Pathophysiological Modelling in Anaesthesia and Intensive Care: Who, How & Why?

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There exists a requirement for the expansion of our knowledge of disease processes and their treatment. Therefore, research is necessary. In-vivo research has several drawbacks, which include the ethics of the use of human/animal subjects, the cost, the labour- and time-intensity, and the questionable usefulness and applicability of noisy data from poorly representative populations.

Modelling can provide patient surrogates for investigation. Such surrogates are free from ethical concerns, may be used repeatedly and can provide incredibly detailed and uniform data. So how is such modelling research performed?

First, we must decide the question(s) that need answering. Then we must develop a model and prove to our audience that it is trustworthy. The validated model may then be investigated in the same way as a patient.

Questions that suit modelling research may address issues inappropriate for clinical research because of ethical problems, expense or feasibility. The modelling researcher must decide whether modelling can provide an answer, and, importantly, whether people will believe the answers provided by the model.

Developing a model is a complex process. It commences with algorithm development; this must take a multi-scalar view, from the microscopic to the macroscopic level. Mathematical processes must be mass-conserving and adhere to the basic laws of physics. Algorithms are generated that usually follow the established pathophysiological theory, although the literature contains remarkably little quantitative description of the volumes, flows and dimensions required in developing a multi-scalar compartmental model. Flowcharts are a good starting point, and linked equations can be tested in a spreadsheet program. Eventually, the algorithm has to be coded, and this may be accomplished using a software programming language (such as C++ or Pascal) or using one of the modelling software toolkits (e.g. MatLab). Custom software runs faster and is more easily modified in real-time. MatLab is more easily verified and can be used to provide reusable model building blocks. Both are acceptable in widespread use.

Perhaps the most difficult (and most important part) of modelling is establishing the validity of the model. In essence, no model can be truly validated, in that absolute truthful replication of a process is impossible and untestable. Instead, the modeller must generate credibility. This comprises establishing trust in the minds of the consumers of the research that the model can adequately replicate the process under consideration. Such credibility may be established through: (1) Comparison with new patient data, (2) Comparison with old patient data, (3) Comparison with accepted theory, (4) Clear and open description of the model to generate a ‘sympathetic confidence’.

Finally, we may use the model. Usually, we investigate it as we would a patient. A protocol is designed and conducted on the model, which has been configured to match the patient/disease/age group of interest. Examples:

- Can we estimate alveolar deadspace from the arterial to end-tidal PCO_2 gradient?
- Why do some COPD patients retain CO_2 when given oxygen?
- How does hypoxaemia progress during apnoea? What factors modify its progression?