

Evaluating our Performance: Tissue Penetration Paradigm Shift

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The term paradigm shift, as introduced by Thomas Kuhn, describes a change in basic assumptions within a ruling theory of science. Such a change in a certain thought-pattern is usually the result of a long process. Applying the paradigm shift model to the measurement of concentrations of anti-infective drugs at the site of infection, we indeed observe a remarkably slow shift in thinking and acting even in the face of compelling reasons for change. For several decades anti-infective drug concentrations at the site of infection have been primarily measured by taking a whole tissue biopsy, grinding it, determining the total concentration in the homogenate, comparing it with the corresponding blood sample, and then judging a drug's clinical value and performance from such a measurement. As has been shown, homogenizing biopsy samples results in a mixture of distinct pharmacological compartments, of bound and unbound drug, and, thus, fails to give meaningful information about concentrations at the infection site. Surprisingly, despite our knowledge of the many well-known problems with interpreting tissue concentrations from biopsy samples, this method remains in fairly common use over many years after the flaws were described. According to Kuhn's definition of a paradigm shift, the anti-infective research community is - like other research communities - reluctant to change and slow to adopt new thinking. This can be attributed to some extent to the lack of reliable alternatives or to challenging issues with new methods. However, if the new paradigm of repeatedly measuring free concentrations in distinct pharmacological compartments - such as extracellular fluid of tissues or various body fluids - is generally accepted, thoroughly explored and executed, the old paradigm will be replaced. We seem to be close to this paradigm shift and thus to more accurate measurement and interpretation of tissue concentrations.

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