Sleep disturbance alters autonomic balance to the heart

Secrets of life from beyond the grave

#Biobakes
Welcome to the Winter 2014 edition of Physiology News

Introduction

05 Editorial

News in brief

06 #Biobakes
LifeSci TRC

07 Student-led ‘Physiology Challenge’ for Biology Week at the University of Leeds

08 Policy Focus

In depth

10 Cambridge physiology scores a century

12 Physiology on the go

14 A tribute to Bernhard Frankenhaeuser 1915-1994

Meetings & events

16 Forthcoming events

17 Meeting notes: Obesity – a physiological perspective

18 Young Life Scientists’ Symposium 2014

19 Meeting notes: International lecture 2014

20 We know where we are going but how do we get there?

Features

21 Human metabolism and obesity: the influence of exercise

25 Exercise: more than just a role in energy balance

28 Sleep disturbance alters autonomic balance to the heart

30 The mighty protein: Insulin-like growth factor type 1

34 Secrets of life from beyond the grave

Membership

36 Great textbooks of physiology

38 An affiliate’s view on networking and mentoring

40 Physiology to pedagogy

43 ETIS: facilitating research and training in in vivo physiology

43 The Benevolent Fund

44 Obituary: Alex Livingston

46 Journal updates

Membership Fees for 2015

<table>
<thead>
<tr>
<th>Membership category</th>
<th>Direct Debit</th>
<th>Non-Direct Debit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Member</td>
<td>£75</td>
<td>£95</td>
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<tr>
<td>Ordinary Retired Member</td>
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Editorial

Mike Collis
Editor, Physiology News

This is my final editorial for Physiology News (PN) as I am standing down as Editor at the end of this year. When I took over as editor in 2012, I posed the question, ‘Why should members pick up Physiology News to read when they have a pile of scientific papers to plough through?’ I also mused about the role of a quarterly hard copy magazine in an era where information can be transmitted almost immediately through electronic media. After acting as editor of PN for the last three years, I am reassured that the magazine is being read widely by members of The Society (84% according to the recent membership survey). Interestingly, about 70% prefer to read the hard copy, so even in a digital age, there is still a need for a paper magazine.

A further question I have asked myself is, ‘What is the unique selling point of PN? Is it primarily a means by which The Society trustees and associated committees communicate with the members? Or is it a vehicle for The Society office to keep members informed of past and new ventures? Is it primarily a publication that highlights new and interesting physiological science? Or a publication that reports on members’ activities – a way for The Society to promote itself to non-members? In truth PN is all of these, but integrating such a wide range of content from different sources needs good team work and a clear alignment of responsibility and authority. Fundamentally PN is (and should remain) a magazine for members, written and directed by members, with the expert help of Society staff.

I have been lucky to have had the support of a very hard working and enthusiastic editorial board. The board have a range of backgrounds, expertise and experience (including chairs of two Society committees) and broadly reflect the membership. Together we have introduced a wide range of articles: Science features and updates, the clinical application of physiological research, discussions on ethics, science policy and research funding. We have published articles on the activities of members, laboratory profiles, book reviews and, sadly, obituaries. A major innovation has been themed issues, which have featured Education, Imaging, The Pharmaceutical Industry and most recently Obesity. I am particularly proud of PN 97, which was produced to coincide with The Society hosting the IUPS 2013 meeting and included articles from many sister societies from around the world.

A new format and design for PN was introduced in 2012. The standardised format of contents has been well-received with the majority of members considering it a more enjoyable read than previously. The original re-design of the magazine received mixed comments from members and the board. We all feel that ‘content is king’ and that the simpler design we have now adopted provides a modern look and feel, without compromising the content or gravitas of Physiology News. Identifying compelling cover images for each issue, which encourage the casual reader to pick up the magazine, has been a challenge. We would welcome relevant images from members of The Society that would fulfil this important function.

This edition (PN 97) contains the usual diverse mix of articles. Scientific features written by members are included that present an area of research in a more ‘digestible’ form than is typical in a research paper or review. Feedback from members indicates that these types of accessible scientific articles are much appreciated and are often useful as teaching aids. Physiology News is of course not a peer-reviewed scientific journal and consequently we ensure that science based articles do not contain unpublished (un-reviewed) data. A delicate balance has to be struck between making physiological research more accessible and oversimplification. I hope that, as a board, we have got the balance right more often than not. The value of these science based articles would be increased if they could be searched easily online and I am pleased to say that there are plans to introduce a new platform for the archive to facilitate this in 2015.

There are many people who I want to thank for their support for PN over the last 3 years: the other members of the editorial board (Siobhan Dennis, Mike Evans, Sarah Hall, Jamie McPhee, David Miller and Keith Siew), the publications staff of The Society and of course all those who have contributed articles to the magazine. I am sure that Physiology News will go from strength to strength under the leadership of a new editor and wish all involved success with this important publication.
The Physiological Society joins the Life Science Teaching Resource Community

For several years, Society members have developed many digital teaching resources but we have not been able to find a mechanism for evaluating, managing, updating and delivering them. It became obvious very quickly that the Life Science Teaching Resource Community (LifeSciTRC) is the answer to this problem.

The LifeSciTRC is a dynamic digital repository managed by the American Physiological Society (APS) which provides teachers and lecturers with a comprehensive and diverse range of teaching aids aimed at students at different stages of their education.

Marsha Lakes Matyas, APS Director of Education Programs, says, ‘We are excited to welcome The Physiological Society as the newest LifeSciTRC partner, and look forward to collaborating in other activities as well.’

Other partner organisations include the Human Anatomy and Physiology Society, the Society for Developmental Biology, the American Association of Anatomists, and the Genetics Society of America.

As a part of this community, Society members can access a range of teaching resources that can be used in their entirety or adapted to specific requirements. In essence, if you need to deliver a new teaching activity, we would strongly recommend you explore the LifeSciTRC to investigate what is already available in your subject area. This can save you time and give you new ideas for activities.

Members of the partner organisations can also submit their own teaching resources for evaluation and review by The Society – if accepted, they will be uploaded for all to use! If you have any particularly useful resources, we would encourage you to submit them so that they will benefit the whole community.

Contributions from Society members will be marked with The Society’s logo, thereby establishing a community for members to use and share resources with each other. A set of FAQs for submission of teaching resources will be available via The Society’s website over the next few months.

Furthermore, we are also looking for interested members to act as referees for submissions to the LifeSciTRC. If you are interested, please contact Angela Breslin at education@physoc.org.

In the meantime, please take the time to register as a member of the LifeSciTRC, which is free, and explore the repository to find out which activities might be useful for your teaching, outreach or public engagement activities http://www.lifesctrc.org/

Student-led ‘Physiology Challenge’ for Biology Week at the University of Leeds

Physiology Friday, the annual event supported by The Physiological Society as a finale for ‘Biology Week’, aims to engage with science in a novel way. This year, the challenge was set by Dr Charlotte Haigh, an associate professor in Human Physiology at the University of Leeds, and James Croft, a final year Human Physiology student, to ‘design and run a fun and engaging stall for the local Leeds public at Leeds Central Library’.

Teams of six, which each contained undergraduate BSc Human Physiology students from each year, engaged the public with a range of physiology themed stands: Alzheimer’s disease and neuro-degeneration, cardio-pulmonary health, diabetes, and the science of hangovers. Rose Bavidge, Outreach Officer for the Faculty of Biological Sciences, said of the event, ‘It always amazes me how much undergraduates want to get involved in these activities and how much effort they put into these events. We will certainly be working with more undergraduates on public events like this in the future.’

Students evaluated the success of their efforts and were marked on the quality of their presentations, impact of their projects and the effectiveness of their engagement strategy. The activities culminated in a social quiz within the students’ union bar, and marks from both the outreach project and quiz were used to select a winning team. James Croft commented, ‘There is a University-wide drive to promote our research findings not only within the scientific community, but also into the public eye. The week ended in a social quiz, and, aside of anything else, outsmarting some of our lecturers was great fun!’

Chris Salmon, a third year student, elected to use peak flow meters to inform the public about obstructive disorders such as asthma, and the effects of smoking, in line with the NHS’s Stop smoking campaign. He said, ‘It was a challenge trying to communicate principles learned in lectures to the public in a fun and easy to understand way, but we think the visitors to our stand were left feeling improved.’

Jordan Appleyard, a second year student, designed a mountain range with the peak flow readings of famous athletes, singers, the average person and smokers to allow people to compare their peak flow readings with those of celebrities. He found the Physiology Challenge ‘a great way to make friends with other Physiology and Biomedical Science students in different years, and a way to engage with members of academic staff outside lectures.’

This outreach activity was a great success and introduced undergraduate students to public engagement on behalf of both our institution and The Physiological Society. We look forward to running the Physiology Challenge again in 2015.

Physiology Feed

Bringing you snippets of the latest intriguing research

Sugar linked to memory problems and brain inflammation in adolescent rats

A diet high in sugar impaired hippocampal-dependent spatial learning and memory in adolescent but not adult rats. This research indicates that consumption of added sugars negatively affects hippocampal function, metabolic outcomes and neuroinflammation when consumed in excess during the adolescent period of development.

DOI: 10.1002/hpo.22368

Mood food – omega 3 supplements beneficial in treatment of depression

Two studies showed that omega 3 supplementation prevents detrimental chronic stress-induced emotional and neuronal impairments by expediting hypothalamic–parietal–amygdala (HPA) axis hyperactivity, as well as depression in hepatocellular carcinoma.

DOI: 10.1126/science.1254426

Researchers watch dynamic motion of HIV as it reads an attack

Researchers at Weill Cornell Medical College have developed technologies that allow them, for the first time, to watch what they call the ‘dance’ of HIV proteins on the virus’s surface, which may contribute to how it infects human immune cells.

DOI: 10.1038/npjhc.1628

How rapies ‘hijack’ neurons to attack the brain

Researchers discovered that the rabies virus ‘hijack’ the brain’s transporting cell components along a neurological pathway straight into the spinal cord. Once in the spinal cord, the virus attacks the first available transmission within the brain, where it wreaks havoc before spreading through the rest of the body, shutting it down organ by organ.

DOI: 10.1371/journal.pntd.0004348

Continues overleaf
Policy Focus

While politicians were enjoying summer recess, The Society’s policy work was at full speed.

Engaging with Parliamentarians

Following the launch of the Engaging with Parliamentarians Scheme at the House of Lords in June, we were delighted to welcome around 30 Society members to Hodgkin Huxley House in September for the Engaging with Parliamentarians training day.

The day was designed to provide information on the policy-making process, encourage members to think about policy development, and provide an opportunity to explore how policy issues are communicated by The Society. This was the first time The Society has run such an event and a number of lessons were learned. In 2015 the Policy Committee will be developing new policy positions on the key issues that were identified at the meeting as core concerns for The Society and its members. The Committee is also keen to ensure that the communication of ongoing policy work is improved, with opportunities for members to help shape policy positions.

The Health of Physiology

The Health of Physiology review is a major project being led by the President and the Chief Executive of The Society. It is reviewing physiology as a scientific, medical and educational discipline in the UK and Ireland, looking at data across a range of metrics including student numbers, research funding and publication data. In September separate stakeholder meetings were held with members and external organisations to gauge opinion.

Interestingly there was much similarity in the discussions, including – the teaching and learning of physiology in schools and universities; academic research and ties with industry; and concern for the profile of physiology and The Society. One of the recommendations for the future was for The Society to be more externally focused, with the external stakeholders encouraging greater collaboration.

The Society is currently gathering the views of industry and will also be seeking student opinion. The findings from all the key stakeholders will be incorporated into the final report and will help shape the future strategy for The Society. The report will be launched in 2015.

Letter to the Prime Minister

On 12 August The Society wrote to the Prime Minister in response to comments made by Norman Baker MP, the Home Office Minister with responsibility for animal research. He was quoted in the media as saying he wanted ‘to see an end to all animal testing’. Our letter strongly urged the Government to understand the clear and vital need for the continued use of animals in scientific procedures and instead he looked forward to the day, ‘in the far–off future, when science has developed techniques that make use of animals redundant’.

We received a response from Mr Baker explaining that he had not called for a ban on all use of animals in scientific procedures and instead he looked forward to the day, ‘in the far–off future, when science has developed techniques that make use of animals redundant’.

Section 24 reforms

In June The Society responded to a Home Office consultation on proposed changes to Section 24 of the Animals (Scientific Procedures) Act. At the time of writing The Home Office has yet to formally announce what changes will be made to Section 24, once they do we will communicate these through The Society’s usual channels.

If you would like to know more about or contribute to the policy work The Physiological Society performs on behalf of its members please email Ed Hayes – ehayes@physoc.org

Interested in these or any other policy related issues? Please contact us via policy@physoc.org

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Cambridge physiology scores a century – 100 years of The Physiological Laboratory, University of Cambridge

Sue Jones & Roger Keynes
Department of Physiology, Development & Neuroscience, University of Cambridge, UK

Physiology took off in Cambridge when Michael Foster arrived there in 1870. He had a remarkable influence, inspiring students and co-founding both the Physiological Society and The Journal of Physiology. As his Cambridge School flourished, it needed to house an increasing number of talented students and young researchers, including future Nobel laureates AV Hill (1922), FG Hopkins (1929), CS Sherrington (1932), ED Adrian (1932) and HH Dale (1936). When two disused coal cellars had been pressed into service as labs, it was clear that a new building was urgently needed. The Worshipful Company of Drapers provided funding for a fine new home, designed under the careful eye of Foster’s protégé, John Newport Langley, and the Physiological Laboratory opened in full ceremony in 1914. One hundred years later, in September 2014, the Department of Physiology, Development and Neuroscience (PDN) hosted a series of events to celebrate the Centenary. Our aim was to give insight and inspiration to a wide audience about what physiology is, what it has achieved and contributed in the past, and what it continues to contribute today.

The opening event took place on 2 September 2014 with over a hundred invited guests: colleagues from across the University of Cambridge, including the Vice-Chancellor; physiologists from nearby Universities and from funding agencies, scientific journals and Societies, family members of our alumni, local Sixth Form students, and the Mayor of Cambridge. After a welcome from our Head of Department, Bill Harris, we heard from Roger Keynes about Foster’s inspirational teaching and Langley’s quest to understand all aspects of autonomic nervous system function, then from Andrew Murray about studies of high altitude physiology, pioneered by Sir Joseph Barcroft, continued by Bryan Matthews, and still a strong area of research in the Department of PDN. Chris Huang reviewed the innovative work of past nerve and muscle physiologists, including AV Hill, Lord Adrian, Sir Alan Hodgkin and Sir Andrew Huxley. Chris also reminded us that Roger Tsien joined The Physiological Laboratory as a PhD student of Richard Adrian and then continued as a Research Fellow. Martin Johnson gave a moving account of the scientific, medical and social impact of Sir Robert Edwards’s research in the field of Reproductive Physiology. Guests then visited interactive displays, where demonstrations, real experiments and a range of physiological measurements were in action. Around 40 volunteers designed and ran the displays, including graduate students, postdocs, academic staff and support staff from PDN, and there was much-appreciated help from our colleagues at Anglia Ruskin University. Sir Colin Blakemore closed the afternoon’s events with a Centenary Lecture – a personal account of his experience as a young neurophysiologist in The Physiological Laboratory. Through his anecdotes and reminiscences we were reminded of further achievements in the one hundred year history of the building. Guests and volunteers then had the opportunity to mingle and ‘network’ at dinner in the Great Hall of Trinity College.

By all accounts the occasion was informative and enjoyable, and served as a positive reminder of the past and continuing importance of physiology. Our volunteers, in their distinctive green Centenary T-shirts, ran their interactive displays enthusiastically on three more afternoons in September for local GCSE students and interested members of the public. Further information about the Centenary events can be found on http://www.pdn.cam.ac.uk/centenary/index.shtml.

The events were supported by the Department of PDN, the Wellcome Trust Institutional Strategic Support Fund, The Physiological Society, Trinity College Cambridge and St John’s College, Cambridge.

References
Langley JN (1883). The arrangement of the sympathetic nervous system, based chiefly on observations upon pilo-motor nerves. J Physiol, 17, 248.

All photographs courtesy of Adrian Newman

More information about the families of our alumni can be found at http://www.pdn.cam.ac.uk/centenary/index.shtml.
Physiology on the go

Vadim Alexeenko
University of Surrey, UK
Anna Shumitskaya
Independent telecommunications journalist

Physiology on the go

Physiology is one of the health sciences that embraced the use of computers as soon as they became available, and has heavily relied on digital equipment ever since. As technology progressed, digital devices grew in capability and shrank in size and weight, ultimately becoming portable and connected, at first via wired networks. A recent boom in mobile communications has enabled portable devices to stay online and maintain the link with data processing centers virtually anytime and anywhere. This change has not yet affected the health sciences, but it is the wave of change that seems to be on its way.

Physiology, as the science of body function, has always needed to record the tissue or organ response to stimuli, and almost till the end of the last century every physiology laboratory had an extensive collection of chart recorders and paper rolls used for analogue data collection and storage. Even now, if you go through the laboratory cupboards, very likely you will find one or two such ‘fossilised’ devices. Most likely they are preserved purely for sentimental reasons, while the ‘real science’ went fully digital long ago. The major driving forces were the prospects of easy access to huge volumes of data, the power of numerical data analysis and the ability to automate the experiment.

The determination to use computers was so strong that the first electronic devices, used to control experiments or treat the patient, were bulky, consequently limiting the subject’s movements to the immediate vicinity of the apparatus (Fogt et al 1978). However, the ultimate aim of life sciences is not to gather physiological data or cure a patient who is tethered by wires and tubes to a computer, but to help them have as normal a life as possible, and this means mobility.

Mobility for a medical device can come in different forms. At its simplest it takes the shape of an external device connected by sensors to a patient, like a Holter heart rate monitor or glucose monitor. More complex technologies that can augment or replace physiological functions include implantable prosthetic devices: pacemakers, defibrillators, cochlear implants, sacral neuromodulators and drug pumps. Such implants do not restrict patient movement and can substantially increase their quality of life. But these implantable digital devices overcome quite a few technological challenges. First, there is a requirement for compact and energy-efficient computers, sporting high precision analogue-to-digital and digital-to-analogue converters to interface the implant. Secondly, an appropriate set of sensors is needed to read the relevant physiological information. The list of such parameters might be long: electric potentials, blood or other liquid pressure, oxygen and glucose concentration; this list is by no means exhaustive. Thirdly, if the implantable device is intended for drug delivery, then a pump is a must. Lastly, and perhaps most importantly, an efficient and compact power source is essential to supply the implant.

Some of these tasks were solved by microfluidics technologies – tiny liquid pumps with the smallest of them being less than a few cubic millimeters. Others were addressed by development of biosensors: for example, it is now possible to detect blood glucose content using optical methods (Ozana et al 2014). A highly competitive telecommunications market has helped to shrink the size of portable electronic devices, hugely increased the capacity of their batteries, and introduced wireless charging technology to the mass market. Application of the same technologies to implantable devices has brought similar benefits of decreased size and power consumption; wireless charging is now available for devices that are implanted several centimetres deep (Ho et al 2014).

However, an important feature of implantable devices that has not been mentioned is that they have the ability to collect data and relay it to external data storage centres for further analysis by healthcare professionals. The increased capabilities of portable electronics make it even possible to perform a limited data analysis on the implantable or wearable device. This can restrict the uploaded data to just those segments that report deviations from the normal state and enabling the device to alert medical services and carers of potentially dangerous situations. A review analysing continuous cardiac monitoring devices, piloted in France, indicated a four-times quicker intervention response compared with conventional monitoring strategies (Maild et al 2014).

The progress of telecommunications has made the link between an implantable device and a remote data centre much more feasible than was previously possible. During the last decade, considerable effort has been directed towards the development of methods to facilitate data exchange between stationary and mobile digital devices – machine-to-machine technology (M2M). Originally conceived for automation and instrumentation, now it also covers various telematics applications, and buzzwords such as ‘connected revolution’ or ‘internet of things’ became a commonplace in the telecommunications world.

Proper functioning of such technologies requires permanent network connectivity and this might have had an influence on the paradigm shift in the design of mobile networks. The development of all previous standards of mobile communication technologies was aimed primarily at increasing the data transfer rate as the most important parameter, and loss of service in some locations was treated as a valid trade-off for high data transfer rates in the neighbouring places. The upcoming standard of fifth-generation mobile network (5G) is expected to be adopted in early the 2020s and, according to Professor Rahim Tafazolli, the head of the 5G Innovation Centre in the UK, the new standard will focus mostly on availability of digital services, with the ultimate aim of the total elimination of ‘bad reception areas’.

Other important features of 5G devices will include increased energy efficiency, reduced delays and latencies, and better management of portable device resources.

It is still too early to make any assumptions on a final shape of the 5G standard, but one can now make some informed guesses as to the possible uses of its features: mobile phones used as portable remote cardiac monitoring base stations is just one of them. The exciting possibilities for other futuristic medical gadgets may emerge very soon. And one of the key things to make it happen is a tight collaboration of telecommunication scientists and health scientists.

References


Bernhard Frankenhaeuser was born in 1915 in the small town of Borgå in the south of Finland where his father was an architect. He went to school in Borgå and then started to study medicine in Helsinki in 1934. Late in 1939 the Soviet Union attacked Finland and the so-called Winter War started. Bernhard was called into the Finnish army and served as military doctor both in the Winter War and in the so-called Continuation War (1941–44). Very much later, he told dramatic stories about narrow escapes from the advancing enemy. When the war was over, Bernhard finished his studies and obtained his medical degree in Helsinki in 1946. In that year he also met Marianne von Wright and they married after having known each other for just a few months. Marianne later became a world authority in stress research. They had their only child, a daughter named Carola, in 1949. She is married (Ludé) and is now a Professor of Occupational and Environmental Dermatology at the Karolinska Institutet.

By 1939, Bernhard had already come into contact with Ragnar Granit, then Professor in Physiology at the University of Helsinki. After the war, Granit helped Bernhard to go to Oxford. There he met William Rushton who made a deep impression on him, as did the whole British School of Physiology. In Oxford, Bernhard undertook the experimental work that was the foundation of his doctoral thesis, which he defended in Stockholm in 1949. Bernhard had been in contact with Granit during the years after the war and moved to Stockholm (with Marianne) in 1946. Granit had already moved to Sweden in 1940 and set up a laboratory at the old Karolinska Institutet. In 1946, Grant was offered a chair at the new Karolinska and his own institute, which he accepted. Bernhard joined Grant at the new Nobel Institute for Neurophysiology in 1947.

Between 1950 and 1952, Bernhard worked on accommodation in single nerve fibres of the frog. He was also interested in the mechanism of saltatory conduction in myelinated nerve fibres. In 1952 Bernhard met Alan Hodgkin at a meeting in Cold Spring Harbor. Hodgkin and Huxley had just published their famous papers on the mechanism of nerve impulse conduction. Their voltage clamp experiments had revealed the voltage- and time–dependency of the Na+ and K+ conductances in the axon membrane; the ‘H–H’ equations gave a quantitative description of the mechanism underlying the nerve impulse. Still, it was not known how the opening of the ion channels in the axon membrane came about. Frankenhaeuser and Hodgkin decided to test the hypothesis that Ca2+ acts as a ‘plug in the hole’ that controls the conductance. This idea originated from the knowledge that the Ca2+ concentration of the external medium influenced excitability. Voltage clamp experiments were again performed on the squid giant axon at the Marine Biological Laboratory in Plymouth. They found that changes in Ca2+ concentration shifted the voltage dependency of the ion conductances – as predicted by the hypothesis – but the effect was not large enough. Nevertheless, the findings about the Ca mechanism were of great importance and this paper has been highly cited.

Hodgkin and Huxley had clarified the mechanism of impulse generation in squid axons. But vertebrate myelinated nerve fibres have a different structure. Huxley and Stämpfli had shown that impulse propagation in myelinated fibres is saltatory. But which ionic currents underlie the nerve impulse at the node? In order to answer this, a method was required that allowed voltage clamp of the isolated nerve fibre. After several false starts, and when Bernhard was near despair, he finally managed to get the method to work. Using negative feedback, the longitudinal currents could be controlled and the membrane potential recorded. This was decisive for allowing control of the membrane potential with yet another feed–back amplifier and obtaining a voltage–clamp system. With the new method in hand, Bernhard made a thorough analysis of the nodal ionic currents and discovered many similarities with the squid axon membrane, but also some interesting differences. Bernhard was one of the pioneers in computer simulation of biological processes and managed, together with Andrew Huxley, to recreate a nodal action potential using his experimental data and advanced programming.

One aim at the onset of the voltage–clamp experiments on the node was to try to resolve ‘quanta’ in the recorded ionic currents. The node is especially suitable for this approach because of the very restricted membrane area. Bernhard did not quite reach his goal, but his method of noise analysis was of a pioneering kind.

Bernhard had a position as researcher at the Swedish Medical Research Council between 1963 and 1965, was Professor in Physiology at the University of Umeå 1965–67, and succeeded Granit as Professor in Neurophysiology at the Karolinska Institutet and as Director of the Nobel Institute for Neurophysiology in 1967 until his retirement in 1981. A characteristic of Bernard as a scientist was his aim at perfection. He could spend many weeks, even months, at refining a technique: it was all or nothing – he would never engage in mediocre science. Bernhard is author of 49 publications listed in PubMed and contributed to at least equally as many as supervisor. For him it was natural to share his vast knowledge generously and to work with the manuscripts of pupils and colleagues.

I remember Bernhard as extremely knowledgeable about electronics: from the beginning in the laboratory he constructed his own equipment – very much the British style. He also designed a large part of the electronic equipment for other people in the department. He was very generous with his knowledge and put together a lab programme for us beginners to increase our understanding of the mysteries of electronics. Bernhard had many collaborators (post-docs) from other countries as well as a number of Swedish PhD students (including myself) of which he took very good care.

Questions about the threat to the environment were something that engaged Bernhard at an early stage. He was an ardent (and very well-informed) opponent of nuclear power and was politically active. He took part in the debate in Sweden which raged in the 1970s. He was also very concerned about phosphate eutrophication and the risk of lack of oxygen in the Baltic, as well as the use of pesticides such as DDT and PCB. Bernhard was in fact one of the pioneers in environmental science, which is now such a hot topic.

Bernhard was not only generous with his knowledge in mathematics and electronics, but also generous outside the lab. Many of us remember his summer parties at his house in Saltöbaden, southwest of Stockholm, close to the water, where the whole department was invited. Not far from his house, his beloved Dulcibella, a relatively big sailing boat, was moored. Some of us PhD students were recruited as crew onboard Dulcibella and sailed with Bernhard in the Åland archipelago where he tried (with mixed results) to teach us navigation and seamanship.

The starting point of this portrait of Bernhard was a photo – collage, made by some of his pupils just before his retirement. The collage was given to Arne Walhorn, a well-known engraver and famous for his miniature engravings for postage stamps. He made a large steel engraving and, from the steel block, a limited number of prints were made. The artist has been playing a little when drawing the voltage clamp circuit and it is up to the reader to discover the error – no prizes given!

References


Jan Lännergren

Karolinska Institutet, Sweden

A tribute to Bernhard Frankenhaeuser 1915 – 1994

‘Bernhard was one of the pioneers in computer simulation of biological processes and managed, together with Andrew Huxley, to recreate a nodal action potential using his experimental data and advanced programming’
Obesity – a physiological perspective

Our first ever Topic Meeting took place at the Newcastle United Football Club, Newcastle upon Tyne. This year’s theme was Obesity: a physiological perspective. With over 200 attendees, 20 symposia and 80 poster presentations, it is safe to say that the meeting was highly successful and well attended.

The conference took us on a journey into the complex nature of obesity. Topics range from causes of obesity, obesity during pregnancy and metabolism, and cardiovascular consequences of obesity, to mechanisms underlying the physiology of appetite control, as well as the impact of obesity on society and possible lifestyle interventions to challenge obesity.

We are looking forward to seeing you at our next Topic Meeting, on Ageing and Degeneration, which will take place on 10–12 April 2015 in Edinburgh.

Meetings & events

2015 Forthcoming events

<table>
<thead>
<tr>
<th>Event Name</th>
<th>Date</th>
<th>Venue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiology 2015</td>
<td>28 Mar–1 Apr</td>
<td>Motorpoint Arena, Cardiff, UK</td>
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<tr>
<td>Ageing and Degeneration: A Physiological Perspective</td>
<td>6–8 July</td>
<td>The Convention Centre Dublin, Republic of Ireland</td>
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2016

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<th>Event Name</th>
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<tr>
<td>Physiology 2016</td>
<td>29–31 July</td>
<td>The Convention Centre Dublin, Republic of Ireland</td>
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The Young Life Scientists’ Symposium (YLS2014) was held at King’s College London on October 2014, with the theme The Physiology & Pharmacology of TRP channels. The symposium was supported by The Physiological Society, the Biochemical Society and the British Pharmacological Society in addition to King’s College London, and was sponsored by various biotechnology companies.

The symposium attracted about over a hundred national and international early-career researchers, and held vivid discussions on the cutting-edge research on the physiology, pharmacology and biochemistry of TRP channels. Additionally, YLS2014 incorporated engaging workshops on the future of publications (F1000) and outreach opportunities, including Dr Julie Keeble’s experience with the Mission Discovery committee. The symposium was concluded with a ‘Spicy TR(i)P’ to Masala Zone for some

Achievements were celebrated with numerous prizes from F1000 and the organising committee. The symposium was concluded with a ‘Spicy TR(i)P’ to Masala Zone for some

Achievements were celebrated with numerous prizes from F1000 and the organising committee. The symposium was concluded with a ‘Spicy TR(i)P’ to Masala Zone for some
opportunity to learn how the reforms in education and social policy initiated by the previous President of Brazil, Dr Lula, had affected physiological teaching and research. It proved to be a revealing visit.

My first stop was in Recife where I was hosted by Carol Leandro and Joao Henrique da Silva Costa of the Federal University of Pernambuco. This is a relatively poor state and the reforms have led to a major expansion of education including the establishment of new universities in deprived areas. The university has a major campus in Recife and a second some one-hour’s drive inland. The Department of Physiology is situated within an Institute of Public Health as well as having links to biomedical sciences. There is an emphasis on research into obesity which is a major national problem as in most western societies. Joao provides a physiological approach to understanding the relationship between obesity and cardiovascular disease. Carol is a leading player in major international programmes studying obesity and its social impact. Their labs were well-developed and I was impressed by the students’ and academics’ commitment to the ethos engendered by the reforms. As in every department that I visited in Brazil, the students were enthusiastic and showed genuine interest in discussion on my presentation and their own research.

My trip finished with a drive north to the town of Joao Pessoa in Paraiba State. Here my visit was hosted by Prof Valdir Birga who heads a thinly staffed department in a recently established biotechnology institute in the Federal University of Paraiba. This has been supported by both government and state resources and seeks to develop novel drugs from the wide variety of plants that are unique to Brazil. The brief on translation does not distract from the keen determination to develop a strong basic science presence. The institute has already identified two lead compounds that will enter preclinical trials. It was clear from my visit to the north-east that the reforms have had a major impact in both socio-economic terms but also in the recognition of the importance of higher education and research in facilitating these advances. Physiology is clearly playing its part!

Features

Human metabolism and obesity: the influence of exercise

This article discusses the effects of physical activity and exercise programmes on human metabolism and obesity. It demonstrates how exercise and physical activity are important regardless of body weight or composition, and reports on a number of successful interventions including community-based exercise programmes that have reduced body fat and improved health outcome markers in overweight/obese individuals.

Dr Naomi Brooks & Dr Stuart Galloway
Health & Exercise Sciences Research Group, University of Stirling, UK

As at its most simple, obesity is considered to be caused by increased energy intake without corresponding energy usage. However, it is not that simple. Environmental and behavioural factors including increased calorie consumption and food intake (foods high in sugar and fat) can influence the energy imbalance. Decreases in physical activity also contribute, some would argue more so, to the obesity crisis. Physical inactivity and sedentary lifestyle are independent risk factors for metabolic disorders. Adequate physical activity is required for metabolic health and acts to reduce risk factors associated with atherothrombotic and metabolic disorders, particularly rectifying high blood pressure, insulin resistance, glucose intolerance, low HDL-cholesterol, high LDL-cholesterol, and high triglycerides. Physical activity in addition to reduced sedentary time (sitting less) is therefore recommended in both prevention and treatment of these metabolic disorders.

An increased body mass, measured by body mass index (BMI) mass (kg)/height (m$^2$), has been consistently reported to be linked to increased mortality and morbidity throughout the lifespan. The recommended BMI for a healthy individual is 18.5–24.9 kg/m$^2$; overweight is defined as BMI of 25–29.9 kg/m$^2$ and obese is defined as ≥30 kg/m$^2$. However, BMI does not take into consideration body composition or location of fat mass.

Obese individuals develop health complications due to an increasing number and size of adipocytes (increasing fat mass). The increased size and number of adipocytes leads to dysfunction and cellular stress which contributes to insulin resistance, increased inflammation and increased circulating lipids (for detailed review see Capurso & Capurso, 2012). Obese individuals develop resistance to the cellular effects of insulin, which displays as an impaired ability of insulin to stimulate glucose uptake from plasma into fat and muscle cells. It is thought that increased fatty acids (FAs) combined with lipid metabolites/signalling molecules interfere with the insulin-signalling pathway and can impair the actions of insulin and contribute to...
Insulin resistance (Fig. 1). The resistance to the action of insulin results in elevated plasma glucose concentration (see Table 1 for normal values). The pancreas continues to secrete insulin in an attempt to reduce blood glucose concentration and eventually the beta-cells fail, and individuals with type 2 diabetes then require insulin therapy.

The adipocytes themselves are not inactive cells but are extremely important in human metabolism. Adipocytes secrete metabolically active proteins (adipokines) such as leptin, adiponectin and resistin, which contribute to healthy metabolism and are altered with obesity. Alterations of adipokine secretion lead to pathological consequences such as insulin resistance and increases in plasma lipid concentration. Adipocytes also contribute to the increased systemic inflammation noted with obesity, including increases in tumor necrosis factor-α, interleukin-6 and α-interferon. Indeed, the capacity to oxidise FA seems an important feature of insulin resistance and CVD. In addition, the resistance to insulin (Fig. 1) is now well recognised that can be more beneficial for health. Vigorous exercise at the high ends of the spectrum could fail, and individuals with type 2 diabetes then require insulin therapy.

Skeletal muscle is an extremely important metabolic tissue and uses glucose and fat as well as amino acids for energy production. Insulin signalling normally increases GLUT4 translocation, but with insulin resistance, glucose uptake into muscle is reduced. Thus, there are strong associations between aerobic fitness, amount of vigorous activity, and adiposity that are important in reducing cardiovascular and metabolic disease risk markers.

Figure 1. Insulin signalling normally increases GLUT4 translocation, but with insulin resistance this is thought to be blocked by accumulation of fatty acids metabolites such as long-chain acylcoA (LCACoA), diacylglycerols (DAG) and ceramides. That is, delivering of fatty acids is greater than the capacity for oxidation and/or storage as triglycerides. Figure simplified from Timmers et al. (2008). More detail from the original review article.

### Table 1

<table>
<thead>
<tr>
<th>Insulin Sensitivity</th>
<th>Healthy</th>
<th>Unhealthy</th>
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<tr>
<td><strong>Fasting glucose</strong></td>
<td>≤ 6 mmol/L</td>
<td>&gt; 6–7 mmol/L, impaired fasting glucose &gt; 7 mmol/L</td>
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<tr>
<td><strong>Fasting insulin</strong></td>
<td>1.4–14 μU/ml</td>
<td>&gt; 14 μU/ml</td>
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#### Lipid profile

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<tr>
<th>Lipid</th>
<th>Healthy</th>
<th>Unhealthy</th>
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<tr>
<td><strong>Total cholesterol</strong></td>
<td>&lt; 5 mmol/L</td>
<td>&gt; 5 mmol/L</td>
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<tr>
<td><strong>HDL cholesterol</strong></td>
<td>&gt; 1 mmol/L</td>
<td>&lt; 1 mmol/L</td>
</tr>
<tr>
<td><strong>LDL cholesterol</strong></td>
<td>&lt; 3 mmol/L</td>
<td>&gt; 3 mmol/L</td>
</tr>
<tr>
<td><strong>Triglycerides</strong></td>
<td>&lt; 1.7 mmol/L</td>
<td>&gt; 1.7 mmol/L</td>
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#### Blood pressure

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<tr>
<th>Blood pressure</th>
<th>Healthy</th>
<th>Unhealthy</th>
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<tr>
<td><strong>Systolic BP</strong></td>
<td>120 mmHg</td>
<td>&gt; 140 mmHg</td>
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<tr>
<td><strong>Diastolic BP</strong></td>
<td>80 mmHg</td>
<td>&gt; 90 mmHg</td>
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**Definitions**

Insulin sensitivity can be assessed by measuring fasting blood glucose and insulin levels and/or levels after a glucose drink (oral glucose tolerance test).

Lipid profile measures various lipids in the blood including triglycerides, total cholesterol, low-density lipoprotein (LDL)-cholesterol and high-density lipoprotein (HDL)-cholesterol.

Blood pressure is measured with a sphygmomanometer and normal values are 120/80 mmHg. Hypertension is considered to be when values are above 140 and 90 mmHg, respectively.

(Healthy values are in Table 1)

Values taken from NHS Choice
Physiology News / Winter 2014 / Issue 97

Exercise: more than just a role in energy balance

Improveing our understanding of the mechanisms by which physical exercise enhances health requires physiologists to isolate the relative effects of exercise per se.

Jean-Philippe Walhin, James Betts & Dylan Thompson
Department for Health
University of Bath, UK

Features

Research studies investigating the impact of exercise on health often show physical activity/exercise to be beneficial. However, energy status (deficit, balance, surplus) can have a profound impact on metabolism. To understand whether exercise leads to health improvements, energy balance needs to be carefully controlled.

Some excellent studies have already started to unpick the relative importance of exercise in the context of an energy deficit. For example, work by the CAREILIE team at Peninsula has used sophisticated designs where weight reduction was achieved either through caloric restriction alone, or through a combination of caloric restriction and increased structured exercise. The energy deficit elicited was matched between groups providing an equivalent role to caloric restriction in terms of energy balance, another study by the same group showed that exercise combined with caloric restriction did further improve metabolic function compared to caloric restriction alone (Larson-Meyer et al. 2010). Although understanding the contribution of physical exercise during a period of energy deficit or energy balance is extremely helpful in the context of weight loss, it is only part of the picture. It is likely that most individuals intermittently experience brief periods of positive energy balance and experimental studies focus on their impact on exercise and physical activity during periods of energy surplus or obesity.
reduced their physical activity to sedentary levels (~4000 steps per day) for 7 days. Half of the group performed a daily bout of vigorous-intensity treadmill running for 45 minutes. Everyone was asked to over-consume their habitual diet: the non-exercising group (SUR group) increased their energy intake by 50% whilst the exercising group (SUR+EX group) increased their energy intake by 50% plus the energy expended during the exercise (so the net energy surplus was matched in both groups). After one week and a surplus of around 17,000 kilocalories, serum insulin responses to glucose ingestion and biopsies of adipose tissue were taken. Results showed that participants from both groups gained weight during the course of the interventions. Fig. 1 shows the matched energy surplus induced in both groups.

The combination of short-term overfeeding and reduced physical activity had a dramatic impact on insulin sensitivity (Fig. 2). We demonstrated that after just 7 days of positive energy balance, fasting insulin concentrations increased and the ingestion of 75 g of glucose resulted in a ~2-fold increase in the insulinogenic response of healthy individuals. Our calculations suggest that excess carbohydrates would have resulted in a saturation of skeletal muscle and liver glycogen stores. It is likely this contributed to a saturation of skeletal muscle and liver glycogen stores. It is likely this contributed to a decrease in insulin sensitivity. Remarkably, the inclusion of a daily vigorous-intensity exercise bout largely prevented these changes from taking place even though extra food was provided to the participants in order to keep the energy surplus the same between groups. Thus, even though the SUR+EX group consumed even more energy in order to match the energy surplus of the SUR group, they were still better off at the end of the week.

Surprisingly few studies have focused on changes in the expression patterns of key genes in adipose tissue during a bout of energy surplus in healthy individuals, considering it is the major site for energy storage. The experimental model used in this study had a significant impact on the expression of several key genes within adipose tissue (Fig. 3). For example, overfeeding and reduced activity significantly increased the expression of both SREBP-1c and FAS transcripts in the SUR group. SREBP-1c is a transcription factor that regulates the expression of the lipogenic enzymes FAS. It is likely that the protocol used would have rapidly saturated liver and muscle glycogen stores favouring a lipogenic environment. The SUR group had little capacity for carbohydrate oxidation as a result of restricted physical activity. SREBP-1c has been linked with de novo lipogenesis (DNL) which has been shown to take place in adipose tissue, thus providing a route for the disposal of excess glucose. Other genes and proteins involved in key DNL steps such as SREBP-2 and AMPK were down-regulated, highlighting a switch of oxidative fuel from fatty acids to glucose. It is possible that these changes within adipose tissue may be a secondary response to the marked hyperinsulinaemia resulting from the positive energy balance induced by the overfeeding and reduced physical activity - although as we discuss in the full paper there are a number of other possibilities. It is particularly interesting that exercise exerted pronounced effects in adipose tissue, even whilst it was expanding (i.e. whilst people were gaining weight).

This study provides some of the strongest evidence to date that exercise is far more sophisticated than simply understanding the exercise component that regulates the expression of the lipogenic enzyme SREBP-1c. SUR+EX group compared to SUR result in highly significant increase in this enzyme.

Figure 1: Schematic representation of the energy surplus achieved by the overfeeding and restricted physical activity model in both groups. CHO = Carbohydrates; PRO = Protein; ETOH = Alcohol; RMR = Resting Metabolic Rate; DIT = Diet Induced Thermogenesis; MAEE = Physical Activity Energy Expenditure. Values are means ± CI.

Figure 2: Serum insulin 2h AUC (A), plasma glucose 2h AUC (B), means ± CI in response to the OGTT before and after a week of overfeeding and reduced physical activity. In *A* denotes a day/group interaction (P = 0.002). *A* denotes values different pre-post within SUR group (P = 0.001).

Figure 3: Relative gene expression of several key genes measured in adipose tissue at baseline and follow-up for the SUR group (n = 10) and the SUR+EX group (n = 12). Dashed line represents no change. Data normalised to PPIA, baseline and internal calibrator. Values are means ± SEM.

**References**


Sleep disturbances such as sleep apnoea can cause a chronic imbalance in the autonomic nervous system, and if left untreated, can lead to cardiovascular diseases.

One of the key consequences of OSA is a chronic imbalance in the autonomic nervous system, which serves to maintain homeostatic cardiovascular function as well as to protect against challenges and perturbations to the cardiovascular system. Both the sympathetic and parasympathetic divisions of the autonomic nervous system regulate neural control of the heart, with parasympathetic activity dominating this balance. A normal resting heart rate of ~60–80 beats/minute is maintained by the tonic parasympathetic activity to the heart, without which heart rate would become exaggerated (~100 bpm) with a higher risk of arrhythmias. While previous work by others has focused on how OSA elicits sympathetic overactivity, the goal of the current study was to study and identify the mechanisms responsible for diminished cardioprotective parasympathetic control of heart rate in OSA.

Parasympathetic cardiac vagal neurons (CVNs) are responsible for parasympathetic activity to the heart. The vagal descending projections from these neurons synapse upon parasympathetic cardioregulatory ganglion neurons located in close proximity to the vagus, to activate the parasympathetic activity to the heart. The changes responsible for diminished vagal control of heart rate were identified by studying the changes in blood pressure, heart rate and neurotransmission to CVNs evoked by acute hypoxia–hypercapnia and CIH. These changes were found to be consistent among different strains, ages and severities of OSA. However, beyond alterations in glutamate receptor density, little was known about how CIH impairs CVN function and what, if any, targets can be identified to restore cardioprotective parasympathetic activity to the heart.

The changes responsible for diminished vagal control of heart rate were identified by studying the changes in blood pressure, heart rate and neurotransmission to CVNs evoked by acute hypoxia–hypercapnia and CIH. The effects of CIH on CVNs were studied in detail in Dyavanapalli et al. (2014). Briefly, in vivo telemetry recordings of blood pressure and heart rate were obtained in adult rats prior to and during 4 weeks of CIH exposure. CIH exposures were performed by placing the rats in a commercial atmosphere controlled chambers, exposed to repetitive cycles of 2 minutes of mild hypoxia–hypercapnia (6% O$_2$, 5% CO$_2$, 89% N$_2$) followed by 3 minutes of normoxia (21% O$_2$, 5% CO$_2$, 99% N$_2$), repeated for 10~15 cycles, for weeks during the light phase. Fluorescently labelled CVNs were visualized and identified in an in vitro brainstem slice preparation obtained from adult rats exposed to either air or CIH for 4 weeks. Neurotransmission to CVNs, including postsynaptic inhibition and excitatory synaptic events, were recorded using whole cell voltage clamp techniques.

Our results have shown that chronic intermittent hypoxia–hypercapnia exposure for 4 weeks increases blood pressure to hypertensive levels and blunts cardiovascular reflexes in response to both acute hypoxia–hypercapnia and CIH. This likely occurs by the observed changes in the neurotransmission to cardiac vagal neurons that normally maintain a low resting heart rate. Specifically, cardiac vagal neurons received an increased frequency of inhibitory (both GABA & glycinergic) and depressed incidence of excitatory (glutamatergic) neurotransmission with CIH. These changes would act in concert to inhibit the activity of CVNs and diminish cardioprotective parasympathetic activity to the heart. These changes in cardiorespiratory network function within the brainstem would act to increase the heart rate, blood pressure and risk of adverse cardiovascular events that occur in patients with OSA.

In addition to identifying the adverse alterations responsible for reduced parasympathetic activity to the heart following CIH, the results from this study would predict that patients who have OSA and take sleep promoting medicines that typically act by enhancing inhibitory GABAergic neurotransmission within the CNS might be at heightened risk for a more significant reduction of critical parasympathetic activity to the heart. This study also provides a foundation for the development of potential therapeutic interventions to restore cardioprotective parasympathetic activity to the heart in patients with OSA.
The mighty protein: insulin-like growth factor type 1

IGF-1 plays a critical role in skeletal muscle growth during development, muscle regeneration and muscle hypertrophy in response to training.

Fan Ye & Stephen E Borst
University of Florida, USA

Muscle atrophy and weakness are common clinical phenomena observed following bed rest, surgery, cast immobilization and injury or disease. The consequences of loss of muscle function are far reaching and include decrease of motor control and overall fitness, development of functional limitations and impairment, and long term disability. The recovery of muscle strength and function following injury or disease is a major challenge in rehabilitation.

The ability to manipulate muscle adaptation and growth has great potential in clinical situations where functional ability and strength are compromised. Administration of growth hormone (GH) has been used successfully in elderly to prevent atrophy during catabolic diseases or following hip fractures (Van der Lely et al 2000). GH administration in these situations resulted in increased insulin-like growth factor 1 (IGF-1) levels, and increased muscle mass and functional ability. IGF-1 plays a critical role in skeletal muscle growth during development, muscle regeneration and muscle hypertrophy in response to training. Several growth factors have been implicated in directing muscle specific gene expression; however, the hypertrophic effects of growth hormone have been thought to be primarily mediated via IGF-1.

IGF-1

IGF-1 was first identified in 1957. It was known by other names including sulfation factors, non-suppressible insulin-like activity, multiplication stimulating activity and somatomedins. It was initially identified on the basis of three unique properties: its mediation of the skeletal growth-promoting actions of GH, its mitogenic properties, and its mimicry of the actions of insulin. This peptide was isolated in Zurich by Rinderknecht and Humbel on the basis of its insulin-like activity, but was renamed IGF-1 when it became apparent that its growth-promoting properties were more important than their insulin-like activities (Rinderknecht & Humbel, 1978).

The IGF-1 system includes ligand IGF-1, its receptor, IGF-binding proteins (IGFBPs) and IGF receptors. The biological significance of the IGF-1 was most strikingly demonstrated when its expression was ‘knocked out’ by homologous recombination techniques. Virtually every component of the IGF-1 system (the various ligands, receptors and IGF-binding proteins) has been knocked out, and the results demonstrate that the IGFs are very important in muscle growth and development. Indeed, a common observation in mouse lines lacking IGF-1 (and/or its receptor) is that embryonic development is impaired but embryos are viable. However, the pups die immediately after birth because they cannot breathe. The central importance of IGFs to muscle development is emphasized by the fact that mice in which expression of myogenin has been knocked out show the same result; i.e there is essentially no functional muscle development in the absence of either IGF-1 or myogenin. The mice with an inactive IGF-1 gene studied by Powell-Braxton et al (1993) were characterized by underdevelopment of muscle tissue, and a ‘generalized organ hypoplasia… including the muscles’. The essential role of IGFs in cell growth is shown by the report that fibroblasts from IGF-1 receptor knockout mice grew very slowly in culture unless they were transfected with a plasmid expressing the IGF-1 receptor. Using the opposite approach in which transgenic animals overexpressed IGF-1, Mathews et al (1988) found that muscle and bone growth were increased approximately 30% when circulating levels of IGF-1 were 50% above control values. There was a substantial increase in weights of spleen, pancreas, brain, and kidney and an increase in DNA content of these tissues. All of these observations are consistent with the view that IGF-1 plays an essential role during normal growth and development. In spite of the association of excess IGF-2 with tumours, in general it is clear that IGF-1 plays a major role in development, growth, cell differentiation, and maintenance of skeletal muscles, both in culture and in intact animals. Most, if not all of these actions are mediated by the IGF-1 receptor, and they are strongly modulated by IGF binding proteins.

Viral-mediated IGF-1 gene transfer

Increasing blood hormone levels may be risky. Specifically, the long-term safety of the activation of GH/IGF-1 levels remains uncertain with regard to tumour growth, as most human solid cancers express IGF-1 receptors. Elevated GH levels have also been linked to impaired glucose tolerance, hypertension and fluid retention. However, given the known autocrine/paracrine actions of IGF-1, local manipulation of IGF-1 expression and secretion by muscle fibres may not only be safer but also more effective (Fig. 1). Recent developments in genetic manipulation are appropriate for the introduction of small regulatory factors, such as IGF-1, into tissue. The recent adenovirus-associated virus (AAV) vector system consists of AAV inverted terminal repeats (ITRs) that are necessary and sufficient for replication and packaging of the virus. AAV lacks virally encoded genes, and therefore can be used to infect adult tissue without rendering an immune response. Viral-mediated gene delivery of IGF-1 has been shown to enable efficient transfer of IGF-1 into both young and adult animals. The AAV-virus is introduced via direct injection of tissue. The recombinant AAV virus (rAAV) consists of rAAV inverted terminal repeats (ITRs) that are necessary and sufficient for replication and packaging of the virus. The rAAV virus is then used to infect the target tissue (Fig. 2). 

IGF-1 and muscle

Numerous in vitro studies have shown that exposure of mammalian muscle cells to IGF-1 promotes myogenic proliferation and differentiation as well as protein synthesis. Other studies have shown that administration of IGF-1 induces an increase in muscle protein content and reduces protein degradation. By injecting the gene-virus package into the muscles of adult mice, we (Ye et al 2013, Stevens-Lapierre et al 2010) have shown that virally mediated gene transfer of IGF-1 increases muscle size under normal loading/ activity conditions (Fig. 3), but that this newly established homeostasis is maintained during cast immobilization, when neuromuscular activity is minimal. Interestingly, despite increased expression of IGF-1, the relative rate of loss of muscle mass and strength is not attenuated in virus- injected versus control muscles. We speculate that the latter is related to a decrease in IGF-1 bioactivity in the absence of neuromuscular activity, due to alterations in receptor density, binding protein, or postreceptor events. Allen et al (1999) previously postulated that the level of neuromuscular activity affects the expression of IGF-1...
the loading state of
motoneuronal survival has been demonstrated
emerging. A critical role for IGF-1 in
survival and motor regeneration is quickly
shown that IGF-1 not only inhibits neuronal cell
during embryonic and early postnatal life, as
demonstrated that successful gene transfer of
IGF-1 increase the muscle’s regenerating
potential of overexpression of IGF-1 in
respiratory and motor limb muscles to directly
innervated adult skeletal muscle induced by exposure
to members of the fibroblast growth factor family and hepatocyte

growth factor–isoforms promotes different responses in


Cerny P & Grandin P (1990). Nerve sprouting in


References


The importance of IGF-1 in
motor neuron survival and motor regeneration is quickly emergent. A critical role for IGF-1 in
evolutionary and early postnatal life, as
well as in spinal cord pathology. In vivo studies show that IGF-1 not only inhibits neuronal cell
death, but also stimulates nerve regeneration in crushed or freeze-injured nerves. Rabinovitch et al. (2003) found that after a
sciotic nerve crush injury in transgenic mice expressing the human IGF-1 transgene, there is an increase in the number of neurons flaking the axons in muscle and an accelerated return of nerve conduction velocity. Similarly, IGF-1 increases intramuscular nerve sprouting 10-fold when administered subcutaneously to normal adult rats (Caroni & Grandes, 1990). Finally, IGF-1 has also been linked to age-related alterations in neuromuscular innervation (Payne et al. 2006). These data indicate that IGF-1 plays an important role in mature motoneuron maintenance, both in the normal state and under conditions where motor neuronal loss is found such as ageing and pathological conditions involving the central nervous system.

It has been shown that AAV1 is retrogradely transported from presynaptic terminals of projecting neurons through the entire length of the axon. Kaspar et al. (2003) took advantage of the retrograde transport ability of AAV1 in a mouse model of amyotrophic lateral sclerosis and injected AAV1 into respiratory and motor limb muscles to directly target the motoneurons and test the efficacy of two neurotranspheric factors, IGF-1 and glial cell line-derived neurotrophin factor (GDNF). They showed that IGF-1 delays the onset of behavioural symptoms and sustains life to a greater degree than GDNF. The marked effects of IGF-1 on onset and survival were accompanied by preserved morphology of motoneurons.

Conclusion
Collectively, these findings demonstrate that IGF-1 is a central trophic growth factor, essential for muscle regeneration and hypertrophy, and motor neural maintenance and regeneration. Given the role of IGF-1 in the regeneration of nerve and muscle, it is worth further investigating the therapeutic potential of overexpression of IGF-1 in different neuromuscular diseases.

IGF-1 and motor neuron

IGF-1 increases the muscle’s regenerating potential of overexpression of IGF-1 in
respiratory and motor limb muscles to directly


Figure 4. Markers of regeneration in the soleus across all experimental timepoints. A, cross-sections of the soleus muscle stained with laminin (red) + DAPI (blue) + Pax7 (green). Pax7 positive fibres (arrows) at 5 days of reloading (5d Reamb). Bar = 50µm. C, cross-sections of the soleus muscle stained with monoclonal antibody against embryonic myosin isoform (green) at 10 days of reloading. Bar = 12.5µm.
The title of the special issue of *The Journal of Physiology* on 1 June 2014 reflected the theme of the opening of the 2013 IUPS Congress: physiology moves back onto centre stage (Noble et al. 2014). The articles focus on ways in which new and often controversial developments in evolutionary biology have opened the door to the discovery of physiological functions, which play a role in determining the variations in inherited characteristics on which natural selection may act. This is known as Lamarckian heresy, which the founders of Modern Synthesis (neo-Darwinism or Synthetic Theory of Evolution) sought to exclude. But did we really have to wait until 2014 for all that to happen?

A recent book by Niemann (2014) shows that if history had taken a slightly different turn three decades ago the answer might well have been no. In 12 June 1986, the great logi-"on 1 June


The first article in this short series (PN94, Spring 2014, p. 8) started with the remarks: 'The age of great textbooks of physiology seems to have passed. Those splendid thousand-page volumes that used to inform and perhaps intimidate, have – like battleships – disappeared. But actually, we can still learn a lot from these books. In this article, I am discussing just a few of the greatest from 40 years ago. In that article, I revisited Ruch and Patton’s Physiology and Biophysics. Now I turn to three more examples of Great Textbooks.

General Physiology
Hugh Davson

Hugh Davson (1909–1996) probably knew as much as any one person could know about general physiology or biophysics. His General Physiology appeared as a single volume in 1951 and in its final two-volume form in 1970. By then, it had become a standard work and few professional physiologists lacked a copy. It is an extraordinary book. Davson’s approach to physiology and his unusually fluent prose style are well shown in the preface to the first edition. He points out that advances in general physiology depended on the recruiting of scientists trained in non-biological subjects (his own training was in chemistry) and noted the difficulties under which those trained only in the biological sciences must labour. His honesty is transparent. How many authors would thank their employers, in his case the Medical Research Council, for having...silenced him...acquired the theft of so many hours, devoted to this book, which might perhaps have been better employed in original research."

How did he write such a book? By spending thousands and eventually tens of thousands of hours, reading and summarising the results of original papers in the library of the Royal Society of Medicine. His approach was straightforward: he read only original papers that interested him and maintained his position as a leading authority on the physiology of the eye and cerebrospinal fluid and as the doyen of membrane physiology. The range of subjects covered in depth in his book is most impressive. From the mechanics of Raggia, DNA, the molecular biology of connective tissue, diffusion processes, electrophysiology, photosynthesis, the gut, the kidney, cardiac muscle – the list is endless. And all in faultless, flowing English.

Davson’s General Physiology was a unique book. It contains much information of classical importance and anybody who thinks he or she has a new idea in membrane physiology would be well advised to read Davson before applying for a grant. But more valuable perhaps than the scientific information is the opportunity to meet Davson. Nobody will write, and certainly nobody will be paid whilst writing this sort of book again.

Principles of Human Physiology
Ernest Starling

According to Sir Charles Lovatt Evans, Starling dictated much of the first edition of Principles of Human Physiology (PHP). Perhaps the text might have been shortened, but as it stands, it links us immediately with Starling: brilliant, impatient and busy. Starling’s pupil Charles Lovatt Evans took over after Starling’s death in 1927 and the book changed. More details, references and historical introductions to sections were added. Lovatt Evans wrote (not edited) all the editions up to the 12th in 1956, and then handed over to Hugh Davson and Grace Eggleton who, as editors and contributors, produced two more – the last appearing in 1968. Again, the book changed. No longer a single author work, it now comprised a series of eight ‘books’ or monographs, each contributed by an expert. It is the final, 14th edition which is considered here.

Even in 1968, PHP looked more like a reference book than a textbook for students. E M Killick, in reviewing the 12th edition, commented that the book had ‘one great defect as a textbook, namely, that medical students find it extremely difficult to read’. A damning comment, but softened by her praise for the work as a reference book for teachers of physiology.

The 14th edition contains contributions of outstanding quality. M de Burgh Daly’s 500 or so pages on blood, the circulatory and respiratory systems (with contributions by Davson), and H H Smyth’s account of the gut are excellent pieces of work. Davson contributed extensively: 558 pages on the CNS and special senses in addition to the introduction and sections on tissue fluids and the CSF. Davson told me that he had written the section on the CNS after having been let down by a distinguished neuro-physiologist. Although the CNS was not Davson’s special area of interest, he excelled in a fluent and exhaustive style, dealing with the anatomy as well as the physiology.

Rush菊’s chapter, ‘Nerve fibres’, is still worth reading today. He wrote in a classical style introducing striking analogies ‘Like ships anchored to their buoys, the K+ ions cannot drift away but all swing on their moorings in one direction with the set of the tide.’

But as sales dropped, Davson deplored the decision to drop the book and responded in one direction with the set of the tide.’

The approach taken by all contributors involved a great deal of detail. Illustrations were adequate but not prolific and the impression received by the beginner was one of long passages of rather solid text. This was off-putting to some; to others the depth of treatment was rewarding and the standard of the work was clearly a long way beyond that of ‘ordinary’ textbooks of medical physiology.

The series of chapters, which seemed to be particularly good were those on sensation contributed by Mountcastle himself. His work on kinaesthesia, for example, is still the standard work in the field.

Medical Physiology
Vernon B Mountcastle

‘Mountcastle’, as the book was usually known, was the largest of the great textbooks of physiology of the 1970s period. Two large volumes, 1858 pages plus an index – a long book. – Medical Physiology. Like the other books considered in this series, had a long history. It appeared in 1918 and was edited for many years by Philip Bard from Johns Hopkins University. The 14th and final edition appeared in 1980. 1999 pages plus 72 pages of index. One volume was devoted to the nervous system (and muscle), the other to the remainder of the subject. Rather confusingly, the order of the volumes was reversed between the 12th and 14th editions.

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Mountcastle’s approach to physiology and the 1980 edition was the last. Students no longer read such long books: the loss is theirs.

References


I turn up at the registration desk for Physiology 2014 in Edinburgh and I escape into my delegation bag and mobile phone as a distraction from the disturbing truth – I do not know anyone. This is the same for many other affiliates, year on year. Though two years on, after diving into the society quiz night and an awkward piano performance at ‘Physoc’s Got Talent’ on that very same first intimidating day of the conference, the thought, ‘I do not know anyone’ could not be further from the truth.

Currently as Affiliate Representative to Council of The Physiological Society and a member of the Policy and Education and Outreach Committees, I know both Physoc staff and countless members and affiliates. In this time I have presented seven scientific posters, given one oral presentation, won two poster prizes and played a role in the policymaking and physiology education and outreach agendas. But this is not about me blowing my own trumpet; instead I’m writing to explain as an affiliate that to start off with, everyone is in the same boat and it is very daunting trying to keep that boat afloat.

As part of the Education and Outreach Committee I took upon myself (with the help of Keith Siew) to revamp the Mentoring scheme and help integrate affiliates into The Society. The aim was to provide interested affiliates with advice on how to get the most out of a conference and the benefits of having a mentor. The revamped consisted of two parts; firstly the Early Career Social (ECS) which at P14 was held in the Abbot pub in Westminster. With over 50 affiliate attendees it was a successful meet and greet social.

On the outside, you would assume I’m an outgoing people, person, willing to engage and debate topics on a peer level with prominent scientists on a council of trustees and not be easily intimidated. But this is far from the truth; this ‘personality’ is a skill that I have developed over time, through all the shy and awkward encounters, through the ‘out of my league’ conversations and seemingly intimidating physiologists. Portraying self-confidence is a mask that many people have to learn to force yourself to flick that switch that turns you into Ms or Mr awkward piano performance at 'Physoc’s Got Talent' on that very same first intimidating day of the conference, the thought, ‘I do not know anyone’ could not be further from the truth.

The key to networking in action at Physiology 2014

Types of mentoring

Mentoring

The mentor is typically senior and may or may not be within your field but regardless, they will still have the experience and support you require. Ensure your expectations of a mentor are realistic. Keep in mind what your aims are, in this way a mentor could help guide you through your chosen career path.

Peer Mentoring

You’ll gain different perspectives/experience from a peer along with it being less intimidating for you to bring your problems to them; they sometimes offer frank advice that a senior mentor might not. Furthermore this is mutually beneficial to both parties as the reciprocal relationship shows you are to be both mentor and mentee.

Networking in action at Physiology 2014

It is false to think that once you have acquired sad mentor (see Box 1), life suddenly becomes easier. ‘Mentors are not knights on white chargers, they are personal trainers who show you the route, act as a guide, but you have to do the work’, said Lucy Donalson. This is a similar ethos to networking, relying on others to introduce you to their contacts is the best and simplest route, but sometimes this is just not possible, and in some cases you have to just bite the bullet and throw yourself into the conference. Knowing the best places to network, be it to find your next collaboration, future employer or potential mentor. It is a mistake to believe that the communication of your poster or oral presentation is the only benefit; remember to take advantage of the social events and talk to new people. Contacts are always important for career progression through academia; therefore attend as many presentations as possible, broaden your knowledge and push yourself to ask questions. Set yourself goals for the conference, mark abstracts and talks that are of key interest ahead of time and make a note of the people you may want to approach – a welcome reception or dinner event is perfect for this. This becomes significantly easier with practice, but to start you off I’ve provided you some top tips, as discussed and agreed upon by our panel of mentors and mentees (see Box 2).

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Occasionally the link between networking and mentoring is unclear. You do not require a lasso and a contract detailing your relationship with your mentor, ensuring they’re tied to you in every way possible. Although having previously been allocated a mentor, I have been supported more by those around me that have not been rubber stamped as my ‘mentor’. They are interviewers who I’ve met after a failed post-doc interview, Physoc Committee Chairs who have listened to my problems and proffered wisdom and encouragement, and fellow PhDs and post-docs that have echoed my thoughts and provided frank advice. This would not be possible without networking: by removing my head from my delegate bag, putting my phone away and walking up to a fellow physiologist.

Networking

Sue also recommends getting on Google and looking at hints and tips for ‘networking for people who hate to network’. So next time, do not hesitate in approaching someone, plaster a smile on your face, proffer a solid hand shake and introduce yourself – the first time is always the hardest.

But regardless of any achievements, I continue to have the same problems as every other affiliate: where will my next job be? who has grants/funding? and the pressures, problems and writer’s block associated with papers. Nevertheless, I am fortunate enough to have mentor figures I can go to for advice and support, and ultimately this is what helps me keep my boat afloat.

Fiona Hatch

University of Surrey, UK

Physiology News / Winter 2014 / Issue 97
Physiology to pedagogy
Nicholas Freestone
University of Kingston, UK

Receiving “Most Helpful Male Lecturer” award from the Kingston University pharmacy students’ association in 2012

Background context
For UK physiologists working as lecturers in universities, research in that discipline is probably what defines them in terms of their professional roles and expertise. However, we are living in changing times and along with being skilled at the practice of our discipline many of us must also transmit physiological knowledge and expertise to our students, who many of us must also transmit physiological knowledge and expertise to our students, who many of us must also transmit physiological knowledge and expertise to our students, who many of us must also transmit physiological knowledge and expertise to our students, who many of us must also transmit physiological knowledge and expertise to our students.

So we have a context whereby we have in the recent past seen a massive expansion in student numbers, a future where the expansion may further increase and a government intent on rebalancing the role of teaching relative to research in part by making student satisfaction one of universities’ key performance indicators. What mechanisms are there in place that might help us deal with these complex and multi-faceted challenges?

Academics’ possible response
Most universities now require new academics to enrol on postgraduate education-type courses. These tend to give rather generic instruction in the fundamentals of learning and teaching, and are underpinned by varying degrees of enthusiasm by the participants. More recently many institutions have added elements of these courses to progression criteria to the revised United Kingdom Professional Standards Framework (UKPSF) launched by the Higher Education Academy (HEA) in 2011. This framework seeks to benchmark ‘success within HE teaching and learning support’ (HEA, 2014). The possibility of progression in the university system by evidencing strengths in learning and teaching underpinned by the UKPSF has encouraged many colleagues to seek Higher Education Academy (HEA) recognition linked to the various dimensions of the UKPSF. To add complexity, some colleagues have aligned elements of their career progression criteria to the revised United Kingdom Professional Standards Framework (UKPSF).

In responding to this challenge the HE sector has, so far, paid lip service to the concept of the professionalisation of university teaching (Cashmore et al., 2013). It is still undoubtedly true that career progression for colleagues across the sector is more straightforward when it is concentrated on the research arm of their practice. Career progression for those colleagues focusing on the learning and teaching aspects of their practice is not so simple. Thus it remains the case that there are very few pedagogical professors in the STEM subjects in UK universities and even fewer in the discipline of physiology.

This may be due to the fact that, as the Higher Education Council stated, ‘at least part of [the] problem might be that universities had not adequately addressed the issue of what makes up quality in teaching’. Therefore, the reluctance of UK universities to promote academics through their teaching ability alone may reside in the fact that objective criteria to compare the ‘excellence’ of different academics’ teaching are absent. This fact contrasts markedly with the promotion pathway for research-oriented academics where objective criteria for progression are explicit, transparent and adhered to (publication outputs, grants received, PhD completions, etc.). This places the learning and teaching specialist at a significant disadvantage in the progression path for advancement within the UK HE sector.

Teaching in the laboratory
However, despite the frustrations that this situation caused, it gradually dawned on me that all of the basic elements of a research career area were readily available. I had become increasingly interested, due to my prolonged and close contact with undergraduate students, in how they learned and negotiated their way through their degree programmes. Getting to know my learners as individuals opened up a vast array of interesting personal circumstances, experiences and learning styles that I could develop this interest in the process of learning into a fruitful area of research?

Here, again I was very fortunate to, almost incidentally, come into contact with the Biosciences special interest group of the HEA. This provided a very supportive, collegial and collaborative environment in which to gain exposure to, and experience of, the application of qualitative social science research methods in pursuit of knowledge about the nature of learning in our UK HE context. I quickly came to realise that such research was not so dissimilar from our quantitative laboratory-based physiological research, i.e. find an interesting research question, use the most appropriate method to investigate that question, obtain data, analyse the data and then disseminate it at conferences and/or in papers (here the Physiological Society deserves a special mention for continuing to sponsor an Education and Teaching Theme at its annual Main Meeting).

Apart from career progression and promotion (which as pointed out previously is not necessarily rewards for engagement with pedagogy) there are many prizes awarded for teaching excellence that may motivate the putative pedagogue. As a prime example, The Physiology Society itself offers not only the annual award for an individual who has quickly thrust the development of a new degree programme important for the sustainable future of my School. It was an opportunity for me, working with my colleagues, to be on the development and subsequent administration of a coherent new learning programme. This, of course, severely restricted my opportunities to develop a laboratory-based research programme in the crucial early years of my academic tenure. However, despite the frustrations that this situation caused, it gradually dawned on me that all of the basic elements of a research career area were readily available. I had become increasingly interested, due to my prolonged and close contact with undergraduate students, in how they learned and negotiated their way through their degree programmes. Getting to know my learners as individuals opened up a vast array of interesting personal circumstances, experiences and learning styles that I could develop this interest in the process of learning into a fruitful area of research?

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ETRIS: facilitating research and training in in vivo physiology

Dave Lewis
School of Biomedical Sciences
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The transposition of EU Directive 2010/63/EU in UK law has introduced new training and competency requirements for scientists working under the Animals (Scientific Procedures) Act 1986. Both the Directive and the amended Act explicitly state that staff must be ‘adequately educated and trained’ and that they shall be supervised in the performance of their task until they have demonstrated the requisite competence. In addition to initial Home Office accredited modular training, there is now also a requirement, throughout a researcher’s career, for them to receive continued on-the-job training, to participate in other continuous professional development activities, and to have a reassessment of their competencies at regular intervals. ‘Training for the acquisition, maintenance or improvement of vocational skills’ is a permissible purpose under the amended Act. The plan is for ETRS to be a repository of resources, which grows and expands over time. However, this will only happen with the help of the community. Therefore if you have any e-learning or training resources, including, but not restricted to, videos, podcasts, guidance notes, software or educational protocols that you are willing to share or know of any relevant resources on open access websites, please contact Dave Lewis at 3j@leeds.ac.uk. Resources do not have to fall within existing categories; resources in other areas not currently covered are also required. Likewise, please use ETRS, share the site with your colleagues, link to it from your institutional or company Biomedical Services or Home Office websites. Your feedback on the nature of their employment can be included. They should only be used, if absolutely necessary, and only during the final stages of training. For example, after the observation of similar studies, viewing or utilising electronic resources, and practising the setting of experimental preparations using cadavers. Electronic resources are increasingly being used in the early stages of this process to supplement hands-on experience. Whilst many excellent e-resources have been developed, significant numbers are locked behind the websites of institutions, commercial or professional organisations, only available to members or subscribers. Those that are freely available are often unknown to the community.

In response to this problem, ETRS (Educational and Training Resources in vivo Sciences, www.etris.leeds.ac.uk) was developed. ETRS is a website which provides direct links to free, open access, or open educational e-resources which deliver training or facilitate research in vivo physiology and pharmacology. In addition to a direct web link to individual resources, each is accompanied by a descriptive paragraph which outlines what is in the resource, its provenance, copyright or access restrictions and suggested usage or audience. All resources are vetted to ensure compliance with the Animals (Scientific Procedures) Act and best practice in the 3Rs. Resources are grouped into 13 categories spanning the entire spectrum of resources required by practising in vivo scientists including animal welfare and husbandry, ethics and the 3Rs, experimental and statistical design, and surgical procedures. ETRS is free to use, and no log-in or registration is required. Individual resources can be located using the search function or clicking on a resource category.

The Benevolent Fund of The Physiological Society (the Ben Fund) is a charity within The Society, which was established by Trust Deed in 1976 ‘for the purpose of assisting Members of The Physiological Society (The Society) and staff and former staff (who by the nature of their employment can be considered to have contributed to the advancement of physiology) employed at teaching, research and industrial establishments who are in necessitous circumstances and their dependants’.

What does this dry legal statement mean in real life?

What it means is that there is a relatively small pot of money that can be called on to help anyone associated with Physiology. The beauty of the Fund is its simplicity and rapid response.

Who can apply?

Anyone can apply but applications usually come from members of The Society who have identified a needy cause. This is not necessarily another Society member; the only criterion is that they have contributed to the advancement of physiology in its broadest sense. So this might be another scientist or a member of their family, or a member of technical or domestic support staff in your institution who contributes to the advancement of physiology in an indirect way. We rely on members to identify a deserving case and alert us.

Who decides on awards?

There is a small committee of elected trustees comprising the Chair, three Society members and two ex officio members (the Society’s President and Treasurer). The committee meets formally once a year, in the past this has been immediately before the AGM, usually to coincide with the main summer meeting. However, most business throughout the year is conducted by email. All applications are treated in confidence and considered on a case-by-case basis.

Who administers the Fund?

The Fund is a separate Trust from The Physiological Society. However, it is administered by The Society’s officers. Our expenses are therefore very low.

Where does the money come from?

The Fund relies from donations from Society members. Typically this is in the form of one-off or regular donations. As we are a charity you can Gift Aid your donation, which increases its value to the Fund by 25%, as we can claim the tax back. A small amount of money is also generated by events like raffles. Retired and Honorary Members of The Society, who no longer have to pay a membership fee, sometimes donate their subscription to the Fund, which is much appreciated.

How much money is there?

The Ben Fund is a very small charity, so awards are relatively modest. In recent years grants have ranged from £200 to £2000. The beauty of the Fund is that we can respond very quickly. In an emergency, even a relatively small sum can make a significant difference to people’s lives.

Some examples of awards:

Health and carer support including assistance towards specialist wheelchairs, home adaptations, mobility equipment and respite care (including welfare breaks).

Short-term financial assistance in the form of grants and donations when you are facing exceptional financial difficulties including funeral arrangements, medical treatment, grants for re-training and childcare arrangements.

What is excluded?

We cannot fund applications for travel to meetings, student fees or stipends, seminars or meetings. This is outside the remit of the Trust and there simply isn’t enough money, however worthy the cause.

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Find further information about the Ben Fund and make a donation on the Fund’s website www.physoc.org/benfund

Do you know about the Benevolent Fund?
Obituary:
Alex Livingston 1930 – 2014

Alex Livingston BSc BVetMed PhD FRCVS Dip ECVPT, a prominent figure in veterinary medicine and science, died of a heart attack after a short illness in June 2014, 10 days short of his 74th birthday.

Alex was recognised for his leadership and research advances in the areas of animal pain, animal welfare and pharmacology of analgesics. He was awarded the Merial Grand Prize for Outstanding Research in Animal Pain in 2001.

Alex grew up in Luton during the Second World War. Here he spent much time with his Granddad who had a collection of shacks where he kept ferrets, dogs, chickens and other animals until he sold them. This experience no doubt led Alex to a love of animals and a desire to study veterinary medicine at university.

He gained a place at the Royal College of Veterinary Medicine in the University of London, where he intercalated a BSc in Physiology in 1962. He continued his course to complete a veterinary medical degree, BVet Med, and MRCVS in 1964. He then moved to Bristol to study for a PhD with Dr K Lederis in CNS pharmacology, which he completed in 1968. His later research focused on the action of chemical messengers in the brain areas involved in pain perception and how drugs that can alter these actions affect the way animals respond to pain. His concern for the welfare of animals made him aware of how little was understood about an animal’s behaviour associated with pain, which he felt was different.

Alex became lecturer, then senior lecturer and then in 1991 acting head of Pharmacology in Bristol. In 1992 he moved to Canada to take up the position of Dean at the Western College of Veterinary Medicine at the University of Saskatchewan making an important contribution to training of students in veterinary medicine and to their position in Canadian society. He retired from the deanship in 2002 and took up a faculty position until finally retiring in 2007. He had a distinguished career becoming a Fellow of the Royal College of Veterinary Surgeons (FRCVS) in 1993 and Diplomat of the European College of Veterinary Pharmacology and Toxicology in 1999. Throughout his deanship Alex was still involved with graduate research, teaching and mentoring of clinical residents. Alex was also active in the scientific community as board member on the Canadian Council for Animal Care and Editor-in-Chief for Research in Veterinary Science. During his career he supervised 15 PhD students and contributed to scientific knowledge with over 100 publications in internationally recognised peer-reviewed journals, and over 20 book chapters. Alex’s passion was scientific research for the benefit of animals, but he still managed to run a small farm with a herd of Charolais–Hereford crossbreed cows.

In his younger days Alex was a keen rock climber, exploring cliffs throughout the UK but particularly active on the limestone of Clifton and Cheddar Gorge as well as the sea cliffs of Cornwall.

Alex will be remembered forever for his sense of humour, his love for his family and for his animals. He was a great story teller. He took great pride in his family and all the students he taught and mentored over the years. His later years were spent continuing his academic research, attending auctions and acquiring antiques. He is survived by his wife of 38 years, Sue, and sons Alex, Andy, Ian, daughter Kate, and grandchildren Ellie, Stephanie and Adam.

John H Coote
Professor Emeritus
School of Clinical and Experimental Medicine
University of Birmingham, UK

The Journal of Physiology publishes important advances in our knowledge of physiology that increase our understanding of how our bodies function in health and disease.

Reasons to publish in The Journal of Physiology:

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- No page or figure limits
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- Immediate ‘In Press’ publication upon acceptance
- Articles published ahead of issue publication in <6 weeks
- Every issue made free after 12 months
- Over 5.7 million full-text downloads in 2013
- 2013 Impact Factor®: 4.544
- Ranks in the top ten of all citation metrics in the physiology category

Notices and full obituaries can be found on The Society website at www.physoc.org/obituary-notices
Physiological Reports

Virtual Issues

To coincide with Obesity: A Physiological Perspective, held in Newcastle on 10–12 September, Physiological Reports produced a virtual issue entitled New Insights in Energy: Homeostasis, Fat and Obesity. Associate Editors Julian Davis and Gareth Leng selected articles on this subject published in the last year. There was another virtual issue to coincide with the annual meeting of the Society for Neuroscience in November, with articles selected by Gareth Leng. These displayed the range of Neuroscience topics covered by the journal. The cover article was an interview with Jonathan Goodchild, at the ESC Congress.

New Editors for The Journal from January 2015

We are delighted to announce that Professor David Paterson, Editor-in-Chief of The Journal of Physiology, has been elected as an Honorary Fellow of the Royal Society of New Zealand (RSNZ).

The Journal at the ESC Congress

Barcelona, host to this year’s European Society of Cardiology Congress, greeted us with warm sunshine and a variety of exciting comestibles. Despite the laid back ‘mañana’ attitude that we often associate with the Spanish, the meeting at Fira Gran Via was well organised and went very smoothly.

In 2013, we attended the AHA Scientific Sessions meeting, but this year we chose to target the ESC meeting as we felt that the programme was more suited to our focus on basic research. This was the first time in recent years that we had attended a major international meeting in Europe and the demographic of the attendees was strikingly different to that of the US meetings that usually form our conference schedule. There were very few people from North America, but many from South America, Eastern Europe and Asia. Of the 300 or so people that we spoke to, over 75 countries were represented – a pretty impressive statistic!

Although aware that we were targeting a new audience, we were still surprised that many people had not heard of The Journal of Physiology. We were therefore pleased to be able to educate them on the long and interesting history of The Journal and The Society, and highlight some of the key papers in the field of cardiovascular physiology that had been published in The Journal. We had virtual issues highlighting both classic and new cardiovascular papers and historical information listing our Nobel Prize-winning authors and seminal works. The 2013 special issue dedicated to arrhythmia was also promoted and was very well-received.

We usually expect to be asked about submission requirements, policies, cost and speed of publication, but the audience here were far more interested in reading our content. This is probably because many of the delegates were clinicians who need to keep up-to-date with advances in cardiovascular research, but are unlikely to look to us as a potential publishing option. Despite this, we are looking forward to building up a relationship with this new community of readers in the coming years.

The Journal at Neuroscience 2014

As ever, The Journal of Physiology had a stand at the Society for Neuroscience’s annual meeting, this year held in Washington, DC. It was another great opportunity to engage with our growing pool of neuroscience authors. The Journal of Physiology compiled a Neuroscience virtual issue, which featured recently published, high-quality research papers and review articles. The selected papers demonstrated the broad scope of our neuroscience content, ranging from research at a cellular and molecular level, to cognitive and behavioural work, as well as studies on the neurobiology of disease.

New EP Editor

Professor L. Ashley Blackshaw from Queen Mary University of London joins EP as a new editor.

His research focuses on gastrointestinal sensory mechanisms in a range of disease indications including pain, obesity and reflux disease.

GL Brown Lecture 2014

The 2014 GL Brown Lecture by David Eisner, Colcem from the heart: from physiology to disease has been published (October issue) and is also available on Youtube: https://www.youtube.com/watch?v=VYsMq5Ok860

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