

# J F Nunn

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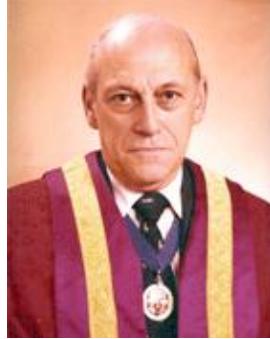
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## **John F. Nunn** **MD DSc PhD FRCS FRCA FGS**

John Nunn is most well known, amongst anaesthesia trainees working for exams, for his book on Applied Respiratory Physiology. He started his academic career as a research fellow in Birmingham (1955-56) and then at the Royal College of Surgeons (1957-64).



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He was the foundation professor in Leeds from 1964 until 1968, when he returned to London to become head of the Division of Anaesthesia of the Clinical Research Centre. Permanent accommodation was completed in 1972 at Northwick Park, Harrow; Nunn retired in 1991.<sup>ii</sup> John Nunn's publications start before, and finish after, the epoch this series of reviews cover. He started in 1948 and finished in 2003. The journals that accepted his work are of the highest reputation, Nature [4], Journal of Applied Physiology [8], Lancet [9], BMJ [7], British Journal of Anaesthesia [89], Anaesthesia [20], Anesthesiology [16] and Respiration Physiology [4], in no particular order.

His first publication is an article on mountain sickness in the Queen's Medical Magazine[1], a student production of the University of Birmingham. It was another five years before a paper entitled "A simple method of administering cyclopropane for very short operations" in the Medical Journal of Malaya[2], known as "Nunn's bag". A year later "An anaesthetist looks at Malaya" was published in the Lancet[3]. He was the first author of 105 papers and the sole author of 64. As he acknowledges himself much credit goes to others who helped, including Irene Manton, JA Kitching, EJ Moran Cambell, Tony Allison and many others.

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<sup>i</sup>Courtesy of the Royal College of Anaesthetists and JFN.

<http://www.rcoa.ac.uk/index.asp?PageID=1460>

<sup>ii</sup> Development of academic anaesthesia in the UK up to the end of 1998

J F Nunn. British Journal of Anaesthesia. London: Dec 1999. Vol. 83, Iss. 6; pg. 916

There is no disputing his contribution to the understanding of respiratory physiology as the vast majority of his publications are in this area, either dealing with the physiology itself or the devices used to study it.

## **Measuring devices**

The first was a time-phased end tidal sampler [4]; it is hard to imagine in the 21<sup>st</sup> century how difficult it was to measure respiratory gases. This paper describes how with a relatively simple differential pressure device an electronic circuit could be triggered which would then start a small suction pump that would aspirate gas through a magnetically controlled valve [controlled from the same circuit]. This enabled a selected portion of gas from the circuit to be analysed using a colorimetric method. Its performance was studied during both spontaneous and controlled ventilation. Following on from this, a year later was a description of the Dräger carbon dioxide analyser [5]. From Nunn's account this device was devised during WWII for use in submarines. This device, in retrospect, is so simple/crude. A known volume of the gas to be analysed (a ten ml syringe) pushes the sample gas into a sodium hydroxide chamber where the CO<sub>2</sub> is absorbed and the volume of gas is then re-measured. There were, as one might expect, lots of careful preparation for accurate results, temperature, humidity of the gas, nitrous oxide and so on but in 1958 this was leading technology. An overview of the problems of gas analysis, storage of gases, absorption of gases in chemical reagents and so on were also examined in detail and modifications to Haldane's apparatus were made in the light of their findings [6]. Nunn worked with Andrew Thornton at this time a produced a paper on the "Accuracy of determination of pCO<sub>2</sub> by the indirect method." [7]

The next equipment/measurement paper was on the coiled cathode oxygen polarograph [8], with co-workers RA Butler and S Askill. This was published in Nature, a short report on an improvement in design that overcame the disadvantages of previous devices – the total volume of the cuvette was 0.2ml. This is accompanied by an overview of the measurement of blood oxygen tension in the Brit. J. Anaesth. also in

1962 [9]. In the opening paragraph he describes how there is a dearth of measurements of  $pO_2$  during anaesthesia because a) anaesthetists think they can detect hypoxia and b) its measurement has been so difficult. This article contains all you would wish to know about the handling of specimens and the measurement of oxygen.

1962 was a busy year, another paper assessed the accuracy of two respiratory flow meters [10]. The respirometer (the Wright Respirometer) turned out to be less accurate at low and high flow rates but all the forces of error evened out during anaesthesia; as the authors point out, the errors exaggerate a departure from normality which one could perceive as a good thing. The ventigrator, being something similar to a pitot tube, measures the difference in pressure on either side of a constricting 'throat' in an air conduit. The sensitivity changed markedly with flow and, more importantly during anaesthesia, with the density of the gas. It was not considered suitable for routine use as, although the device itself is robust, the paraphernalia required to make the measurements were unlikely to "withstand dropping on the floor."

Over the next thirty years a variety of instruments were assessed, paramagnetic oxygen analysers [11, 12], refractometers [13, 14], anaesthesia related equipment – a new halothane vapouriser [15], the Quantiflex machine [16], and a modification to the Brompton Manley ventilator to facilitate intermittent mandatory ventilation [17], another ventilator tested was the Ohmeda CPU-1 ventilator – a very sophisticated device at the time [18]. Later 1988 and 1990 there were a further two papers, one on the oesophageal detector device [19] and one assessing three indirect calorimetry devices for assessing metabolism in critically ill patients [20]. These devices are used during artificial ventilation and were tested on a lung model where butane was burned in a gas-tight combustion chamber. The combustion of oxygen and production of carbon dioxide characteristics are known. They investigated the effect of oxygen concentration on the accuracy of the instruments with fixed set ventilation parameters. It would appear from their results that the Datex Deltratrac Metabolic Monitor came out best. This is a far cry from a clinical study [which would be

extremely difficult] but it demonstrates the ingenuity of the team effort. In 1984 they had developed a lung that could represent spontaneous breathing (as well as being able to be artificially ventilated) and it had the ability to trigger ventilators as patients do in the real world [21]. There are other equipment/measurement related papers [22-27]

## **Lung Perfusion and ventilation**

Nunn is known internationally for his work on respiratory physiology, particularly relating to the practice of anaesthesia. In 1962 there were papers on the topics of predictors for oxygen and carbon dioxide levels during anaesthesia [28] and hypoxaemia after anaesthesia [29].

The 'hypoxaemia' paper was a joint effort with Jimmy Payne [see his bibliography], they were both Lecturers at the time at the Postgraduate Medical School, Hammersmith Hospital. "All patients undergoing minor operations under general anaesthesia were found to be hypoxic for several hours after operation...The cause of the hypoxaemia appears to be a disturbance of ventilation/perfusion relationships within the lung." This is the crux of all the work, the avoidance of hypoxia and hypercarbia. There are many interrelated papers and so only a selection will be described.

Much of the work started in the late 1950s.

"A comparison of artificial ventilation and spontaneous respiration with particular reference to ventilation-blood flow relationships." 1958 [30]

"Anatomical subdivisions of the volume of respiratory dead space and effect of position of the jaw." 1959 [31]

"Gaseous exchange during halothane anaesthesia: the steady respiratory state." 1959 [32]

"Ventilation nomograms during anaesthesia." 1960 [33]

"Respiratory dead space and arterial to end-tidal carbon dioxide tension difference in anesthetized man." 1960 [34]

"The respiratory effects of resistance to breathing in anesthetized man." 1961 [35]

"Factors Influencing the Arterial Oxygen Tension during Halothane Anaesthesia with Spontaneous Respiration." 1964 [36]

"Ventilation-perfusion relationships after haemorrhage." and "Problems of Oxygenation and Oxygen Transport during Haemorrhage." 1963 and 1964 [37, 38]

"Influence of Age and Other Factors on Hypoxaemia in the Postoperative Period." 1965 [39]

"Factors influencing the arterial oxygen tension during anaesthesia with artificial ventilation." 1965 [40]

"The influence of cardiac output on arterial oxygenation: a theoretical study." 1967 [41]

"A comparison between the effect of nitrous oxide and nitrogen on arterial PO<sub>2</sub>." 1967 [42]

"Influence of duration of hyperventilation on rise time of P-CO<sub>2</sub> after step reduction of ventilation." 1968 [43]

"Influence of anaesthesia on the regional distribution of perfusion and ventilation in the lung." 1969 [44]

"Influence of anaesthesia on the regional distribution of perfusion and ventilation in the lung." 1970 [45]

"Distribution of gas and airway closure." 1971 [46]

"Expiratory muscle activity and changes in functional residual capacity during anaesthesia." and "Factors influencing the development of expiratory muscle activity during anaesthesia." 1973 [47, 48]

Functional residual capacity during anaesthesia, I, II and III 1974 [49-51]

This is a fraction of all the papers on this aspect of physiology as it relates to anaesthesia; a huge body of work from a wide range of team workers; Alagesan K, Bergman NK, Campbell EJ, Coleman AJ, Ezi-Ashi TI, Freeman J, Hewlett AM, Hill DW, Hulands GM, Kelman GR, Matthews RC, Peckett BW and Webb SJ. My apologies to any I have missed.

There are another 41 references in this section. 51-92]. [22, 23, 28-31, 33-41, 43-93]

## **The cellular effects of anaesthesia**

Another interest was that of the cellular effects of anaesthesia, this work started in 1968 and over 20 years was carried out in collaboration with many people; Alison, Bottiglieri, Chanarin, Chapple, Deacon, Dixon, Jones, Keeling, Kimball, Konieczko, Lovis, Lumb, Monk, O'Morain, Pope, Rostain, Royston, Sharp, Skacel, Snape, Sturrock, Wardley-Smith, Webster and Wiklund (apologies to any I have missed).

The first was on the possible mechanism of anaesthesia by a study of cellular microtubules [94]. This was a review article – a good way to start an investigative project. Microtubules are found in many cellular sites that are affected by anaesthetics. Cold, high hydrostatic pressure and colchicine can produce narcosis and they also reversibly depolymerise the microtubules. How the depolymerisation caused narcosis was unknown but the abundance of microtubules in neurons may suggest a role in neurotransmission. The authors were hypothesizing that anaesthetic agents may also reversibly depolymerase the microtubules.

The first presentation of an experiment was at the Anaesthetic Research Society held in London in November 1968, with JA Sharpe and K Dixon. They studied the movements and mitosis of cells cultured from mouse lung and thymus. They filmed the cells for a control period and then exposed them to 2% halothane. Of the different cell types cultured only the lymphocytes exhibited significant loss of motility – mitosis also took twice as long. It was speculated that it was a direct effect on microtubules as they had been implicated in both motility and mitosis<sup>iii</sup>.

They then moved from cell culture to living organisms, protozoa with spherical bodies, *Actinosphaerium* [95]. These organisms have thin cytoplasmic projections called axopods and their inner cores are axonemes which can cause the axopods to bend. These protozoa were exposed to a number of anaesthetic agents, chloroform, diethyl ether, divinyl ether, methoxyflurane and halothane. They discovered that the effects were proportional to that found in man; evidence for the site of activity had been strengthened.

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<sup>iii</sup> Hirsch, J. G., and Fedorko, M. E. [1968]. *J. Cell Biol*,38, 615.

There were another three papers in 1970 [96-98]; "Effects of halothane on the single cell", "Reversible effect of an inhalational anaesthetic on lymphocyte motility." (a letter to Nature) and "The effects of halothane on bacterial division rate." The Nature letter – this described how the mobilization of neutrophils was suppressed by halothane. And the B.J.A. article (ARS) bacterial growth rate was inhibited in a dose dependent manner by halothane but only if it was in a concentration greater than 3%, this led on to other aspects of the effects of anaesthetic agents on cellular division – see below.

There were a variety of publications over the next few years [99-103] but we will now jump to 1974 [104]. They studied the effect of six anaesthetic agents on the swimming velocity of *Tetrahymena pyriformis* (a ciliate protozoon). The concentrations resulting in a 50% reduction in motility were of the same order as in man (cyclopropane was an exception). No cellular damage was seen at these 'clinical' concentrations but was at 10x the normal dose, but even this was reversible after time.

In 1975 a further study [105] using halothane on the contraction and relaxation of *Spirostomum ambiguum* and *Vorticella* sp. were studied. In these animals, contraction was stimulated; two sites of action were postulated, the microfilaments of the myonemes or the stimulatory system that controlled contraction. It wasn't until 1978 that another 'cilia related' paper was published, this time it was an investigation of the effect of ambient pressure on the depression of cilia activity by halothane [106]. It was a test of the critical volume hypothesis of anaesthetic action<sup>iv</sup>. Simply put, the hypothesis was that high ambient pressure could reverse the actions of anaesthetic agents. The swimming speed of *Tetrahymena pyriformis* was studied at high pressure and at different concentrations of halothane. The results were contrary to expectations of the critical volume hypothesis and it was suggested that the pressure reversal of the narcotic effect of anaesthetic agents must be different to the effect on cilia. A study in 1986 [107] also studied the effect of pressure 'reversal'. Rats were compressed in a

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<sup>iv</sup> The Pressure Reversal of General Anesthesia and the Critical Volume Hypothesis. Miller K. W. Paton W. D. M. Smith R. A. and Smith EB. *Molecular Pharmacology* March 1973 vol. 9 no. 2 131-143

helium-oxygen mixture until they convulsed. The rats were given either saline or barbituric acid (a non-anaesthetic), those with the barbituric acid infusion remained convulsion free to higher pressures. Again the results suggested that anti-High Pressure Nervous Syndrome activity involved "at least one site which is different from that responsible for anesthetic activity."

The critical volume hypothesis was soon replaced by another, and then by another, time and time again.

There were other studies on motility, now of neutrophils [108-110]; in brief, halothane did not seem to reduce motility, nitrous oxide did.

This just about completes this aspect of their work on anaesthetic agents and cellular mechanisms but another aspect was the effect of anaesthetic agents on DNA synthesis and cell division and mainly the effects of nitrous oxide.

Following on from Wardley-Smith's ARS presentation on the effects of halothane on bacterial division rate [98] Allison followed up with a general article on the cellular effects of anesthesia [99] and Nunn with a paper in the Annals of the Royal College of Surgeons on anaesthesia and cell division [100]. Over the next decade there were other such 'general' articles [103, 108, 111-113].

## Further cellular effects

### The research

This can be divided into the effects of the 'aromatic' anaesthetic agents, those of nitrous oxide (particularly on bone marrow) and those showing the bad side of oxygen.

### Aromatic agents

The effects of halothane on mitosis was published in 1969 [114] and the arrest of mitosis by halothane [101] in 1971. These papers were on plant-based experiments where changes in the chromosomes were likened to the effect of colchicine; after four hours exposure the chromosomes had contracted to about 50% of their normal length and were twice as thick, the ED50 was within the range 0.5-0.9%. Unpublished work by Forer, Allison and Nunn had shown a similar effect of mitotic spindle dispersal in the sea-urchin egg. It was also suggested that halothane may interfere with DNA synthesis. They mentioned the work by Ostergren 20 years previously as being extraordinarily far-sighted<sup>v</sup>. The effects were completely reversible and they commented that although this may occur in Man the duration of a standard anaesthetic was much shorter than the cycle of mitosis.

Two other points were made, a. the possibility of teratogenesis and b. the use of anaesthesia to synchronise cell division for cell cultures.

The full paper on the effect of halothane on bacterial growth [102] appeared in 1971. In essence there was no significant effect of clinically used concentrations and the effect that did occur at higher concentrations was reversible.

From plants and bacteria the team moved on to animal preparations. DNA synthesis in hamster fibroblasts [115], an ARS presentation. The cellular cycle has a pre-DNA-synthetic phase (G1), a DNA-synthetic phase (S) and a post-synthetic phase (G2) followed by mitosis. This study was designed to see at which point the effect of halothane occurred. The conclusion of several experiments was that something

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<sup>v</sup> Ostergren, G. [1944]. Colchicine mitosis, chromosome contractions, narcosis, and protein chain folding. *Hereditas* [Lund], 30, 429.

happened in the G1 phase in response to low, clinically relevant, concentrations and resulted in a delay in mitosis.

In 1975 there was a study on mitosis in mammalian cells following exposure to anaesthetics [116] . This was a more comprehensive study (methoxflurane, trichloroethylene, chloroform, halothane and diethyl ether) of the effects of these agents on the Chinese hamster fibroblasts. All agents caused dose-dependent inhibition of cell multiplication that seemed to be related to the oil-gas partition coefficient. In this study effects in the G2 phase were also noted. It was commented that the pollution of operating theatre air by anaesthetic agents was of too low a concentration to cause problems but chronic exposure to long-lived products of metabolism could have potential side effects.

“Effects of halothane on DNA synthesis and the presynthetic phase (G1) in dividing fibroblasts” [117] came out in 1976 and seems to be a full account of the 1974 ARS presentation.

In '76, in the last of this series of studies, Sturrock demonstrated that nitrous oxide alone had no significant effect on the production of abnormal cells in the Chinese hamster cell fibroblast preparation. However, when combined with halothane, which had a dose dependant effect (1% halothane caused 12% abnormalities in cells undergoing mitosis) the percentage of abnormal cells increased to 22% [118, 119]; a synergistic effect, whereas the effect on growth rates was additive.

## Nitrous Oxide

To paraphrase Deacon et al's introduction to the subject... in 1956 four out of six patients who were given nitrous oxide during the management of tetanus developed megaloblastic red cells<sup>vi</sup>. It was thought that cobalt-ligand complexes in vitamin B12 broke down nitrous oxide and this then resulted in an oxidation of active cobalamin to an inactive form<sup>vii</sup>. Methionine synthetase and methylmalonyl CoA

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<sup>vi</sup> Lassen, H. C. A., Henriksen, E., Neukirch, F., Kristensen, H. S. *Lancet*, 1956, i, 527.

<sup>vii</sup> Banks, R. G. S., Henderson, R. J., Pratt, J. M. J. *chem. Soc.* 1968, section A, p. 2886.

mutase are the only two enzymes requiring Vit B12 in mammals. Deacon et al's study [120] involved the measurement of the activity of both, in rats, in the presence of nitrous oxide. They showed that nitrous oxide rapidly caused inactivation of the cytosol enzyme methionine synthetase, but the mitochondrial enzyme, methylmalonyl CoA mutase, was unaffected. This difference was unexpected.

An editorial on the subject was published at almost the same time [121]. Several points were made...one was that significant depression of bone marrow was not seen in vitro, citing their own work in 1976 and it was also pointed out that the work by Banks in 1968 (see footnote) was not recognized for its clinical significance, "a sad reflection on interdisciplinary communication".

At that time the methylfolate-trap hypothesis suggested that 5-methyltetrahydrofolate [5MTHF] becomes metabolically trapped. 5MTHF cannot be metabolised via the methionine synthase pathway or converted to its precursor methylene-tetrahydrofolate and the cause.....B12 deficiency.

The 'team' investigated the effect of nitrous oxide inactivation of vitamin B12 on rat hepatic folate and this had implications for this hypothesis [122]. Their data did not support the hypothesis. They found no 'trapping' of 'methyl' folate, and suggested that a failure of folate polyglutamate was the major defect.

Two years later they investigated "serum methionine and hepatic enzyme activity in anaesthetists exposed to nitrous oxide" [123]. The report was very reassuring at a time when scavenging of exhaled anaesthetic gases was in its infancy. Serum concentrations of methionine, leucine, isoleucine and valine were normal, as were the activities of aspartate transaminase and gamma glutamyl transpeptidase. However in the same year they described megaloblastic haemopoiesis after multiple exposures to nitrous oxide", Lancet [124]. This was diagnosed in a patient with porphyria who used Entonox (50% nitrous oxide:50% oxygen) for physiotherapy. In the same year they wrote a letter to Anesthesiology [125] explaining their experience

with folinic acid as a therapeutic prophylactic agent to prevent the megaloblastic response. This had been described by O'Sullivan et al<sup>viii</sup>. They found it didn't work.

A study published in 1983 [126] showed that the effects of chronic exposure to nitrous oxide were dose dependent. They failed to demonstrate any effect at 450ppm, the ED 50 being 5400 ppm; they thought the American recommendations of 25 p. "unduly restrictive".

Further studies on the haemopoietic toxicity of nitrous oxide in patients [127] showed that haematological changes did take place – however the patients were ventilated with 70% N<sub>2</sub>O for up to 24h; an abnormal time when compared with normal clinical practice. Some of these changes [megaloblastic] had reverted after a week but there were still dyserythropoietic effects.

Three years later Nunn et al published a paper that seemed to contradict their earlier letter to the Lancet, they used folinic acid to protect against nitrous oxide teratogenicity in the rat [128]. Their hypothesis was that some teratogenic effects were due to interference with folate metabolism and that folinic acid may prevent them. The rats were exposed to 70-75% nitrous oxide on day nine of their pregnancy with or without folinic acid. No significant differences in fetal survival occurred but the number of ossified sternebrae was reduced only in the nitrous oxide group not receiving folinic acid. Major skeletal abnormalities in the untreated nitrous oxide group were significantly increased to five times that of the control groups; their hypothesis was proven true.

Another study that seemed to contradict their Lancet letter (unless I am mistaken) was "Megaloblastic bone marrow changes after repeated nitrous oxide anaesthesia. Reversal with folinic acid" [129]. A patient required a second anaesthetic seven hours after a previous N<sub>2</sub>O anaesthetic and was treated with 30mg folinic acid as a prophylactic and did not develop bone marrow abnormalities.

They studied the effect of short-term administration of nitrous oxide on plasma concentrations of methionine, tryptophan, phenylalanine and S-adenosyl

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<sup>viii</sup> O'Sullivan H, Jennings F, Ward K, et al. Anesthesiology 1981;55:645-649

methionine in man[130] [tryptophan was reduced by 30% but there were no significant changes in methionine and phenylalanine concentrations] and later, in rats where they detected interference with thymidine synthesis in bone marrow associated with a highly significant reduction in hepatic methionine to 62% of control [131].

In 1987 Nunn wrote a review on the "Clinical aspects of the interaction between nitrous oxide and vitamin B<sub>12</sub>" [132]. He addressed wound healing and infection [no effects reported], pregnancy ("...it is the view of the author that the use of nitrous oxide in pregnancy during the period of organogenesis is inadvisable in the light of present knowledge." This was in the absence of any direct evidence), exposure to trace concentrations (in contaminated operating theatre there did not seem to be problem but in the poorly ventilated dentist's surgery with high flows of gas dU suppression tests and abnormal polymorphs had been reported), nitrous oxide abuse (subacute degeneration of the cord) and the problem of the patient with subclinical B<sub>12</sub> deficiency (synergy with nitrous oxide exposure makes the problem worse; note: vegetarians may also be at risk because man's only source of vitamin B<sub>12</sub> is from animal products).

## **Teratogenicity**

There had been a great interest in the teratogenicity of anaesthetic agents over the previous decade and in 1987 Nunn's team wrote on the "Fetotoxic potential of general anaesthesia in relation to pregnancy." [133]. The bottom line on this audit, in this author's view, is that there is no clinical evidence showing an adverse effect of anaesthesia on the incidence of congenital abnormalities, and this view was supported by four other studies acknowledged in the paper. However, they still persisted with the statement "in our view, it seems inadvisable to administer nitrous oxide to any woman known to be in early pregnancy."

## **Oxygen toxicity**

The next gas to come under scrutiny was oxygen used in high concentrations...it is commonly known that even breathing 21% oxygen can lead to death after about 70 years.

This work started quite early, in 1978 [134]. Hamster lung fibroblasts were grown in culture and exposed to oxygen (40 – 90%) for up to four days. The damage to the cells' chromosomes was dose related; 100% of nuclei were affected by 95% oxygen after 72h. A similar study two years later examined the effect on pulmonary macrophages and alveolar epithelial type II cells [135].

The cells stopped dividing after 17 hours and started to die after three days. One conclusion from this study was that these cultures were good test-benches for the testing of drugs efficacy against oxygen toxicity.

It should be noted that at least hyperoxia has no effect on methionine synthetase activity in rats." [136]

In the 1970s and '80s intensive care units were becoming mainstream clinical units and patients with severe pulmonary malfunction were being cared for. Many received high concentrations of oxygen to maintain arterial oxygen levels; this however was accompanied by the risk of causing further cellular damage. In a study published in 1990 they describe the changes in lung permeability in rats exposed to 100% oxygen [81]. They discovered that changes started at 48h and that by 60h there was sufficient damage to cause pleural effusions.

The following year they found an early marker of lung injury and also described the usefulness of antioxidants in the amelioration of the lung damage [137]. The marker was oxygen uptake by a purified mitochondrial fraction in the presence of succinate and ADP; this was reduced by 20% after three hours. The antioxidants were N-acetyl cysteine, dimethyl sulphoxide and allopurinol.

There are many more papers worthy of discussion<sup>ix</sup> but these above should suffice...an extraordinary output. Let's finish with a few less physiology based publications [138-142].

1977: Egyptian antiquities at the Royal College of Surgeons of England. As might be expected this is a cataloguing of antiquities that were given to the College of Surgeons by Sir John Bland-Sutton in 1943. At the time of writing anaesthesia was still a faculty of the College – Nunn's qualifications at that time reflecting this state of affairs – MD, PhD, FFARCS (Fellow of the Faculty of the College of Surgeons).

1996: Ancient Egyptian medicine

1997: Staffs as walking aids in ancient Egypt and Palestine – illustrations of Egyptians using staffs abound but very few depict individuals in imperfect health. This was due to artistic convention of the day. However some have survived and this paper deliberates on the various postures, and in one case what appears to be an example of a shortened leg with an equinus deformity.

2000: Tropical diseases in ancient Egypt – this is a detailed treatise on a variety of diseases and the examinations of the patients as described in medical papyri.

John Nunn is an acclaimed academic and not only did he write the respiratory physiology 'bible' for anaesthesia trainees (Applied Respiratory physiology with special reference to Anaesthesia, Butterworth & Co Publishers Ltd, 1969 (ISBN-10: 0407109404, ISBN-13: 9780407109407) he also wrote a book on Ancient Egyptian Medicine, Red River Books, 2002 (ISBN-10: 0806135042 ISBN-13: 9780806135045)).

What this author was delighted to find was a third book, The Tale of Peter Rabbit by John F. Nunn and Richard B. Parkinson, with some historical help from Beatrix Potter.

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<sup>ix</sup> The laryngeal mask airway<sup>205</sup>. "All we said was "Push it down as far as it will go and blow up the cuff". Our staff had 98% success rate and that led directly to the launch of the laryngeal mask revolution. It was not very academic, but the consequences were impressive." Personal communication from JFN.

This is the Tale of Peter Rabbit “faithfully translated and transcribed page for page into the hieroglyphic script of an Egyptian of the Middle Kingdom”. I assumed [I now know] that this is the JF Nunn that you have been reading about. What a finish.

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