

HISTORICAL ARTICLES

Lyon Playfair (1818-1898) and Compulsory Vaccination

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Abstract

Lyon Playfair was born in India but brought up by his uncle in St Andrews. He studied medicine in Glasgow and Edinburgh but never practised as a doctor. Instead he worked for the chemist Thomas Graham in London and then studied for a PhD with Liebig in Germany. While serving on a government commission he became very interested in public health, particularly the control of infectious diseases. In 1883, while a member of parliament, he made a passionate speech in support of a government bill in favour of compulsory vaccination against smallpox. He was violently attacked for his speech in a pamphlet by William White, an adherent of the teachings of the Swedish mystic Emanuel Swedenborg. Playfair died in 1898 and is buried in St Andrews.

In 1800 Dr James Playfair (1738-1819), minister of Meigle Parish in Perthshire, was invited to become Principal of the United College of St Salvator and St Leonard in the University of St Andrews, as well as minister of St Leonards church. This move initiated a connection between the city of St Andrews and the Playfair family that lasted several generations. One of James Playfair's sons, George, qualified as a doctor and worked for most of his professional life in India, latterly as Inspector-General of Hospitals in Bengal. He married Janet Ross and one of their sons, the subject of this article, was named Lyon after his paternal grandfather. At the age of two Lyon Playfair was transported from India to his uncle's house in St Andrews and it was there that he spent the rest of his formative years. At the age of 14 he enrolled as a student at the University of St Andrews but thought the courses he attended rather uninspiring. On leaving university he first tried a commercial career in the office of his uncle James in Glasgow but found it unbearably tedious. In 1835 he enrolled as a medical student at the Andersonian College in Glasgow, where one of his fellow students was David Livingstone. While at the College he came under the influence of the lecturer in chemistry, Thomas Graham, and spent more time studying chemistry than other subjects in the medical curriculum. Graham moved to University College London and Playfair left Glasgow to continue his medical training in a more conventional way at the University of Edinburgh. Unfortunately he had to discontinue his studies as the vapours of the dissecting room and hospital caused severe eczema. Playfair wanted to return to science but his father,

still in India, urged a commercial career and set him up in a trading company in Calcutta. He enjoyed the voyage out to India, remarking in his journal:

*'The voyage was pleasant, for at that time, numerous young ladies went out to India to look for a career also.'*¹

He survived the journey but the work in Calcutta proved as tedious as that in Glasgow and he quickly returned to London to work for Thomas Graham. Graham advised him that, to make a career in science, he needed a German doctorate and so Playfair enrolled as a doctoral student in Justus von Liebig's laboratory in Giessen. In 1840 he returned to Britain with the coveted doctorate, the goodwill of Liebig and an excellent command of German. His first task was the translation of Liebig's influential work on agricultural chemistry.² His first salaried appointment was as chemist at the then-famous Primrose calico works in Clitheroe but changing public taste resulted in the rapid closure of the works and Playfair was forced to take an unpaid job as lecturer at the ill-fated Royal Institution in Manchester. In 1842 Liebig was a visitor to Britain and Playfair was his guide and companion, meeting many influential people in the political field.

Out of the blue came a letter from no lesser person than Michael Faraday at the Royal Institution in London asking if he would like the chair of chemistry at the University of Toronto. When news of this offer reached the government there was an immediate response. The prime minister, Robert Peel, met Playfair and urged him not to accept the post but to stay in Britain. He was flattered enough to fall into line and returned to his unpaid post in Manchester. Remunerative work soon came his way. The British Association for the Advancement of Science asked the German chemist Robert Bunsen, of bunsen burner fame, to examine the gases coming from blast furnaces. He, in turn, asked Playfair to join him and it was during this project that Playfair met his first wife Margaret Oakes, the daughter of a Lancashire ironmaster. They married in 1846. In a very significant development Peel asked

Playfair to join the Royal Commission on the Health of Towns. He studied conditions in a number of Lancashire towns and was appalled at the overcrowding, filth and disease that characterised the lives of the working classes. This commission started his life long interest in what he called 'sanitation' and what we call public health. Later this concern was to dominate his life leading, in 1898, to the award of the Harben Gold Medal of the Royal Institute of Public Health.

To further his career he needed to be in London and a post was found for him at the Geological Survey. It was there he made his most significant chemical discovery: a group of salts called the nitroprussides.³ The sodium salt is marketed under the name Nipride as a vasodilator, used in vascular surgery and the management of myocardial infarction. It is a good vasodilator but the presence of the cyano groups makes death of the patient by cyanide poisoning an ever-present possibility.

He continued to serve in government commissions, including a study of the potato famine in Ireland and the lavatories in Buckingham Palace. Apparently the latter were primitive even by Victorian standards. The most important of his government posts came in 1850 when he was invited to be a Special Commissioner for the Great Exhibition at Hyde Park housed in an enormous greenhouse (the Crystal Palace). In spite of an inauspicious start, the Exhibition was a great success and led to a life long friendship between Playfair and the Prince Consort and, unlike the Millennium Dome, made a very considerable profit used to purchase the ground on which the Victoria and Albert Museum, the Albert Hall and Imperial College London were built.

In March 1852 he became secretary of the government's newly established Department of Science and Art and he used this post to promote his vision of a network of science schools. He met with little success and in 1858 he abandoned his government work and accepted the chair of chemistry at the University of Edinburgh. During his time in Edinburgh he did little scientific research, although he did supply James Young Simpson with various materials to test as anaesthetics. Instead of research he played a large part in the administration of the university. He reorganised the teaching of chemistry and provided encouragement for his colleagues. He was president of the Chemical Society, now the Royal Society of Chemistry, 1857-59 but, by the late 1860s, chemistry played only a small part in his life and in 1868 he quit the chair at

Edinburgh to take up politics fulltime. After a vigorous campaign he was elected the member of parliament for the Universities of St Andrews and Edinburgh and took the Liberal whip. He spoke frequently in the House on education and public health. For a time he was Deputy Speaker but without great success owing to the disruptive behaviour of some Irish members. He was knighted in 1883. He represented the constituency of Leeds South from 1885 to 1892 when he was raised to the peerage and took his seat in the House of Lords as the first Baron Playfair of St Andrews.

One issue exercised him greatly as part of his concern for public health: legislation enforcing compulsory vaccination against smallpox. The consequences of contagious diseases upon the working classes were brought home to him forcibly during a number of Royal Commissions and smallpox was one of the most deadly of these diseases. It had been around in most of the world since earliest times but it was the growth of cities that made it a major problem of public health. Unlike cholera the means of controlling smallpox was known in the 19th century. The simple observation that few people contracted smallpox twice led to the practice of inoculation, or variolation as it was called in the case of smallpox. The healthy victim was given an attack of smallpox and, if he recovered, he would be free from smallpox for the rest of his life. It was a hazardous business as the victim might die or be scarred for life. The technique of variolation was perfected by the Chinese in the 18th century⁴ and passed to Arab physicians. Lady Mary Wortley Montagu witnessed variolation by Greek women in Constantinople when her husband was ambassador there and brought the therapy back to London, where it was called engrafting. Lady Mary was very active in encouraging aristocratic mothers to have their children treated in this way but it had very limited use as a public health measure amongst the working classes. Edward Jenner's genius was to see a safer way of achieving the same end. He noticed that milkmaids, who nearly all suffered from a mild disease called cowpox, which they contracted from cows, rarely suffered from smallpox. He reasoned that whatever mechanism stopped people from getting a second attack of smallpox could be equally well activated by an attack of cowpox. The effect was confirmed by experiments with orphans and vaccination against smallpox was born. The practice was slow to be accepted but grew during the 19th century and, with increasing concern for public health, was seen as a way of controlling epidemics. This meant *compulsory* vaccination and it was

the compulsory aspect that caused so much opposition. Societies arose to oppose compulsory vaccination as the government proposed legislation to enforce it. Those who resisted compulsory vaccination were known as 'conscientious objectors'.

Playfair was adamant that good public health demanded the control of smallpox by compulsory vaccination but other public figures differed. As part of the opposition, on 19 June 1883 the following motion was introduced in the House of Commons by the member for Leicester:

'That, in the opinion of the House, it is inexpedient and unjust to enforce vaccination upon those who regard it as inadvisable and dangerous.'

Playfair made a fine speech⁵ against the motion in which he marshalled all the scientific evidence for the benefits of vaccination. It cannot have been easy listening; even Playfair suggests,

'I fear I have wearied the House by statistical results.'

But this was a fine scientist speaking with authority and the amendment supporting compulsory vaccination was carried by 286 votes to 16. One would have thought that this was the end of the matter. However, some months later a long pamphlet⁶ was issued containing a virulent attack on Playfair, with the intriguing title 'Sir Lyon Playfair taken to pieces and disposed of'. It questioned his stature as a scientist and he was deeply hurt by the attack. The author of the pamphlet was an unknown writer, William White.

The pamphlet does not make captivating reading. It is verbose (168 pages long) and strident. None of the evidence adduced by Playfair stands up to scrutiny by a rational person, or so William White claims. A short quotation will give the flavour of the complete work:

'Always curious and eager to hear what can be urged in justification of a practice which is a survival from the pre-scientific age, we followed Sir Lyon Playfair attentively, but anything more hopelessly commonplace than his discourse it would be difficult to imagine. The stalest fallacies of the vaccinators were recited as if they had never been answered. The freshness consisted in the business-like assurance and plausibility, after the Scots manner, with which the speech was delivered. Not a single novel point was made.....We all love to have our prejudices flattered, and never more than when we suspect them to be questionable.'

White's diatribe might be dismissed as political knockabout were it not for the serious consequences of a smallpox outbreak.

Throughout the pamphlet White questions Playfair's statistics. The latter quoted many examples where the incidence of smallpox in two groups, one vaccinated and the other not, was compared. In all the cases he quotes, unsurprisingly, it is lower in the former. However, by modern standards, the groups are not well matched and effects other than vaccination *could* explain the effect. White credits the differences to changes in hygiene and public sanitation which had had such a beneficial effect in reducing the incidence of other infectious diseases such as typhoid and cholera. With modern knowledge of the causation and transmission of smallpox it is clear that this cannot be the case but White could not know that. A few distinguished scientists, including Alfred Russel Wallace, were also unconvinced by the statistical evidence. Others, including many clergymen, objected to compulsory vaccination on moral or spiritual grounds. The Genesis story of creation sets man apart from other animals and to introduce something into a man from a diseased animal was to deny man's status. Secretly, some saw smallpox as a way of controlling the size of the working class population. At the same time, in working classes circles there was a curious suspicion of vaccination. They rarely saw a doctor and their most frequent contact with the medical profession was when there was an epidemic. The simplistic conclusion was that doctors brought disease and compulsory vaccination was another part of the capacity of doctors to generate illness rather than cure it.

Playfair, in his House of Commons speech, attempted to deal with the question of personal freedom and the control of smallpox epidemics. His conclusion was that it should not be left to the conscience of the individual:

'A man may burn down his house if he injures no-one but himself. If he affects his neighbours we punish him. Likewise smallpox vaccination.'

In reading White's polemic against Playfair it is clear that White is not a scientist and it seems likely that his fundamental objection was moral or religious and he uses scientific data merely to substantiate his view. But why was he so bitterly opposed to compulsory vaccination?

White wrote a short and generally unrevealing biography.⁷ He was born in Glasgow of Quaker stock but rebelled

against the tedium of Quaker meetings for worship and the evangelical zeal of the boarding school to which he was sent. His rebellion against organised religion was reversed when he read, quite by chance, a book by the Swedish scientist and mystic Emanuel Swedenborg. Swedenborg is, today, an almost forgotten figure but, in his time, was a person of some substance. Born in 1688 in Stockholm, the son of a Lutheran bishop, he studied at Uppsala, entering the university at the age of eleven. Later he travelled extensively in Europe to broaden his intellect but returned to Sweden in 1722.

In 1724 he was made secretary to the Swedish Board of Mines by Charles XII and later published a massive book on mineralogy *Opera Philosophica et Mineralia* which won for him praise from savants throughout Europe and allowed him to correspond with the leading scientists and philosophers of his day. Later he set about writing books describing the state of understanding of all branches of natural philosophy. The language he used was Latin. At the age of 55 he underwent a curious conversion that caused him to switch from science to theology. From then on until his death in London he was the author of many wordy books in Latin based, so he claimed, on conversations he had with angels on religious matters. He set out to describe the soul and the heavenly kingdom in the same detail he achieved for the earthly world and to reinterpret Scripture in the light of these conversations.

The most complete statement of his insights is given in the twelve volumes of the *Arcana Caelestia*, the first volume of which appeared in 1749. The new doctrines have attracted the attention of some distinguished people including William Blake, Ralph Waldo Emerson, August Strindberg, William Butler Yates, Elizabeth Barrett Browning and, somewhat incongruously, John Wesley. The best known modern commentator is the poet and Blake scholar Kathleen Raine, one of whose poems gave Gavin Maxwell the title of his trilogy 'Ring of Bright Water'. To summarise Swedenborg's ideas briefly is impossible but, for present purposes, it is sufficient to say that he blurred the distinction between the material and the spiritual. He writes:

*'Man was created as to be at the same time in the spiritual and in the material world.'*⁸

There is no resurrection of the body in Swedenborg's system; the life after death is a continuation of what we have now. White embraced Swedenborg's teachings with

enthusiasm and became manager of the bookshop of the Swedenborg Society in London. Unfortunately he was dismissed under a cloud and much material relating to him was destroyed.

According to the current secretary of the Swedenborg Society, there is nothing in the teachings of Swedenborg to oppose vaccination and he feels that White's commitment to the teachings was not the origin of his opposition. However, the distinguished medical historian, Roy Porter, takes a somewhat different view. He writes:

*'Influenced by the teachings of the mystic, Emanuel Swedenborg, some groups went further, discarding medicine altogether and trusting to the healing power of Nature, aided by water, prayer, self-control and spiritual illumination.'*⁹

The end of that road was, of course, Christian Science, which denies the reality of sickness. A further influence on White may have been William Wilkinson, an officer at the Swedenborg Society at the same time as White, whose brother, James John Garth Wilkinson, was a well-known homeopathic doctor and bitter opponent of compulsory vaccination.

In view of this and of Porter's judgment on the influence of Swedenborg on alternative medical therapies in Victorian times, it is not unreasonable to conclude that White's bitter opposition to compulsory vaccination, expressed so forcefully in his reaction to Lyon Playfair's speech was, in some measure, due to his association with the Swedenborg Society but his intemperate language is alien to the mild-mannered Swedenborgian movement. Subsequent events have proved, of course, that Playfair was right and White was wrong. The anti-vaccination movement is now a pale reflection of its former self and in the global eradication of smallpox, completed in 1975, Jennerian vaccination played an essential part.

Swedenborg died in London, as he predicted, in 1772 and is now largely forgotten. Playfair, greatly honoured by a grateful nation, died in 1898 and is buried in the Eastern Cemetery in St Andrews. His physical memorial is a water fountain near the Royal and Ancient clubhouse but his contribution to public health is his true memorial.

Acknowledgment

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For references see www.smj.org.uk

ABSTRACT OF SOCIETIES

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Oral Presentations

Angiotensin II receptor blockers as potential anti-inflammatory agents

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Objective Angiotensin II (AngII) plays an important role in regulating blood pressure via the renin-angiotensin-aldosterone system. Subsequently, it was found to have pro-inflammatory properties and long-term effects on tissue structure. Studies on angiotensin converting enzyme inhibitors (ACEi) and AngII receptor blockers (ARB) have suggested that their therapeutic effects are mediated by inhibiting AngII. In theory, ACEi and ARB could be used as anti-inflammatory agents. Captopril is already established as having anti-inflammatory properties, mediated by the thiol moiety unique to the drug. The purpose of this study was to establish in an animal model of arthritis whether ARBs have anti-inflammatory effects and in a retrospective audit to establish the anti-inflammatory effects of ARB by comparing inflammatory markers of rheumatoid arthritis patients who were on ACEi (ramipril or lisinopril), or ARB or neither. **Study Method** Adjuvant monoarthritis was induced under anaesthesia in the rat knee joint (n=6) treated with vehicle or the selective AT₁ receptor antagonist losartan (15mg/kg s.c. alternate days), these being administered both prophylactically and therapeutically. Joint swelling was monitored as an indicator of inflammation. Patients were identified from 2 centres – Glasgow Royal Infirmary (GRI) and Gartnavel General Hospital (GGH). Data were collected by patient questionnaire at GRI and by computer database at GGH. Data included disease modifying anti-rheumatic drug (DMARD) therapy, ACEi (ramipril and lisinopril) and ARB use, and corresponding C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) values. Results of CRP and ESR values of all patients were consolidated and statistical analysis performed. **Results** Rat joint swelling was significantly (P<0.0001) reduced (≥50%) by losartan treatment, both with prophylactic and therapeutic (day 12) intervention. Mean (± SD) ESR from RA patients on ARB (n=42), was lower (25.1±22.5) than that from patients on ACEi 30.8±29.2, n=58) or those on no angiotensin inhibition therapy (control group: 40.1±29.4, n=38), and these differed significantly (P=0.02, 1-way ANOVA, log₁₀ transformed). *Post-hoc* testing (Bonferroni) revealed only the ARB-treated group differed significantly (P=0.021) from the control group. Although a similar trend between groups was apparent for CRP, this was not significant using non-parametric statistics (data set not normalized by log₁₀ transformation). Adjusting for statin use, the difference in ESR between groups remained significant (P=0.036, 1-way ANCOVA). **Conclusions:** Inhibiting AngII has anti-inflammatory potential and ARB may be more effective than ACEi.

Mast cell deficient mice produce less circulating IL-6 and exhibit less cardiac tissue damage than their littermates following myocardial ischaemia reperfusion injury.

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Background Myocardial ischemia reperfusion (IR) injury complicates all forms of coronary artery revascularization. Circulating interleukin-6 (IL-6) has been implicated in cell death following a variety of stimuli. To date macrophages, platelets, neutrophils and the endothelium have been shown to release IL-6 after IR injury. Cardiac mast cells have been implicated in IR; however, their involvement has never been quantified. In this randomized prospective study, we compared cardiac tissue susceptibility and serum IL-6 changes between the mast cell deficient (W/W^v) mice and their normal littermates (+/+). **Methods** Twenty-four male W/W^v mice and their +/+ littermates were anaesthetized with 2.5% isoflurane. The left coronary artery (LCA) was ligated for 30

minutes or a sham procedure was performed. After 6 hours of reperfusion, the animals were sacrificed. The muscle viability was assessed on fresh whole-mount slices by the nitroblue tetrazolium (NBT) histochemical assay and serum IL-6 concentrations measured with ELISA. **Results** Cardiac muscle viability was significantly higher in W/W^v than the +/+ mice. Serum IL-6 levels were higher in the +/+ sham mice (163 ± 11 pg/ml, n=6) than the W/W^v mice (65 ± 11 pg/ml, n=6), p < 0.001. The IL-6 levels increased significantly after reperfusion only in the +/+ mice (245 ± 14 pg/ml, n=8, p = 0.001), while it remained similar in the W/W^v mice (71 ± 17 pg/ml, n=8, p = 0.783). **Conclusions** These results show that the absence of mast cells reduces the myocardial damage associated with IR injury. Furthermore, there is an attenuation in the inflammatory response, as measured by serum IL-6 levels, following this local insult. This finding entertains the prospect of developing prophylactic therapy - targeting selective inhibition of cardiac mast cell activation, in clinical situations involving medical or surgical myocardial revascularization.

Fluvastatin inhibits hypoxia-induced proliferation in pulmonary artery fibroblasts: role of prenylated signaling proteins

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Rationale Excessive proliferation of pulmonary artery fibroblasts (PAFs) is an early and important process in the pathophysiology of pulmonary hypertension and is seen in acute and chronic hypoxic models. Blocking this excess proliferation is a key goal for potential new pulmonary hypertension therapies. To further explore hypoxic signaling in PAFs we assessed the effect of fluvastatin on acute hypoxic proliferation. **Methods** PAFs were established in primary culture and used between passages 4-9. Cell proliferation was assessed by [³H] thymidine assay. Cells were quiesced in serum free media then stimulated with 1% serum +/- fluvastatin 1μM (F), mevalonic acid 1mM (M), squalene 25μM (Sq), farnesyl pyrophosphate 0.5μM (FPP) or geranylgeranyl pyrophosphate 0.5μM (GGPP). Cells were then maintained in normoxic or hypoxic (PO₂=35mmHg) conditions for 24 hours. **Results** [³H] thymidine incorporation was significantly increased in PAFs exposed to hypoxia. Mevalonic acid and its products had no individual effect. Fluvastatin blocked hypoxia-induced proliferation. Repletion with squalene (intermediate in cholesterol synthesis) had no influence on the statin effect but repletion with mevalonic acid, FPP or GGPP negated the statin's inhibitory effect. **Conclusions** Hypoxia-induced proliferation in PAFs is inhibited by fluvastatin at a pharmacologically relevant dose. Intact membrane lipid rafts are not implicated in hypoxic signaling in PAFs. Reversal of the inhibitory statin effect by GGPP implicates a geranylgeranylated signal protein such as Rho A as a key mediator of hypoxic responses in this cell type. This important signaling pathway is a promising target for the treatment of pulmonary hypertension.

BEST ORAL PRESENTATION**In-situ generation of N-nitroso compound from dietary nitrate via nitric oxide in the human upper gastrointestinal tract**

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Background The incidence of adenocarcinoma at the gastric cardia and, in patients with acid reflux, the distal oesophagus has increased markedly in the past 25 years. Scotland has the highest incidence of oesophageal adenocarcinoma in the world. The mutagen responsible for the rising incidence of adenocarcinoma at these sites remains unknown. We have previously demonstrated that high luminal concentrations of nitric oxide are generated from dietary nitrate where acid meets saliva in human subjects. Laboratory studies have shown that this nitric oxide can lead to the formation of carcinogenic N-nitroso compounds within the epithelial compartment of a stomach model. **Aim** To ascertain if the luminal nitric oxide derived from dietary nitrate exerts localised nitrosative stress and generates N-nitroso compounds