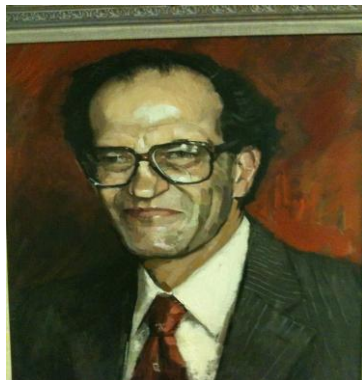


Cyril M. Conway MB BS FFARCS

In 1976 Cyril Conway was a member of the Magill Dept. of Anaesthetics in the Westminster Medical School. Professor Conway became head of the combined anaesthetic departments of Charing Cross and Westminster Hospitals in 1983. He died in 1986.



Many 'new researchers' start their publication list with a case report or description of some clinical problem...this was the case with Cyril Conway [1]. This was followed by an assortment of papers [2-4] until 1962 when, with Jimmy Payne, he had a publication in Nature [5]. This was about standard bicarbonate values of whole blood. In all Conway had nine publications in collaboration with Payne and most of them are associated with hypoxaemia in one guise or the other [5-13]. More details of these papers can be found in Payne's bibliography. There was one more publication on the topic of "Arterial oxygen tensions in surgical patients" with Conway as the sole author [14].

Conway's interest in pharmacology was reflected in a variety of papers [2, 4, 7, 15-20], the subject matter included the anaesthetic ethers, the cardiovascular effects of various induction agents, the effect of anaesthetic agents on myocardial contractility (see below) and, of some academic interest, the Antoine equation coefficients for inhalational anaesthetic agents [19]. This is not a paper but a letter to the British Journal of Anaesthesia about an article by Rodgers and Hillⁱⁱ. It points out errors that the authors acknowledge. As the authors state, Professor Conway diligently examined

ⁱ Photograph courtesy of Neil Soni, Imperial College London.

ⁱⁱ Rodgers, R. C, and Hill, G. E. (1978). Equations for vapour pressure versus temperature derivation and use of the Antoine equation on a hand-held programmable calculator. Br.J. Anaesth., 50, 415.

their paper in great detail. From his work on breathing circuits, detailed below, he obviously had a great eye for mathematical precision.

Cardiorespiratory physiology

In 1970 a paper was presented, with Blackburn JP as the primary author, ... this was on 'Myocardial carbon dioxide response curves' [21] and this was followed in 1971 with "The effects of anaesthetic induction agents upon myocardial contractility" [18], an abstract. There were five papers all with Blackburn as the primary author on aspects of myocardial contractility. To quote a section of their paper on 'An analogue device for measuring the pre-ejection period (PEP)' [22] "The pre-ejection period (PEP), may be derived from the three waveforms by subtracting left ventricular ejection time (LVET) from total electromechanical systole time (EMT)" and this had had to be done manually.

A paper on PaCO₂ and PEP [23] was published in Anesthesiology in 1972. Using $1/PEP^2$ as an inotropic index they studied the myocardial response to changes in arterial carbon dioxide tension, in dogs and humans. An initial rise in inotropy with carbon dioxide was thought to be due to sympathetic stimulation ...in dogs this had been able to be blocked with beta-blockers. With high levels of carbon dioxide myocardial depression occurred. In dogs halothane shifted the response curve downwards and the final thought was that the PaCO₂/myocardial response curve could be used to evaluate drugs that affect the myocardium.

In the 1970s analogue computers for analysis in medicine were in their 'heyday', they very useful for pharmacokinetic and hydrostatic (cardiovascular) type modelling. Blackburn et al here describe a complex analogue system for determining the beat-by-beat PEP value. This was quite a 'tour de force'. They compared hand-calculated values to computed values and the r value was 0.976. There were obviously problems (noisy phonocardiogram and ill-defined dicrotic notches the main ones).

In their final joint publication they studied the effect of the Valsava manoeuvre on systolic time intervals under various conditions, on healthy patients,

prior to surgery. Postural change, beta-blockers, ganglion blocking agents and halothane and methoxyflurane were all assessed.

With 'light' anesthesia the majority of subjects responded appropriately even after beta blockade and ganglion blockers. Adding more volatile agent to the anaesthetic abolished the response, PEP changed markedly whether the responses were blocked or not.

This concluded the work with Blackburn et al.

Measurement

Like all academic anaesthetists devices of measurement are the most important of research tools and Conway also had his share of studies of measurement devices. He evaluated "a battery of coagulation techniques" [24], the "Rapox" paramagnetic oxygen analyser [25, 26], three electronic respirometers [27] and he wrote an article on "Anaesthesia and measurement" for the Proceeding of the Royal Society of Medicine [28]. However he is probably best remembered for his mathematical analysis of the dynamics of breathing systems.

Circuits

1976 was a productive year for Conway's experimental and mathematical appraisal of breathing systems. The first publication in 1976 [29] was in fact an abstract from that Anaesthetic Research Society held in London in October 1975. He was working at this time in the Magill Department of Anaesthetics in the Westminster Medical School. He explains in the abstract how in any semi-closed rebreathing system some rebreathing will occur if the fresh gas flow is below a critical value and that the values of the oxygen-carbon dioxide mixtures in various parts of the circuit, if plotted on an oxygen/carbon dioxide graph, all lie on a single gas exchange line, see below for more details. He goes on to explain how with a single modification of the alveolar air equation alveolar concentrations of gases can be determined. He states, "The behaviour of any circuit can be deduced if the composition of vented gas can be forecast."

Two papers in the same journal were then published, and cited each other[30, 31]. The first was “A theoretical study of gaseous homeostasis in the Magill circuit” [30] and was a more detailed description of the findings of the ARS abstract. Mapleson, almost twenty years earlier, had deduced that the Alveolar CO_2 (F_aCO_2) = CO_2 production / fresh gas flow. The F_aCO_2 was not affected by changes in ventilation. This paper is a purely mathematical treatise on the subject and it assumed that the subject was breathing spontaneously, in a steady state and that the gases breathed were oxygen and nitrogen. Through a lengthy series of equations, along the lines of the alveolar air equation, he was able to show that whether there was complete gas mixing, no gas mixing, or partial gas mixing, the mean inspired gas concentrations (oxygen and carbon dioxide) will be the same. The last paragraph of this paper is interesting in that there is a short discussion on the use of controlled ventilation using the Magill circuit (normally wasteful on fresh gas) where he states ““Replacement of the usual simple expiratory valve of the Magill circuit by a valve which does not permit gas venting during inspiration would allow this simple analysis to be extended to include the passively ventilated subject”. The author believes that this was the basis on which the Carden ventilator was constructedⁱⁱⁱ.

Following on was “An experimental study of gaseous homeostasis and the Magill circuit using low fresh gas flows”. The Magill circuit was probably the most commonly used breathing system in the UK at that time. Volunteers were used to breathe a “non-narcotic” mixture of gases through a standard Magill circuit using various gas flow rates. Previous work in this field had indicated that rebreathing should not occur unless the fresh gas flow rate was at or below the ‘minute alveolar ventilation’^{iv}. This study confirmed this finding but also showed that variations in ventilation could perturb the system, in particular, following a deep breath at low flows the exhaled carbon dioxide could reach the reservoir bag and change the dynamics of

ⁱⁱⁱ Fletcher IR et al. *Anaesthesia* 1983;38:1082-9. Tham EJ et al. *Brit. J. Anaesth* 1993;71:741-746

^{iv} Kain ML and Nunn JF. *Anesthesiology* 1968;29:964

the circuit. The end-tidal gas concentrations changed very little even when this change was associated with marked changes in ventilation and inspired gas concentrations.

The next paper[32] continued the description of the concept of being able to deduce alveolar gas concentrations from the gas mixtures in the breathing system, and this paper generalized the idea to all semi-closed systems. Conway, again, was the sole author. Here he describes a 'black-box' approach to the analysis. He refers to the geometrical approach for the solution of the alveolar air equation that was suggested by Leigh and Tyrrell in 1968^v; this geometrical approach is based on the fact that all gases (inspired, expired, and vented) must all contain "mixtures of varying proportions of fresh and alveolar gases" and these values can be plotted on an oxygen vs. carbon dioxide diagram (x-y graph) and a straight line relationship exists which can be used to advantage. The line plotted (the gas exchange line) is related but not equal to the respiratory exchange ratio; Conway himself had collaborated with Leigh in 1972 when they determined the interrelationship between FiO_2 and the gas exchange ratio in the oxygen-carbon dioxide diagram [33].

The final paper of this series in 1976 was an experimental paper on the newly introduced Lack circuit^{vi}. The advantages of the Lack over the standard Magill (Mapleson A) was that the expiratory valve was proximal, rather than at the patient end, and that the reservoir bag was near the fresh gas inlet rather than on the expiratory limb as found in the Bain circuit. The manufacturer's information leaflet states that the "fresh gas flow requirements [*for a Mapleson A system is*] theoretically equal to a little more than the alveolar ventilation, i.e. 4-5 litre/min for a 70kg adult". The paper, first author PK Barnes, found that the resistance to breathing was unacceptably high and that rebreathing occurred in spontaneously breathing volunteers when the gas flow rate was equal to the minute ventilation; minute

^v Leigh JM and Tyrrell MF. Br J Anaesth. 1968;40:430

^{vi} The Lack circuit is a co-axial breathing system that has the characteristics of the classic Mapleson A type. It was designed and developed by Dr Alistair Lack and Bill Quick of MIE. <http://www.historyofmie.co.uk/viewproduct.asp?id=lack>

ventilation being significantly more than alveolar ventilation. They suggested a flow rate of 1.5 x minute ventilation.

In 1977 two 'circuit' related papers were published, first a theoretical and experimental study of the Mapleson D system [34] and then an analysis of the Bain system [35], a co-axial modification of the Mapleson D.

In the first paper a mathematical analysis was carried out along previous lines of thought and the coaxial version of the Mapleson D (a Bain circuit) was used when ventilating the lungs of dogs. A significant endpoint of the study was the production of a series of multiple regression equations that related carbon dioxide levels in a linear way to fresh gas flow and total ventilation. The last figure in the paper is a graphical nomogram whereby knowing the fresh gas flow and the ventilation the PaCO₂ can be predicted. This was followed by a volunteer study breathing a non-anaesthetic gas through a Bain circuit. It was recommended, "at least three times the minute volume appear to be necessary to prevent rebreathing". These findings were not universally accepted; some years later, following further publications, Spoerel and Bain disagreed with the recommendations in the correspondence section of the B.J.A. and could not understand how the Bain (coaxial D, T-piece) could differ so markedly from the non-coaxial T-pieces^{vii}, Conway replied [36] in defence of his position. In 1980 another paper on the Lack circuit was published, this time in Anaesthesia [37]. There was a great deal of controversy about the required gas flow rates and the importance of rebreathing, another worker, David Humphrey from South Africa, entered the fray in 1982 where he compared the Lack, the Magill and the Bain breathing systems all under the same conditions^{viii}. The Lack system seemed to come out best for spontaneously breathing adults.

In 1981 Conway turned his attention to circle systems – the first being on the factors that affect carbon dioxide homeostasis [38] and the second on "alveolar gas relationships with CO₂ absorption" [39]. The first used an experimental lung model with controlled ventilation without carbon dioxide absorption. In brief carbon dioxide

^{vii} Spoerel WE and Bain JA. Br J Anaesth 1986;58:819-822

^{viii} Humphrey D. J Roy Soc Med. 1982;75:513-524

removal was most efficient at low respiratory frequencies and was well correlated with fresh gas flow and minute ventilation if the frequency was kept constant. The mixing of fresh gas and exhaled gas was thought to be responsible for some paradoxical results when frequency was changed. The second paper a Conway classic. Again he uses the 'black-box' analogy and creates a myriad of equations to determine the dynamics of the system, again using the oxygen-carbon dioxide diagram originally described by Rahn and Fenn 1955^{ix}. Take a weekend and read this paper. Accurate alveolar gas concentrations cannot be predicted but the black box approach does indicate how the system should be used, high flows at the beginning of the anaesthetic (for 20 minutes) when the system is least stable, and then low flows – the long time constants of the system making any changes in alveolar gas concentrations very slow...at very low flows the gas composition should be monitored. A critical letter about his analysis (more along the lines of the futility of it) was rebuffed [40]. Conway would have been in his element with modern monitoring.

Two papers in 1984 [41, 42], the first addressed the factors that should be considered when using closed and low flow systems (*Acta Anesthesiol. Belg.*) and the second on the concentration and second gas effects (where the fast uptake of one gas increases the concentration of the other and therefore enhances its uptake) in circle systems. These factors were more comprehensively explored in the subsequent years and in 1986, the year he died, a further three papers on gaseous homeostasis in circle systems were published [43-45]. The first one was the description of a model and the second a validation of the model.

The model consisted of two parts, the subject and the breathing system. The multi-compartment subject model described by Mapleson^x was used, the lung component modified to accommodate a variety of gases. The model of the circle system assumed complete mixing of gases and complete carbon dioxide removal. The paper needs to be read to understand all the intricacies of the calculations...the program was written in Pascal. The subject model made calculations on a heartbeat to

^{ix} Rahn H and Fenn WO. *American Physiological Society* 1955

^x Mapleson WW. *B.J.A.*;45:319 and *B.J.A.* ;50:731

heart beat basis and the gas concentrations in the breathing system were calculated for every respiratory cycle. There is an extensive discussion on the intricacies of the model and its problems; because of the calculations rates for the subject and the circle are different some errors are “both summated and compounded” at low fresh gas flows.

In the second paper, the model's performance in several tests, including a nitrogen washout test when 'breathing' oxygen and the estimation of the model's functional residual capacity by using helium, tested the 'functionality' of the model. The performance of these tests was good and reproduced the results of some previous studies, including the use of nitrous oxide. It was therefore deemed to be a good test bed for the prediction of the behaviour of circle systems.

The final paper was an application of the model to the dynamics of a classic anaesthetic mixture, Oxygen, nitrous oxide and halothane (or methoxyflurane). A range of flows and concentrations were used and the effects on gas concentrations by the concentration and second gas effects studied. As is known, a circle system, when compared with a non-rebreathing high flow system, will reduce the rate of uptake of anaesthetic agents and this will increase in magnitude as the fresh gas flow decreases. The whole paper is a work of great magnitude and displays the value of models in the understanding of the real world where clinical studies of this nature would have been even more difficult with many more confounding factors.

Cyril Conway died in post in 1986.

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