers of CTE may allow plaintiffs to bring suit during their lifetimes, without having to wait for a definitive autopsy. Challenges will continue to exist, however, even with that development. The paramount question is whether the biomarker, which will likely be probabilistic and not determinative, is sufficiently predictive of the full-blown disease to qualify as proof of causation. In other words, testing to determine the presence of a specific protein does not yet tell us how likely it is that an individual will develop cognitive disorders because of exposure to head trauma. This evidence may need to be supplemented by traditional, population-based epidemiological studies that estimate exposure and risk of disease.

Defendants facing civil liability will use the absence of biomarkers to argue the lack of causal proof. This may create an even higher hurdle for plaintiffs in meeting their burden of proof. Further, as more biomarkers are identified, plaintiff's burden on this element of their claim may only be increased.

Defendants may also use biomarkers of effect to argue alternative causation.[321] Plaintiffs claiming that they acquired CTE through the negligent behavior of defendants will need to demonstrate that their symptoms stem from defendants' activities. Defendants will argue that the symptoms stem from other diseases, like Alzheimer's, which the plaintiff may have acquired anyway. Given that 20% of the population may develop Alzheimer's,[322] the absence of a biomarker of effect in that individual patient may buttress the defendants' arguments. Furthermore, a plaintiff may have been serially exposed to head trauma—in youth, college, and professional sports, for example—and therefore, linking the plaintiff's condition to any particular defendant could be problematic.[323] Advances in biomarkers research may not resolve the causal indeterminacy problem presented in this context. This may be

321. *See, e.g.*, Fisher v. United States, 705 F. Supp. 2d 57, 67-68 (D. Mass. 2010) (discussing whether a seizure disorder could have been caused from prior football concussions or from another cause).

322. *About Alzheimer's Disease*, ALZHEIMER'S FOUND. AM., http://www.alzfdn.org/AboutAlzheimers/statistics.html (last visited Feb. 13, 2016).

323. *See* Julie M. Stamm et al., *Age at First Exposure to Football Is Associated with Altered Corpus Callosum White Matter Microstructure in Former Professional Football Players*, 32 J. NEUROTRAUMA 1768, 1768 (finding a greater risk of brain-development alterations for players who played tackle football between the ages of ten and twelve than those who started playing later).

further complicated when a plaintiff's own negligent conduct, such as failure to report symptoms of a concussion, may be a competing potential cause of his harm, as discussed below.

4. *Defenses*

Affirmative defenses such as assumption of risk and contributory fault, which can limit the duty of schools, sports teams, and leagues to participants, will also be affected by the development and implementation of biomarkers.[324] The assumption-of-risk defense focuses on a participant's subjective, individual awareness of the risk and the voluntary nature of consent to encounter that known risk.[325]

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324. The classic defense of assumption of risk or informed consent in this context raises a host of questions about the validity of and power to consent, as well as absolving the sponsoring entity from liability. The underlying premise of the doctrine is that individuals have fully consented to incur a risk which they thoroughly comprehend. DOBBS, *supra* note 210, at 535-37. If the consent is valid, it will ordinarily relieve the defendant of the duty that may have otherwise existed. *Id.* at 541-43. This means that the consent may overcome duties like the duty to screen, inform, accommodate, or exclude. For example, although the NCAA requires testing for SCT, the athlete can waive the right to receive the results of the testing. *Sickle Cell Trait*, NCAA, http://www.ncaa.org/health-and-safety/medical-conditions/sickle-cell-trait (last visited Feb. 13, 2016). But there are public policy limits on consent. *See* DOBBS, *supra* note 210, at 542 ("Possibly . . . schools should not be allowed to condition a student's participation rights on a general release of all liability for negligence."). At the other extreme, courts generally view participation in interscholastic sports as a privilege rather than a legally protected right, so that a school can refuse to allow an athlete to play, even if the athlete or parent proffers a waiver. *See, e.g.*, Farver v. Bd. of Educ., 40 F. Supp. 2d 323, 324 (D. Md. 1999) (noting the Due Process Clause does not protect a student's interest in extracurricular activity participation, including sports); Peterson v. Indep. Sch. Dist., No. 811, 999 F. Supp. 665, 674 (D. Minn. 1998) (finding there is no protected interest in student's extracurricular activities); Mancuso v. Mass. Interscholastic Athletic Ass'n, Inc., 900 N.E. 518, 527-28 (Mass. 2009) (finding no constitutionally protected right to participate in extracurricular athletics). Full comprehension of risks and voluntariness of consent raises a host of questions. For example, how well-known are the risks and the extent of the risks? Would the athlete need to know the nature and extent of the eventual harm, such as CTE, or is it sufficient that the player be willing to undergo risks of some brain injury, like a mild, temporary concussion? As knowledge of the science of concussions changes, how will the duty to warn affect informed consent? What if the student athlete wants to sign the waiver, but the parents do not, or the parents are divorced and disagree about consent? These questions will increase with the development of biomarkers and the expanded understanding of concussions as a spectrum of injury.

325. *See* RESTATEMENT (SECOND) OF TORTS § 496(C) (AM. LAW INST. 1965).

Defendants have traditionally been successful in asserting assumption of risk defenses in sports, including football.[326]

Availability of biomarkers may affect the assertion of an assumption-of-risk defense. This is because these scientific developments will affect the knowledge of the parties involved with regard to the prevention, diagnosis, and treatment of concussive injury.[327] Use of biomarkers will change the diagnostic process and remove much of the ambiguity surrounding "medical clearance" to play.[328] A player's subjective knowledge of injury may become more readily provable with the development and availability of biomarkers. A player who goes on the field despite that knowledge may be deemed to have subjectively and deliberately assumed the concussion risk. Similarly, use of biomarkers may help clarify the validity of the player's consent, since neither the player nor the evaluator will need to rely solely on the player's processing of his own symptoms.[329] With more precise information will come a more informed consent to play.

At the same time, a significant question is whether the decision to participate can be truly autonomous, especially when the injuries themselves might impair the ability to consent in the future.[330] Neurocognitive impairment may be delayed. This raises questions, in turn, about the extent to which participants understand the risks of acquired brain injury and the extent to which they can voluntarily

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326. *See, e.g.*, Heather MacGillivray, *Where Is the Awareness in Concussion Awareness: Can Concussed Players Really Assume the Risk in a Concussed State?*, 21 JEFFREY S. MOORAD SPORTS L.J. 529, 529 (2014) (stating the risk of concussion in football is generally known); Cailyn M. Reilly, *Where Is Concussion Litigation Headed? The Impact of* Riddell, Inc. v. Schutt Sports, Inc.*, on Brain Injury Law*, 20 JEFFREY S. MOORAD SPORTS L.J. 517, 517 (2013) (noting that concussions are "the reality of contact sports").

327. *See* MacGillivray, *supra* note 326, at 551 (noting that the "devastating long-term effects of concussions have become glaringly clear due to an explosion of scientific research and public attention" to lawsuits against sports leagues).

328. *See cf.* Joseph M. Hanna & Daniel Kain, *NFL's Shaky Concussion Policy Exposes the League to Potential Liability Headaches*, 21 N.Y. ST. B. ASS'N ENT. ARTS SPORTS L.J., Fall/Winter 2010, at 33, 36 (2010) (explaining that the NFL could argue that plaintiffs were contributorily negligent "by (1) failing to report their concussive conditions to team doctors, and (2) returning to play before their concussion symptoms completely disappeared").

329. *See* Alex Taylor, *Neuropsychological Evaluation and Management of Sport-Related Concussion*, 24 NEUROLOGY 717, 717 (2012) (citing evidence that suggests that "up to 90% of sports-related concussions may go undetected or unreported").

330. *See generally* MacGillivray, *supra* note 326 (arguing that an athlete in a concussed state cannot validly assume the risk of continued play).

assume those risks. This issue is also plagued by questions of coercion and competing interests.[331] Even if a player can knowingly and voluntarily assume the risk of a concussion, this does not speak to the awareness and knowledge of the heightened risk of a second concussive injury or the long-term effects of repetitive concussions and cognitive decline. Nor does it speak to the risk of subconcussive impacts that may have similar effects but do not present with observable concussive symptoms.[332] In that case, the player is not aware of the risks presented, particularly of playing in a concussed state. These problems throw the player's capacity to consent into question.

Furthermore, given the quickly changing developments of science in this area, it is unclear whether parents and students can ever validly consent to exposure to such an uncertain and changing risk. Would consent that is knowingly and voluntarily given still be binding when new risks come to light?

Similarly, if individuals are found to be susceptible to concussion, whether by biomarkers or because of previous injury, then this finding will pose the question whether the individuals (or their parents) can lawfully assume the risk of injury. This may depend on the degree of susceptibility the test indicates. Certain levels of susceptibility may always require exclusion from assumption of risk and participation. These questions are explored below.

B. Legal Implications of Biomarkers of Susceptibility

Development of biomarkers of susceptibility will help distinguish individuals more susceptible to concussive injury than the general population. Biomarkers of susceptibility are subject to the same constraints as biomarkers of effect: They are likely to be probabilistic rather than determinative, so there are unlikely to be bright-line demarcations between affected and non-affected, and susceptible and non-susceptible, individuals. A further complication is that susceptibility may be affected by various circumstances such

331. *See* Benitez v. N.Y. City Bd. of Educ., 541 N.E.2d 29, 33 (N.Y. 1989) ("Though the risk is foreseen, an assurance of safety generally implicit in the supervisor's direction supplants the plaintiff's assumption of the risk by requiring action despite prudent cautionary concerns.").

332. *See* McAllister et al., *supra* note 78, at 66.

as the number and type of concussive injuries suffered, gender, age, or even ethnic background, or a combination of these factors.[333]

Notwithstanding these variables, recent findings suggest that biomarkers of susceptibility are likely to be identified in the near future, as discussed above. In particular, the presence of the genetic variant APO ϵ4 may be an important biomarker for susceptibility to concussions.[334] In addition, concussion susceptibility is present in those who have previously suffered brain injuries.[335] With the growing capability to determine concussion susceptibility based on biomarkers, we can anticipate a commensurate impact on the legal landscape.

1. *Duty to Screen for, Warn, and Potentially Exclude from Activities Individuals with Increased Concussion Risk*

Whether a duty to screen players for susceptibility to concussive injury exists involves implementation of the classic cost–benefit analysis in tort law: The likelihood of injury must be high enough and the risk severe enough that that the "costs" of the potential injury outweigh the cost of screening.[336]

While it is not yet established whether the ϵ4 allele actually increases susceptibility to TBI and CTE,[337] this Article assumes that it does to demonstrate the complexity of this analysis. The frequency of the ϵ4 allele is approximately 14% in the general population.[338]

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333. *See* Frederica P. Perera, *Environment and Cancer: Who Are Susceptible?*, 278 SCIENCE 1068, 1070-71 (1997) (discussing age, gender, and ethnicity as influencing susceptibility of cancer).

334. *See supra* Subsection I.C.3.

335. *See supra* note 80 and accompanying text.

336. *See* United States v. Carroll Towing Co., 159 F.2d 169, 173 (2d Cir. 1947) (discussing the "Learned Hand formula" of duty; balancing the magnitude of the loss if an accident occurs, the probability of the accident's occurring, and the burden of taking precautions that would avoid it).

337. *See supra* Subsection I.C.3.

338. *Alzgene - Meta-Analysis of All Published Ad Association Studies (Case-Control Only) APOE_E2/3/4*, ALZFORUM, http://www.alzgene.org/meta.asp?geneID=83 (last updated Jan. 29, 2010); Nader Ghebranious et al., *Detection of ApoE E2, E3 and E4 Alleles Using MALDI-TOF Mass Spectrometry and the Homogeneous Mass-Extend Technology*, 33 NUCLEIC ACIDS RES. e149, e149 (2005) [hereinafter *Alzgene Meta Analysis*]. The allele frequency is the percentage of a particular allele among all chromosomes. *Allele Frequency*, SCIENCEDAILY, http://www.sciencedaily.com/terms/allele_frequency.htm (last visited Feb. 13, 2016). In this case, 14% of chromosomes in the general population contain the APO ϵ4 allele, as opposed to carrying the ϵ2 or ϵ3. *Alzgene Meta Analysis*, *supra*, at e149.

The homozygous ϵ4 genotype is found in approximately 2% of the population.[339] These data show that the ϵ4 allele is relatively rare and the ϵ4 genotype is only found among a small percentage of the population, suggesting a lower percentage of the population is at risk. Severity of injury must be taken into account as well, however, which could be substantial in the concussive injury area.

An analogous precedent of this analysis is the obligation of the NCAA football teams, pursuant to a settlement agreement in litigation brought by the family of a deceased college football player, to genetically screen their players for sickle cell trait (SCT).[340] Carriers of SCT may be at an increased risk for serious harm from strenuous activity.[341] SCT affects approximately 1.3% of the population and 8.3% of African Americans in the United States.[342] As 34% of college football players are African Americans, it could then be estimated that approximately 3% of college football players have SCT.[343] While this is a small percentage of the overall population and also football players, the risk is significant enough that the NCAA has adopted program-wide screening for SCT for all contact sports.[344] Researchers have estimated that one death would be prevented within four years of implementing the program and that seven would be saved in ten years,[345] with the cost of implementation estimated to be between $1,441,810 and $2,883,620 (based on estimating the cost of testing for SCT to be between $10 and $20) over the course of

339. *Alzgene Meta Analysis*, *supra* note 338, at e149. As previously noted in the Article, the ϵ4 genotype has been found to correlate to an even higher risk of TBI and CTE than a single copy of the ϵ4 allele. *See supra* notes 193-207 and accompanying text.

340. *See* Deborah Levenson, *College Athletes Should Get Sickle Cell Trait Tests, NCAA Advises*, 152A AM. J. MED. GENETICS C1, fm ix (2010).

341. *See* Beth A. Tarini, Margaret Alison Brooks & David G. Bundy, *A Policy Impact Analysis of the Mandatory NCAA Sickle Cell Trait Screening Program*, 47 HEALTH SERVS. RES. 446, 454-55 (2012) (explaining that "[t]he relationship between exercise-related death and SCT has long been debated," although case reports "suggest a compelling pattern").

342. *See* Jonathan C. Goldsmith et al., *Framing the Research Agenda for Sickle Cell Trait: Building on the Current Understanding of Clinical Events and Their Potential Implications*, 87 AM. J. HEMATOLOGY 340, 340 (2012).

343. *Id.* at 341.

344. The agreement to screen was part of a settlement agreement and not actually found as a duty to screen as a matter of law. *See In re* NCAA Student-Athlete Concussion Injury Litig., No. 13 C9116, 2014 U.S. Dist. LEXIS 174334, at *13-14 (N.D. Ill. Dec. 17, 2014); *In re* Nat'l Hockey League Players' Concussion Injury Litig., No. 14-2551 (SRN), 2015 BL 82307, at *8 (D. Minn. Mar. 25, 2015).

345. Tarini, Brooks & Bundy, *supra* note 341, at 453.

four years.[346] This is in comparison to the cost of determining one's APOE genotype, which is available commercially as an Alzheimer's susceptibility test for $150 per test.[347] While this cost could be lowered by large-scale purchasing, it may still be significantly higher than the cost of SCT screening.

The duty to screen may vary depending on the sport involved, since concussion injury is more common in certain high-risk sports than others.[348] Furthermore, screening may require more than testing for the presence of biomarkers of susceptibility, since susceptibility to concussive injury also increases with further head injuries.[349] Screening for both medical history and biomarkers could more effectively narrow the list of players where action may be taken.[350]

Even assuming the development of biomarkers of susceptibility to concussive injury will engender a duty on school and sports organizations to screen athletes for susceptibility, questions remain about when to screen and what to do with this information. At one extreme, conducting screening may implicate a duty to exclude from play those individuals with susceptibility biomarkers. Short of exclusion, the activity sponsors may have a duty to warn those individuals of increased risk, monitor them more closely throughout the season, provide accommodations, and implement additional preventative measures to avoid concussion.[351] These measures also

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346. *Id.* at 451, 453.

347. Press Release, SpectraCell Laboratories, SpectraCell Laboratories Offers Apolipoprotein E Genetic Testing (Apr. 21, 2010), http://www.prnewswire.com/news-releases/spectracell-laboratories-offers-apolipoprotein-e-genetic-testing-91763674.html.

348. *See* James M. Nobel & Dale C. Hesdorffer, *Sports-Related Concussions: A Review of Epidemiology Challenges in Diagnosis, and Potential Risk Factors*, 23 NEUROPSYCHOLOGY REV. 273, 276-77 (2013) (noting higher concussive risk in football, soccer, and hockey). However, the NCAA decided to screen all college athletes for SCT regardless of the differential risk between sports. NCAA, NCAA SICKLE CELL TRAIN (SCT) TESTING—WHAT YOU NEED TO KNOW 1 (n.d.), http://www.ncaa.org/sites/default/files/SCT%20testing%20brief%202014.pdf.

349. *See* Tracey Covassin, Ryan Moran & Kristyn Wilhelm, *Concussion Symptoms and Neurocognitive Performance of High School and College Athletes Who Incur Multiple Concussions*, 41 AM. J. SPORTS MED. 2885, 2885-86 (2013).

350. Relatedly, development of biomarkers of susceptibility may engender a duty on employers to screen in the workplace. Workplaces with high incidences of concussive injury include transportation, material moving, farming, fishing, forestry, and installation and repair occupations. *See* Svetla Slavova & Terry L. Bunn, *Work-Related Concussive Surveillance*, 58 AM. J. INDUS. MED. 40, 41 (2015).

351. The SCT provides a relevant precedent here too. The University of California at Berkeley football team offered SCT screening to its players, and player Ted Agu tested positive for the sickle cell trait. Nanette Asimov, *Cal Football*

depend on whether effective intervention measures are available and cost-effective.

Another approach to susceptibility, and one commonly followed, is universal warnings and intervention, rather than universal screening and exclusion or accommodation. In other words, whatever warnings and accommodations are administered to reduce the likelihood of concussion during play (such as changing rules of play or requiring certain equipment) could be applied across the board to all players.[352] In general, information on individual susceptibility will allow policy makers, as well as schools and other sports sponsors, to make concussive risk management decisions based on the probability of injury.

2. *Balancing the Duty to Screen and Warn Against Privacy Interests*

Screening for biomarkers of susceptibility will raise confidentiality and privacy concerns regarding a patient's health information similar to those raised with the development of new technologies[353] and medical tests, such as functional magnetic resonance imaging (fMRI) or genetic testing.[354] The entity performing or ordering the screening for susceptibility will likely be held to a duty to warn the susceptible individual of an increased risk, and this may include disclosure to third parties, such as the

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Player Ted Agu's Family Files Suit against UC, SFGATE (Aug. 6, 2014), http://www.sfgate.com/collegesports/article/Family-sues-UC-over-Cal-football-player-s-death-5670060.php. During an intense practice session, Agu died from his sickle cell condition, and his family has sued the team for its failure to take appropriate action to protect the susceptible player. *Id.*

352. *See* Tarini, Brooks & Bundy, *supra* note 341, at 457-58 (concluding that universal SCT screening will identify a substantial number of sickle cell carriers). It is unclear whether screening is a necessary step to prevent exercise-related sudden death in student–athletes, and successful intervention measures are needed as well. *Id.*

353. The development of electronic recordkeeping and the Internet urged the federal government to adopt privacy regulations for health care providers in the Health Insurance Portability and Accountability Act (HIPAA). Health Insurance Portability and Accountability Act of 1996, Pub. L. No. 104-191, § 264, 110 Stat. 1936, 2033; BARRY R. FURROW ET AL., HEALTH LAW: CASES, MATERIALS, AND PROBLEMS 104 (7th ed. 2013).

354. *See* Stacey A. Tovino, *Functional Neuroimaging Information: A Case for Neuro Exceptionalism?*, 34 FLA. ST. U. L. REV. 415, 416 (2007).

individual's parents, coach, or employer.[355] Releasing that information to others may conflict with the privacy interests of the susceptible individual in his medical information.[356] At the same time, the results may have important implications for family members and others, and the issue arises whether those individuals have a right to that information as well.

One important question is whether this information requires special or heightened privacy protections.[357] This argument has been made regarding neuroimaging data and genetic testing in general.[358] Like genetic testing, biomarkers of susceptibility will be newer and more complex than other medical tests and therefore will require careful consideration of privacy concerns associated with it. A significant issue is whether this information is likely to carry a stigma, so that other policy reasons may dictate that it is important to control access to this health information.[359]

A number of third parties, like parents, employers, coaches, and insurers, will likely have a countervailing interest in obtaining the results of susceptibility testing. Generally, the Department of Health and Human Services (HHS) regulates information privacy through its Privacy Rule,[360] but this only applies to "covered

355. *See* Stanley v. McCarver, 92 P.3d 849, 856 (Ariz. 2004) (holding that a doctor performing a screening test owed a duty of care to the patient even in the absence of a doctor–patient relationship because he was in a unique position to prevent future harm).

356. *See* Michael K. McChrystal, *No Hiding the Ball: Medical Privacy and Pro Sports*, 25 MARQ. SPORTS L. REV. 163, 164 (2014).

357. For example, HIV and AIDS test results have been treated with "exceptionalism" with regard to confidentiality and privacy. *See, e.g.*, 35 PA. STAT. AND CONS. STAT. ANN. § 7607(a) (West 2015) (making it unlawful for persons in control of HIV-related information to disclose or be compelled to disclose such information except in limited circumstances); Joyce J. Shin, Comment, *Closing the Gap: Protecting Predictive Neuroscience Information from Health Insurance Discrimination*, 64 EMORY L.J. 1433, 1435-36 (2015). Other health-related records receive special protection as well. *See, e.g.*, 42 U.S.C. § 290dd-2(a) (2012) (specifying that records maintained in relation to substance abuse research, rehabilitation, or programs should remain confidential); 50 PA. STAT. AND CONS. STAT. ANN. § 7111 (discussing privacy of mental health records).

358. Tovino, *supra* note 354, at 416.

359. In reaction to the stigma attached to seeking help for substance abuse issues, for example, Congress enacted confidentiality regulations relating specifically to substance abuse patient records. 42 U.S.C. § 290dd-2(a); Emily Shrift, *Subpoenas of Substance Abuse Patients Records*, 39 MD. B.J. 49, 49 (2006).

360. 45 C.F.R. § 164.500 (West 2015).

entities," such as physicians, hospitals, and health insurers.[361] This leaves employers, leagues, courts, educational institutions, and others without many regulations and with strong potential interests in obtaining private medical information.[362] The Genetic Information Nondiscrimination Act (GINA) prohibits employers and health insurers from accessing or utilizing genetic information,[363] but it does not apply to other entities, such as life and disability insurers and schools, and does not apply to non-genetic information, such as brain scans.[364]

The use of concussion biomarkers in litigation could present some significant privacy concerns. In some cases, plaintiffs may seek to use their own biomarker data to make their case, but in other cases, the defendant may seek to discover sensitive biomarker data from the plaintiff. If the plaintiff objects, a judge must decide whether the defendant can gain access to the biomarker data under Rule 35.[365] Because the plaintiff has put his or her health at issue, and given that plaintiffs may use the biomarker data themselves if the results favored their arguments, the court will likely allow the defendants to discover the plaintiffs' biomarker data if there has been a basic showing of likely relevance.[366]

This compelled disclosure of biomarker status could have adverse consequences for the plaintiff. For example, APOE status not only discloses concussion risk, but also indicates risk of

361. 45 C.F.R. §§ 162.1101-1802, 164.104(a) (West 2015); *see also* Tovino, *supra* note 354, at 448.

362. Tovino, *supra* note 354, at 449. The Privacy Rule also contains many exceptions allowing health care providers to use or disclose health information for law enforcement purposes, adjudicative proceedings, disease prevention and control, and even to prevent serious threats to the health and safety of the public or an individual person. 45 C.F.R. § 164.512 (West 2015).

363. Genetic Information Nondiscrimination Act of 2008, Pub. L. No. 110-233, 122 Stat. 881, 884, 907 (2008); *see also* Daniel Schlein, *New Frontiers for Genetic Privacy Law: The Genetic Information Nondiscrimination Act of 2008*, 19 GEO. MASON U. CIV. RTS. L.J. 311, 313 (2009).

364. Some states have adopted their own privacy laws that go beyond the federal protections. *See generally* Tovino, *supra* note 354, at 457. For example, Arizona and California prohibit life and disability insurers from requesting genetic information from their clients. ARIZ. REV. STAT. § 20-448.02 (2015); CAL. INS. CODE § 10143(a) (West 2015).

365. FED. R. CIV. P. 35 (authorizing courts to order physical and mental examination of party where that condition is in controversy).

366. *See* Favale v. Roman Catholic Diocese of Bridgeport, 235 F.R.D. 553, 555, 558 (D. Conn. 2006) (compelling examination when condition of party is in controversy and there is good cause for ordering an examination).

developing Alzheimer's disease, something plaintiffs may not want to know about themselves and almost certainly would not want others to know.[367] A college-level player hoping to be drafted may not want professional teams to learn that he has a susceptibility to concussions, as it may diminish his chances of being drafted.[368] These privacy and disclosure issues are likely to create delicate situations for litigants, attorneys and judges.

3. *Comparative Fault Implications*

Susceptibility information will raise unique comparative fault questions. Typically, once liability is determined, damages in a tort lawsuit are based on restoring plaintiffs back to their prior position before the defendant breached his or her duty of due care to them.[369] This rule applies to harms that are foreseeable,[370] but in applying the foreseeability test, courts distinguish between the nature of a harm and its extent.[371] Under the eggshell skull common law rule, courts hold that negligent actors take plaintiffs as they find them, even if the extent of injury is not foreseeable.[372] Under that rule, the award of damages does not take into account whether the plaintiff is more susceptible to injury, even if the defendant had no reason to know of the plaintiff's susceptibility.[373]

Even under this doctrine, however, the question remains whether a susceptible individual has the same right to recovery as a non-susceptible individual, or whether the injured party's compensation should be reduced based on comparative fault or assumption of risk.[374] In any event, measuring harm from concussive

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367. Baugh et al., *supra* note 91, at 249.

368. A professional sports team likely has an employer–employee relationship with its players, and so it could not require genetic testing of players under GINA. However, such information could be publicly released if disclosed during a court case or through testing by a college team, which likely is not considered an employer under GINA. While a protective order may be available to help protect the information disclosed in judicial proceedings, there will remain some risk of disclosure.

369. *See generally* DOBBS, *supra* note 210, at 1047-53.

370. *Id.* at 464-66.

371. *Id.* at 464.

372. *Id.* at 464-65.

373. *Id.*

374. *See, e.g.*, Marchant, *Genetic Susceptibility*, *supra* note 278, at 79, 88 (discussing the "thin skull" doctrine and susceptibility versus non-susceptibility in the context of toxic injury litigation as well as the possibility of an assumption of risk defense).

injury is difficult when the long-term consequences of concussion remain uncertain and yet can be so severe.

Alternatively, a defendant may potentially assert the idiosyncratic response defense when an individual's susceptibility to concussion is rare and unpredictable.[375] The defense would be that the defendant cannot be held liable for an injury resulting from the plaintiff's unusual susceptibility that a substantial portion of the population does not share.[376] This defense has been applied in products liability actions.[377] Defendants in toxic tort litigation have

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375. *See* Marchant, *Genetics and Toxic Torts*, *supra* note 113, at 960-61 (describing defense in products liability cases).

376. There are two early cases recognizing the defense. Griggs v. Comb, Inc., 456 So. 2d 790, 790-93 (Ala. 1984) (noting that the manufacturer "could not have known 'by the application of reasonable, developed human skill and foresight'" that its product could cause the type of injury suffered by the plaintiff; the product was not defective when the plaintiff suffered an allergic reaction to benzocaine, the active ingredient in a topical analgesic); Bennett v. Pilot Prods. Co., 235 P.2d 525, 527 (Utah 1951) (dismissing plaintiff's action against beautician for applying a hair cold wave solution containing ammonium thioglycolate, which caused blistering and inflammation, reasoning that the court "cannot require the merchant to assume the role of absolute insurer against physiological idiosyncrasy").

377. *See* Mather v. L'Oreal USA, Inc. 695 S.E.2d 693, 693-95 (Ga. Ct. App. 2010) (addressing a self-tanning lotion that caused pus-filled abscesses; noting that L'Oreal did not know that the product could cause such a reaction since its active ingredient, hydroxyacentone, was commonly used and accepted in dermatology as safe, and the manufacturer did not receive similar complaints during testing; summary judgment for manufacturer affirmed); *see generally* DAVID G. OWEN, PRODUCTS LIABILITY LAW § 9.4 (2015); THOMSON REUTERS, AMERICAN LAW OF PRODUCTS LIABILITY § 32:52 (3d ed. 2015).

The idiosyncratic plaintiff defense originates in the Restatement (Second) of Torts, which states that a manufacturer has duty to warn of an allergic reaction to an ingredient where a "substantial number of the population are allergic" to the ingredient, and "the ingredient is one whose danger is not generally known, or if known is one which the consumer would reasonably not expect to find in the product." *See* RESTATEMENT (SECOND) OF TORTS § 402A cmt. j (AM. L. INST. 1977). The Restatement (Third) of Torts maintains the defense. It recognizes that "virtually any tangible product can contain an ingredient to which some persons may be allergic," and thus,

> The general rule in cases involving allergic reactions is that a warning is required when the harm-causing ingredient is one to which a substantial number of persons are allergic. The degree of substantiality is not precisely quantifiable. Clearly the plaintiff in most cases must show that the allergic predisposition is not unique to the plaintiff. In determining whether the plaintiff has carried the burden in this regard, however, the court may properly consider the severity of the plaintiff's harm. The more severe the harm, the more justified is a conclusion that the number of persons at risk need not be large to be considered "substantial" so as to require a warning.

argued successfully that they are not liable for harm from products that affect only genetically hyper-susceptible individuals.[378] The difficulty in applying this defense is determining what responses are considered idiosyncratic and the applicable percentage cutoff.[379]

CONCLUSION

This is a transformative moment in society with regard to concussive injury. We are confronted with a public health crisis: Substantial risks of concussive injury already inhere in a variety of settings, ranging from sports injury, transportation accidents, military combat service, workplace injuries, falls, and domestic relations. The lack of objective tests for diagnosis, prognosis, and tracking of concussions, as well as the inability to measure individual susceptibility and response to concussions, is impeding effective policies for preventing and allocating responsibility for this concussion crisis. Yet the explosion of research to meet this public health crisis is leading to the identification of biomarkers that tell us who is more likely than not to be susceptible to harm and the extent of harm they may have already suffered. These developments have dramatic implications for the distribution of loss in terms of fault allocation, duty, and causation.

Arriving at this inflection point demands that we reexamine how we apply basic tort doctrine to concussive injury cases and

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RESTATEMENT (THIRD) OF TORTS § 2 cmt. k (AM. L. INST. 2012).

378. *See* Marchant, *Genetics and Toxic Torts*, *supra* note 113, at 961 (The "defense represents a policy judgment that a non-negligent manufacturer should not be held liable for producing a product that is beneficial and harmless to most persons, even if it may injure a small number of unusually susceptible individuals."). *See generally* Marchant, *Genetic Susceptibility*, *supra* note 278, at 80-84.

379. Although it is beyond the scope of this Article, availability of this defense will have implications for products manufacturers of equipment in sports, such as helmet manufacturers. Manufacturers are held to a duty of producing a non-defective product, which includes a duty to adequately test their products, as well as to warn of the limitations of the safety of the product. *See generally* RESTATEMENT (THIRD) OF PRODUCTS LIABILITY § 2 (1998) (describing three types of product defects). Manufacturers may also have a duty to test their products on individuals with different genetic susceptibilities. Manufacturers may be charged with providing a warning to an identifiable subgroup of susceptible individuals, especially if the individuals constitute a significant proportion of the product users. *See* Marchant, *Genetic Susceptibility*, *supra* note 278, at 79, 88 (discussing the "thin skull" doctrine and susceptibility versus non-susceptibility in the context of toxic injury litigation as well as the possibility of an assumption of risk defense). This would assume that the susceptible individuals have access to information that would identify their susceptibility.

make broad social policy decisions as well. Recall the examples in the Introduction. We need to reexamine whether athletes like Curtis Parker should reasonably expect his coach to be able to determine accurately whether he suffers from concussive injury. We also need to reconsider the implications of long-term damage. Should an athlete like Chris Benoit be entitled to a latent injury claim, such as medical monitoring, to address his increased risk of CTE? Could either Curtis Parker or Chris Benoit have made an informed choice to confront the risks of concussive injury in sport? And do players like Chris Borland have an obligation to be tested for susceptibility to concussive injury? In general, we need to confront whether the availability of biomarkers of effect and susceptibility should limit the players' recovery in tort, or whether the primary responsibility for this population should be placed on the gatekeepers of the athletic field, such as athletic trainers, coaches, and schools.

The biggest challenge in this area has always been one of imperfect scientific information, but we are on the cusp of making the unobservable observable.[380] Scientific advances likely will bring further recognition of diseased states of concussive brain injury, which will dramatically alter what we mean by injury, risk, as well as causation in tort suits involving concussive injury. These elements may lose their sharp definitions as we are able to trace back earlier into what we think of as a diseased state. Proof of biomarkers of effect should shed light on causal issues in tort lawsuits, as well as duties, and may help to substantiate latent injury claims through the ability to examine long-term effects and injuries. Development of these biomarkers will shift legal responsibilities in the diagnosis and management of youth sports-related mTBIs to those most directly involved in the player's participation, including trainers, schools, parents, and the players themselves.

Biomarkers of susceptibility will identify a vulnerable population. This development will modify responsibilities in the duty to mitigate risks, the duty to monitor players in the short term as well as the long term, the duty to exclude or provide accommodations, the duty to inform, as well as the ability of players to consent to risks of head trauma. Practical concerns will also influence these responsibilities through application of the classic cost–benefit

380. *See cf.* Daniel A. Farber, *Toxic Causation*, 71 MINN. L. REV. 1219, 1247 (1987) ("The only real difference between the automobile case and the toxics case is that better information is available about the events in the automobile case whereas the relevant biological events in the toxics case are unobservable.").

analysis that permeates tort law and public policy decisions. As the availability of biomarkers increase and their costs decrease, their use will become standard in concussive injury management. At the same time, increasing reliance on biomarkers will raise concerns relating to privacy and confidentiality.

Ultimately, development of biomarkers should lead to a more accurate and just result in litigation surrounding concussive injury. At the same time, courts will be challenged to deal with the data presented in appropriate ways, since the data will be presented in ranges, and will likely not be determinative but rather probabilistic. Furthermore, these data may be complicated by other factors, such as gender, ethnicity, and age. Moreover, because use of this data may be unduly persuasive, courts will need to evaluate the information presented carefully in their role as gatekeepers of admissibility of scientific evidence. Finally, concussion biomarkers are likely to raise difficult privacy issues, which courts will need to address on a case-by-case approach given the lack of applicability of most federal medical privacy laws to the litigation context.

Identification of biomarkers will also have an impact on the normative questions generated by activities that involve the risk of repetitive head trauma. Safety is a relative term. As we increase our understanding of the risks involved, society will confront on a more informed basis what risks are acceptable and for whom. Development of biomarkers may confirm that the risk of mTBIs or the associated risks of CTE changes depending on the age or gender of the individual or other factors. This will make us confront questions as fundamental as whether parents, coaches, schools, and others owe a duty to restrict children from the playing field.