Saving lives through pressure ulcer research: revisiting our decade-old perspective of aetiology


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In a joint editorial published in the inaugural issue of this journal a decade ago (Clark and Gefen, 2009), we highlighted the work of Reswick and Rogers (1976) as being the first published study to link the magnitude of sustained pressure upon humans with the time of exposure to these forces within the context of pressure ulcer prevention (PUP). The Reswick and Rogers paper was the first attempt to explain how the extent and duration of bodyweight loads relate to the aetiology of pressure ulcers/injuries, and despite that this paper failed to provide a clinically useful tissue injury threshold, it did point to the importance of the time dimension. It is now the 10th year anniversary of *Wounds International* and a decade since we have published our original editorial in this journal, which is a good opportunity to revisit our views from that time and perhaps refer to that classic paper from the 70s again, with the new knowledge that has been generated since.

As already noted in our editorial from 2009, the Reswick and Rogers work was an attempt to determine a quantitative tissue damage threshold for insensate or immobilised patients, which has been, and still is considered to be, the 'holy grail' in PUP. In the more than 40 years since their study was published, that injury threshold remained elusive. However, perhaps the most important research breakthrough that we have achieved in this context is that we now understand that a quantitative, absolute and generic injury threshold will forever remain intangible, much like the proverbial pot of gold at the end of the rainbow.

We will briefly elucidate the reasons for this in our present editorial, however, interested readers are encouraged to find detailed information and in-depth explanations with examples in recent review articles and the upcoming Aetiology Chapter of the International Guidelines for Pressure Ulcer Prevention and Treatment (Gefen, 2017; 2018a; 2019).

The majority of new scientific knowledge on pressure ulcer aetiology and its implications to PUP arise from mechanobiology. Mechanobiology is an emerging field in bioengineering where the focus is on the relationships between mechanical forces and biological function at the microscopic cell and tissue levels. The damage occurring to the cytoskeleton and plasma membrane when cells are chronically distorted and deformed, as in a weight-bearing static posture or when sustained external forces are acting on tissues (e.g. from a medical device), is the root cause of the formation of all pressure ulcers (Weihs and Gefen, 2016). The magnitude of these cell and tissue deformations will always depend on the characteristics of each individual because they are functions of the internal anatomy, tissue composition and mechanical properties — which are, in turn, a function of age and chronic conditions. The basic understanding that cell and tissue damage results, first and foremost, from exposure to internal tissue deformations, which are always different across individuals (even if the forces or pressures at the body-support interface are similar), is relatively new. This then implies that internal tissue damage cannot be predicted based on measurements that only describe the mechanical conditions at the surface of the body.

We did know that bodyweight loads distribute in very distinguishable patterns in bodies and tissues of different individuals, even at the time of writing our decade-old editorial (Clark and Gefen, 2009). Nonetheless, we did not know about the degradation of the plasma membrane and the subsequent loss of control over transport through the cell's plasma membrane under sustained and intensified loads, which only revealed themselves several years later when we developed the mechanobiological scientific tools (combining setups for cell distortion, advanced microscopy and image processing) for conducting these studies (Slomka and Gefen, 2012; Leopold and Gefen, 2013).

Moreover, the new mechanobiology perspective, which allows examination of the origin of pressure ulcers at a cell level, rather than when a wound becomes macroscopic and clinically identifiable, points to the cascade of events causing secondary and tertiary damage within hours after the first cells have died due to exposure to sustained deformation. Specifically, we now understand that inflammatory damage — which has been overlooked before — contributes to the escalation of cell and tissue death and, hence, inflammation should be managed and controlled (Gefen, 2018a; 2018b). This important understanding concerns not only the aetiology of pressure ulcers, but also offers practical interventions, since inflammatory markers,

such as biocapacitance, can be employed to assist the early detection of damage evolving under intact skin (Gefen, 2018a; 2018c) and, therefore, facilitate early intervention. The ischaemic damage pathway was believed to be the "one and only" cause of tissue damage in Reswick and Rogers' time.

It is now considered a tertiary contributor to damage occurring after direct deformation damage and inflammatory damage have already substantially compromised tissue viability (Gefen, 2018a). Referring again to the elusive nature of the injury threshold sought by Reswick and Rogers, the above microscopic, mechanobiological perspective that considers inflammatory processes and later build-up of ischaemic damage over time, points to the (perhaps disappointing) fact that there is no universal tissue injury threshold.

A person's inflammatory response depends on numerous factors, including age, gender, nutrition and lifestyle, any chronic or acute state of disease, and health of the inflammatory system. The health of the inflammatory system is also age-dependent and treatment-dependent (e.g. medication or chemotherapy-dependent). All these factors will influence the effectiveness of the immune response of an individual and whether that response would involve a secondary damage to tissues, e.g. due to prolonged inflammatory oedema. Likewise, any cardiovascular condition or chronic disease (arterial, diabetes) affecting the quality of perfusion, or issues of blood oxygenation (e.g. episode of pneumonia) or availability of other metabolites or hormones in the blood stream will shape the severity of the tertiary cumulative ischaemic damage. The ischaemic damage with its specific onset time-point and rate of accumulation, will be superimposed with the aforementioned primary direct-deformation damage and secondary inflammatory damage, in a highly individualised pattern.

Mechanobiology, the bioengineering approach and methods of examining the interplay between mechanics and biological function at the cellular scale, has developed and now emerged as a new biomedical subfield in the past decade, complementing our understanding of pressure ulcer aetiology and prevention. It is mechanobiological research that was able to explain the colossal failure of generations of researchers who were seeking the holy grail of a universal injury threshold value. That failure was manifested, for example, in guesstimating a pressure of 32 millimeters of mercury as the 'safe' exposure to skin surface loading, which was (embarrassingly) common industry standard for so many years to demonstrate the value of patient support surfaces. Other various attempts to find alternative values of physical properties that can be measured at the body-support interface and used as injury thresholds were, likewise, doomed to fail. We now understand that for early-detection of an evolving pressure ulcer/injury in an individual, we need to monitor the tissue physiology of that specific individual and compare their present status to their own historical or reference values, much like with analyses of blood lipids or other health status biomarkers. It is most encouraging that contemporary PUP technologies are targeting these newly discovered damage routes and their associated biomarkers, aiming at inflammation, in particular, as the phenomenon to detect and control for effective PUP (Gefen 2018a; 2018b; 2018c). WINT

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