Ulster Medical Society

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Professor Dennis Johnston
Dionysus, Witches and Saints—From Poisons to Pills
Queen's University of Belfast

Dr Montgomery:

Well Dr Cupples, ladies and gentlemen, I'd like to welcome you all here this evening, and offer a special welcome to our 2011 Professor Gary Love Lecturer, Professor Dennis Johnston. Can I thank Dr Cupples and the officers of the Ulster Medical Society for their co-operation and help in arranging our meeting.

Dennis Johnston really needs no introduction to this audience, as the Whitla Professor of Therapeutics and Pharmacology and Consultant Physician to the Belfast City Hospital, he brings a lifetime of experience and personal study to his chosen subject. For 30 years, he's had a special interest in the management of poisoning. He's been an active researcher and a popular teacher of undergraduates and postgraduates in clinical pharmacology and internal medicine.

When the Ulster Society for the History of Medicine ran the student-selected component in the History of Medicine, in second-year medicine, Dennis willingly accommodated us within his department. He also contributed to the course, and supervised and examined our students, so we remain grateful for that exceptional support.

Tonight his lecture will trace the use of various therapeutic agents over the course of time, in different cultural settings, and he will also discuss the role of pharmacology in the context of current medical practice. The title is: "Dionysus, Witches and Saints–From Poisons to Pills". Thank you.

Professor Johnston:

Madam President, ladies and gentlemen, I'm really delighted to give this lecture this evening, and given my background with clinical pharmacology and toxicology, I think it's reasonable to assume that this is the theme for this evening.

I'd like to thank Robert Montgomery and Ethna O'Gorman for selecting me, after what is 33 years in the Department of Therapeutics, and coincides almost exactly with my retirement in one year, in one week's time.

Just to say that I've very fond memories of Gary as a wonderful teacher, and as a fantastic physician, and the thing I remember is, we were trying to establish a Northern Ireland formulary, and what struck me with Gary is that we spoke about it in the car, and at the end of the car journey, he knew everything that I knew at the beginning of the car journey. He had a fantastic memory and a fantastic ability.

So my title is "Dionysus, Witches and Saints", and I often have these fairly cryptic titles. Dionysus, you might know better as Bacchus, in the Romans, who is associated with Bacchanalian orgies; witches, who extended the use of drugs during the Middle Ages, from the hedgerows; and then saints refers to certain diseases which were attributed to poisons and certain medication.

So I'd like to start with Dionysus, Witches and Saints. Now, before modern chemistry, most things were derived from natural vegetable, animal and mineral origins, and in the days when it was the wrath of the gods, or possession by demons, then it was the priest physicians' position to devise the various treatments. In Ebers Papyrus, published in 1550 BC, there were no less than 800 different formulae for the treatment of disease. Most of these were useless. Some of them were dangerous, but occasionally certain ones were developed which might, over the years, and at a lower dose, produce a beneficial effect.

The title then is Dionysus, Witches and Saints, and the Latin epigram is, "abusus non tollit usum", which says that the abuse of a substance should not weigh against its good and proper use.

So the first group of substances I'd like to discuss are called the solanaceae, and you'll see, on the left-hand side, that these are very important for foodstuffs: tomato, potato, aubergine and capsicum, and then the other side we have the poisonous ones: nightshade, thorn apple, mandrake, henbane, and of course probably the most toxic of all, tobacco and nicotine.

So I'd like to talk about deadly nightshade. Now, this is the best-known member of the nightshade family, and is known as atropa belladonna, and Atropos was one of the three fates in Greek mythology, who cut the slender thread of life, so it was obviously associated with poisoning. Of course, it was instilled into the eyes of the ladies in Venice and the Spanish court to beautify their eyes, and hence the term 'belladonna', a beautiful lady, and men apparently are attracted more to women with dilated pupils, and it is one of the earliest signs of sexual arousal. The other advantage, of course, for the men was that they couldn't focus terribly well, and identify whether the men were attractive or not, and it's probably the main ingredient of the effect on the sailors from Odysseus' ship, here is the sorcerer, Circe, and she's giving him a potion, which turned them mad and they became animals. This effect is sometimes seen in young men these days with alcohol, so these are the sailors on Odysseus' ship, and the witches then continued this during the Middle Ages, and it was the favourite flying plant, and was mixed with mandrake and henbane and mixed then with bear's grease and applied to the skin, and produced delusions, hallucinations, and a sensation of flying, and small amounts were used for fortune-telling. Eventually it was included in the medical pharmacopoeia of the Edinburgh Dispensary in 1803.

I'm not sure that atropine or belladonna is particularly useful for plague, but these are other things that they thought it might be useful for, but I might suggest that whooping cough is beginning to suggest that, one of the effects of atropine, of course, is to make your mouth dry, which my mouth is drying now, and that's a sympathetic response, and it might be the

beginning of understanding that it had a significant effect on the autonomic nervous system.

Sir William Whitla, in 1882, suggested belladonna might be useful for spinal paralysis–I'm not sure, certainly to reduce saliva and breast secretion, it's a possibility. I'm not sure it would be a good idea for bowel obstruction, because it would reduce motility, but of course these drugs have a new lease of life in ipratropium, tiotropium, as antimuscarinic agents, gallstones and renal calculi, and again whooping cough coming in there, so beginning to think of a way of reducing secretions.

Here we have, "A large dose produces active brain excitement, and pleasing delirium." Presumably this is a fairly large dose. "Hallucinations, illusions and eventually sleep–the heart rate becomes excited," that is increased heart rate, "Blood pressure goes up, saliva is reduced, and sweat is stopped and the bladder becomes paralysed", and these are features that we see quite frequently in the wards, as the result of drugs which have this so-called antimuscarinic or anticholinergic effect … or alternatively, "Hot as a hare, blind as a bat, dry as a bone, red as a beet, and mad as a sometimes March hen", is referred to the effects of belladonna.

Now, it is still used for anterior uveitis. It is also the main treatment for organophosphate poisoning, which I'll mention later on, and combined with anticholinesterases and anaesthesia, and to treat symptomatic bradycardia, and as I said, some of these agents are now used for asthma.

When I came to the Department of Therapeutics in the mid-Seventies, there was a study called "Chemical Denervation of the Heart", and chemical denervation of the heart involved large doses of propranolol and large doses of atropine. I gave to George Carruthers 52 milligrams of propranolol iv, and 5.2 milligrams of atropine, for chemical denervation of the heart, and they were trying to get the heart rate to plateau, so that it wouldn't be influenced by the two systems.

John Kelly, a smaller individual, received a dose of atropine and propranolol, and reported vivid hallucinations and vivid dreams during the night, and had difficulty sleeping, and had a bit of difficulty swallowing as well. In the morning, they decided that maybe we should need to increase the dose, at which time Kelly's Law was introduced, that anyone who thought of an experiment should be the first to do it.

The next member of the solanaceae is the mandrake, and those who are Harry Potter fans will have heard of the mandrake, and it is so called because the root looks like a man, and it has a bifid root, and the top looks like a dragon, and here they often used the dogs to dig it out of the ground, and perhaps this dog has got a bit of dryness of the mouth as a result of digging up the mandrake.

Now, this is a really bizarre story. The roots were considered to be magical, and in Romeo and Juliet, it says, "the shrieking of the mandrake when uprooted, so that living mortals hearing them run mad." It has a long and turbulent history involving the Jews, the Greeks, the Romans, the Europeans, and a quote from the 30th chapter of Genesis, and it says, "When Jacob came from the field in the evening, Leah went out to meet him and said, 'You must come into me, for I have hired you with my son's mandrake.'So he lay with her that night, and God healeth Leah, and she conceived and bore Jacob, a fifth son." So for the Jews, it was good for procreation; the Greeks also referred to it as the "apples of love", but the Arabs decided it was the Devil's apple, because of its ability to inflame the passion. The Greeks had worked out that it had some narcotic properties, but also used it for gout and erysipelas, and of course as a love potion.

One common legend at the time was, Hannibal, when fighting the African rebels, left jars of wine fortified with mandrake in the camp, pretended to retreat, and the rebels came into the camp, consumed the wine, and were easily defeated. In 1490, Hugo de Luca developed what was called a sleeping sponge, which was an early form of anaesthetic. It contained opium, henbane, hemlock, mandrake, and could induce sleep for several hours, during which amputations could be performed. Sometimes you needed a bit of extra whisky to produce the effect, and sometimes the patient didn't wake up, so it was a bit of a variable feast, but hyoscine, unlike atropine, is the main ingredient, so we're talking about hyoscine, and some of you will remember taking Quells, do you remember Quells?–and it was not a good idea take it with alcohol, as I remember. It tended to potentiate the effects of alcohol, and another compound that they used was omnopon and scopolamine. I'm sure some of the older members will remember omnopon and scopolamine, and I was surprised to find it's still in the BNF, and it's not a great drug to use because it's very hard to work out the dose, but the anaesthetists in this part of the world loved it for a long time as a pre-med, was omnopon and scopolamine.

My next one is henbane, which is another source of hyoscine, and it was used to fortify beer, and was also used as a poison at the French court during the time of Louis XIV, and 400 people died as a result of poisoning. I'm not sure what they were doing, but 87 people were executed, and after the death of Catherine Voisin the practice of killing people with this agent ceased, but the most famous case of hyoscine poisoning was Dr Crippen, who killed his wife after she found out he was having an affair, and he buried the body underneath the house, and had extracted some of the internal organs, but the forensic people were able to remove the organs, and extracted half a grain of hyoscine. I think this is beautiful–they found that it had a melting point of 193 degrees Centigrade, and when instilled into the St Mary's cat, dilated the pupil, and on the basis of this evidence, forensic evidence, Hawley Crippen was convicted.

Here is a flying witch, and here is Hawley Crippen, and here's his wife and mistress, and there they are on the boat, and I was telling this story to my sister, and she said, it's also the first time anyone was retrieved from a boat, and it was the first use of the

telegraph. Hawley Crippen was convicted of murder on the basis of that evidence, and that was just over a century ago.

So that was Hawley Crippen. I'd like to move to drugs which have the opposite effect on the autonomic nervous system, and my interest in this is when the Chief Medical Officer asked me to look at a group of farmers who were exposed to organophosphates. Now, most of these farmers were depressed, they had chronic fatigue syndrome, irritable bowel syndrome, and what we were looking for was the cholinergic syndrome, which was the opposite to that with belladonna. We had one patient who thought he had acquired the syndrome from passing a sheep dip, and one of the problems was that Dr Jamal, a neurophysiologist, did a series of tests on these individuals for the tidy sum of £1,200, and would nearly always conclude that they suffered from organophosphate poisoning. And then it transpired that this might be a factor in Gulf War syndrome, and the organophosphates might be related to that, and Dr Jamal was involved with that as well. Unfortunately he made up some of the results and was removed from the register.

The drug which is well known to produce the cholinergic syndrome is the Calabar bean, and this comes from an area in modern Nigeria, or it would be modern Nigeria, and it was used for two purposes. If they thought you were possessed by a demon, or were a witch, they would give you large quantities of the Calabar bean, and if you didn't die, then you weren't a witch, I think, or some variation on that theme anyway!

The other was in duels, where they would divide the bean into two, give one to one individual and one to the other, and the last man standing was the winner. The secret was not to chew the bean, and if you swallowed it whole, it had very little pharmacological effect, so that was the Calabar bean, and it is the poison used in Poirot's Last Case in Agatha Christie's Curtain.

Now, an alternative way to achieve this effect is to use drugs which stimulate the muscarinic receptors–this sounds like old pharmacology, muscarinic receptors, and this is an early source of muscarine, Amanita muscaria, or known as the fly agaric mushroom, and this is a source of muscarine. It's not very clear why it's called the fly agaric mushroom. It may have had some insecticide properties, or it may be that it gives a sensation of flies entering your head, but you may know that it often appears on Christmas cards, New Year's greeting cards, good luck, often accompanied by elves, gnomes and fairies, and it's intimately tied up with the little people in Europe, and I just wonder if the hallucinations may be distortions of size? It's also been implicated in the Santa Claus legend, which I don't believe for a minute, but it was the red-and-white cloak, and the reindeers would eat it and get intoxicated, and certainly those in northern Europe would take it and get hallucinations of flying, so many, a subliminal message there on flying reindeers.

So, the effects which we were looking for for the organophosphate poisoning for acute cholinergic syndrome has the acronym, SLUDGE, so increased salivation, increased tear production, increased urine production, diarrhoea, abdominal cramps and pinpoint pupils–exactly opposite to belladonna, which is the main thing. You say, well what use is this stuff? Well, we sometimes use it for atropine poisoning, I agree it's not very common, but of course, the development in Myasthenia gravis, so the physostigmine, and I remember Robin Shanks telling me that Professor Myers was known as Physo. Presumably that was his interest in physostigmine , and he had an interesting method of teaching, he started at A and went to Z, and when he was going rather slow, they would say, faster Physo, so he was known as Mr Physo, Professor Physo. Not used so much for glaucoma, but of course, these drugs now, the anticholinesterases, are now being used for the increased cholinergic activity in the brain in dementia.

Now, my next topic is ergot of rye. This is a fascinating subject, and I remember I was watching a Dr Finlay's Casebook, and I think I got the diagnosis before Dr Finlay. I said, this is St Anthony's Fire. The story was that in Tannochbrae—do you remember Tannochbrae?–the miller had contaminated the wheat with the rye, and it was a bit old, and they were suffering from a burning sensation and seizures, and I said, I think that's ergot poisoning. That's intimately associated with the growing of rye, and in wet times the fungus would grow, and there are two main types: there's the gangrenous, which would cause the blood vessels to contract, could cause a burning sensation and cause pain, and then there was the other type, convulsive, which also caused major problems, but just an example of the really vascular type of problems occurring with ergot poisoning. In 1093, Gaston de Valloire formed the Hospital of the Brothers of St Anthony to treat patients with ergotism, and ergotism was a real problem. St Anthony's Fire was a real problem in the Middle Ages, and it would break out in various parts of Europe, and this is an example then of gangrenous ergotism, and here is a woodcut, a medieval woodcut of St Anthony. Here is the sufferer with the amputated foot due to ischaemia, and here the sacred fire is coming from his hand.

So, ergot has various interesting effects. If women had ergot poisoning, lactation stopped, and this was due to inhibition, later on shown to be, inhibition of prolactin. It was also used to accelerate labour, until a New York physician, David Hosack, had decided that this wasn't a good idea because it increased the risk of stillbirths. It has been used over the years successfully to reduce post-partum haemorrhage, and I think it's still used, I haven't spoken to the obstetricians lately, but it's been used within the last ten years.

Then there was ergotamine and methysergide, which became treatments for migraine, until in the 1970s, when the non-steroidal anti-inflammatory drugs came in, and then there's the famous story of Hoffman, who was looking at the alkaloids of ergot,

and his apparatus broke, and he got contamination on his hands, and he was riding his bike back and he has this vivid hallucinations, a kaleidoscope of colours, and he came back to the lab and he had found LSD - lysergic acid diethylamide, so LSD was derived from ergot, and in fact it is one of the principal building blocks of many of the compounds of ergot.

So here is Sir William Whitla on ergot, extraction of rye. "It is invaluable in uterine and other haemorrhages, where it can be given under the skin, and when the patient is vomiting."

So just to look at the interesting compounds of ergot: ergometrine was used for post-partum haemorrhage; ergotamine, which was in the past used for the treatment of migraine; some of the older people may remember nikethamide, which used to get you out of your bed at night, and give to patients with respiratory failure, and they would always rub their nose–do you remember them rubbing their nose, you knew that was nikethamide. I don't think it did any good, but it was really something to do in the middle of the night! I'm not sure it had any impact on respiratory failure, and the practice of giving respiratory stimulants declined.

Then we have bromocriptine and the dopamine agonists, which are used in the treatment of Parkinson's Disease, and then our old friend LSD, and there are, of course, some people here from the Sixties, that generation, the flower people and so on, and I don't think there are any major benefits from LSD. It was tried in psychiatry and various other disciplines, with limited success, it would be fair to say.

My next topic is one which is dear to my heart, because it's the basis of my MD thesis, and it is digitalis purpurea, or the digitalis plant, and most of the compounds come from the leaves of the purple foxglove, or the white foxglove as well, apart from maybe the seeds of the strophanthus gratus, but there are other sources of the glycoside, and maybe going back to the witches again, dried toad skins used during the Middle Ages, mostly for emesis and the treatment of constipation. Sea squill used by the Romans, and in fact the Egyptians used this also as an emetic and as a laxative, and oleander, and the interesting thing about oleander is that we use anti-digoxin antibodies to treat digoxin poisoning, and if you eat too much oleander, it will respond in the same way, so you can use anti-digoxin antibodies to treat oleander poisoning, but I'm not sure I would know an oleander really, all that well.

Now, the first account of the effects of digitalis was in the second century BC, by the Roman historian Catullus. The son wanted to kill his father, who was at death's door with the dropsy. He probably had atrial fibrillation and congestive heart failure, but the son made a concoction which contained the leaves of the foxglove, and to his annoyance, he got better, and looked as though he was going to live for a long time, so the son eventually had him strangled. So as I say, the glycosides were used as laxatives, emetics, during the Middle Ages, and it was included in the pharmacopoeia of 1722, but because of what we call the narrow therapeutic index, the dose was hard to arrive at, and many deaths were reported, and as a result, the drug was withdrawn for almost a century, until William Withering's famous account of the uses of digitalis, and this is a wonderful treatise. He was a very eminent botanist and physician, and it is full of many useful observations and statements. So here is our friend, William Withering, and this is his portrait, and on his knee you see the digitalis plant. This sits above the Dean's desk in Birmingham, and when Owen Wade was Dean, he would have had William Withering above his desk.

Account of the foxglove, very important, and this is probably one of the most incisive statements, I think, relating to treatment at that time. "It is much easier to write upon a disease than upon a remedy. The former is in the hands of nature, and the faithful observer, with an eye of tolerable judgement, cannot fail to delineate a likeness. The latter will always be subject to the whim, the inaccuracies and blunder of mankind", and I think this is the story of therapeutics throughout the years. So despite this, digitalis became a cure-all. It was used for tuberculosis, epilepsy, depression, typhoid, pneumonia, diphtheria, scarlet fever, measles, goitre, haemorrhoids, and in fact in Potter's Materia Medica published in 1911, it was recommended as an aphrodisiac.

One of the most interesting speculations about digitalis is whether it had a contribution to Van Gogh's paintings, and we know that high doses of digitalis will cause a bias towards the yellow-green end of the spectrum, and also cause haloes around objects, and it's been speculated that perhaps Van Gogh was receiving digitalis, and here is the portrait of Dr Gachet, who was Van Gogh's physician, and on the table in front of him we have the foxglove, and then might I suggest, I'm not saying it's true, might I suggest that the choice of colours may be slightly different than normal, but particularly these bright objects, and that could be pure style. It would be nicer to think of it as style, wouldn't it?–or it could be cataracts, some people have suggested it's cataracts, but it's a reasonable speculation, and we know that he was receiving digitalis.

Now, in 1969, Hurwitz and Wade produced a paper which was published in the BMJ, on adverse drug reactions, and at that time, over 20% of all adverse drug reactions were due to digitalis, so 21% of all adverse reactions were reported on admission to hospital, and George Carruthers and myself found an incidence probably between 10 and 15% throughout into the Seventies and early Eighties, and I had one patient who was on 750 micrograms daily. He came from the Department of Medicine. Six times the recommended dose. I presume he was just kept on the loading dose, I think that was the problem.

The other one, we had a physician in the City Hospital who would give large doses to make them vomit, and that was his way of digitalising the patient. When Owen Wade's article was published in the BMJ, a headline appeared in the Belfast Newsletter. It was called, "Wrong Drugs Given to Patients at the Royal

Victoria Hospital", and he was met by two senior irate members of the Hospital, to explain how this could happen, who settled down when they realised that the study had been done at the City–and clearly the bad prescribing would not happen at the Royal. Now, we don't use very much digitalis, very little is used, and it's well down the drugs that you would use for heart failure, but it's still used a bit, and it's still used in part for heart failure with atrial fibrillation.

I apologise to the anaesthetists, I thought I couldn't leave out curare, because it is such a poison, and it's such a good example of a poison. I have no intimate knowledge of curare, but I thought it was such a good one to select, and curare of course, as you know, was used by the South American Indians, in their blowpipes and their arrows, to kill their prey, and to kill their animals.

So, Pietro Martire d'Anghiera, a leading churchman in the court of Queen Elizabeth, published De Orbe Novo, the New World, in 1516. Here is a copy of De Orbe Novo, and here is a quote which is a translation. "This Indian king laid waste our men, and fought so fiercely with their venomous arrows, that they slew them 40 and 7, for that poison is of such force, that albeit the wounds were not great, yet they died thereof immediately." So during the 16th and 17th century, 50 similar cases were described by visitors to South America. Laurence Keens, who served with Walter Raleigh, in his expedition, compiled a list of poisons which he called urare, and this became known as curare, which was good for hunting, killing the animal and decomposing on cooking.

In the late 17th and early 18th century, La Condamine, a French astronomer, investigating two theories on the shape of the earth, made detailed observations of Indians making arrow poison, and they used the roots and creepers and other plants, put it into their longbows, and the animals died quickly, and the Indians were not harmed by eating it. He then injected into a hen, and concluded that the effect was due to respiratory paralysis, and he reckoned that the meat was tender and more tasty than he'd ever tasted before, and he brought it back to Leiden to demonstrate its poisonous effects.

The next most important then was Benjamin Brodie, who kept a poisoned cat alive by blowing air into its lungs for 40 minutes, and then Claude Bernard, the great French physiologist, reported impulses travelling down the nerve and impulses normally in the muscle, and concluded that the problem was between the nerves and the muscle. Finally, Henry Deal and others showed that it was a blockade of the acetylcholine receptor in the muscle.

In the 19th century, crude extracts were used to treat rabies, tetanus, epilepsy, with limited success. In 1935, Harold King found the active ingredient, tubocurarine. In 1942, Thomas Cullen, a GP and part-time anaesthetist, used it to reduce the amount of inhaled anaesthetic, and for the next ten years, it was used to relax muscles during intubation in abdominal surgery, and of course, neuromuscular blockers are very important in the practice of anaesthesia.

My last example is bothrops jararaca, and this is a South American pit viper. Now, so far, I have dealt with drugs which have been simply extracted from plants and animals, and I'd like to finish off with something which is more subtle, and that is the development of the ACE inhibitors. So in 1970, Ferrara, a Brazilian, described the effects of the venom of bothrops jararaca. It caused marked flushing and falls in blood pressure. I met Ferrara in Brazil about 15 years ago, and my connection with Brazil I owe to Robin Shanks. I was sitting in my office, and this chap, Luiz Caldas, came into the room, and he said, "I am Luiz Caldas–Professor Shanks has given me your name." I said, "Oh". He said, "Queen's have an exchange between Rio. It's called the UFF Hospital in Rio, with Queen's, and Queen's would pay transport to Rio, and they would pay for me, and vice-versa." I said, "What are you interested in?" He said, "I'm interested in snake and spider bite", so I felt like saying, "You've come to the wrong place"!–but he stayed with me for four weeks. We got him over to the poisons centres in England and Scotland, and then he said, "You must come back, come back to Rio. Will you give a talk"? I said, "Well, what about snake bite in Ireland, before and after the arrival of St Patrick?"

I gave a different talk! Anyway, the interesting thing was then that this snake bite caused vasodilatation, and also caused the blood pressure to drop, and John Vane, working with Ferrara, they identified an ingredient of the venom. It was a nine-amino acid peptide, and couldn't be given orally, and they concluded that its action was to prevent the breakdown of vasodilators, such as bradykinin, and to prevent the formation of vasoconstrictors, such as angiotensin II. So the company, Squibb, looked at 2,000 different molecules, based on the terminal amino acid, its likely interaction with the receptor, and I see Brew Atkinson is here. Brew was involved with the early studies in Captopril, and this was the development of Captopril, which made a big impression. The ACE inhibitors have made a big impression in cardiovascular disease.

Now, they're used for all grades of heart failure, for hypertension, post-myocardial infarction, possibly for patients also at high risk, diabetic nephropathy and neuropathy.

So my final conclusion, as the great man, Paracelsus said, "All things are poisonous, and there is nothing that is not harmless, the dose alone suggests that something is no poison." I think this translation has too many negatives in it, but that's the one that I got.

So in conclusion, we have looked at the solanaceae, which have been around from the mists of time, the mandrake of the Middle East and Rome, and onto Europe and mediaeval Europe, and witchcraft and necromancy. Atropine and hyoscine still have roles, but have been very important in unravelling the secrets of the autonomous nervous system. Ergot is still developing, and dopamine agonists in the treatment of Parkinson's Disease, the Calabar bean, and physostigmine and anticholinesterases are still used

for the treatment of myasthenia gravis, and are now finding a new role in the possible treatment of dementia. They all hark back to these toxic effects which have been described in the past.

Digitalis is a good example of a drug where you need to be careful about the change of dose, and my second theme is that, despite the developments in genetics and molecular biology and so on, we shouldn't forget about the plants and animals and the origins of drugs which are already in use, and just as an example, possibly in part for Paddy, it's interesting that many of our most useful anti-cancer drugs have been derived from a vegetable origin. These are mostly derived from fungi, and of course the yew bark, and the periwinkle, so these are still used. They're quite useful anti-cancer drugs, and they are derived from living organisms. The ACE inhibitors provide a more modern example, not exactly extracting the drug, but using the natural material to work out how you might develop a useful drug. So thank you very much.

Professor Margaret Cupples:

Can I say, thank you very much indeed, Professor Johnston, Whitla Professor of Therapeutics and Pharmacology at Queen's. You've given us a very interesting historical perspective. I would imagine there are some questions for you in the audience. I have John Craig, I'm sure you're happy …

Professor Johnston:

I can't give a lecture without trying to get a laugh, but it's been my technique over the years. I got a few anyway!

Professor Margaret Cupples:

Could I ask you, obviously William Whitla himself was a keen botanist and physician, what do you think of his contribution compared to his contemporaries?

Professor Johnston:

Well, I suppose his big claim to fame was that his pharmacopoeia was used by the Royal Navy, and Robin, I've got a book in my room, and I was surprised to find, this is a first edition of William Whitla's book, and it was written by William Whitla and signed by him. Is that mine? Maybe we could give it to the Ulster Medical Society, or Queen's maybe?

Professor Robin Shanks:

Whitla's books became available just over a hundred years ago and they were adopted by the Royal Navy and by the Merchant Navy, and any ship that did not have a doctor had to have Whitla's two books, and at that stage, there were tens of thousands of books.

Professor Johnston:

There were lots of them, but it says in the front that this is the first volume of the first edition?

Professor Robin Shanks:

That's right.

Professor Johnston:

Now, that's a useful book to have, 1882–Robert knows about these things, don't you, Robert?

Robert Montgomery:

Well, I mean, I gave it to the …

Professor Johnston:

Oh, you gave it? Sorry, Robert.

Robert Montgomery:

It goes to the Whitla Chair.

Professor Johnston:

Right, okay. I should have remembered that you gave it to me, yeah, that's right. I only got £20 for it!

Dr James Douglas:

What is jimson weed, is it confined to the United States? I mean, it's an atropine-like substance?

Professor Johnston:

I don't know. I have a lovely book on herbs that I was given, I'll look it up for you. It's not in my brain. Jimson weed, you think it's good, like atropine?

Dr James Douglas:

I've seen it in American textbooks, and I don't know what it is. I assume it's something that grows in the States, and we don't have it here.

Professor Johnston:

There's a lot of plants that have similar problems. We mentioned digitalis and oleander and various other things, and particularly drugs which have antimuscarinic activities, there are masses of them. It seems to be almost part of the plant kingdom, it's a very common effect.

Dr John Logan:

I presume that all these compounds are used by the plants for their own defence?

Professor Johnston:

Yeah, I think so, yeah. That's why these complex molecules have been made through a long process, and they're pretty subtle. I think we should still be looking for things of plant and animal origin.

Audience member:

Are people still looking out?

Professor Johnston:

Yes, I think they are. One of the sad things is, certain areas have gone down quite a lot, because of the developments in genetics and molecular biology. I think big companies, and cardiovascular, Pfizer for instance, has almost withdrawn from cardiovascular development, so there's been a withdrawal from particularly cardiovascular drugs, which are often the ones which are best examples, including statins and so on. These are all derived from plants.

Dr Stanley Hawkins:

The early botanists and physicians worked very closely together, through the Society of Apothecaries, and along with friends, set up the Chelsea Physic Garden, and there was quite an exchange of plant material between Chelsea and Leiden, and there are recent histories of the Chelsea Physic Garden [Nicholas Cluney?]. They also developed, for the first time in Chelsea, hot houses to help propagate tropical plants. These people went off to foreign parts, trying to bring back plants and propagate them to make a more rational....

Professor Johnston:

I mean, the Amazon jungle has always been the classical place to develop them.

Dr Michael Scott:

Talking of which, isn't that one of the other reasons, apart from trying to slow down global warming, of protecting the Amazon jungle, because it contains so many plants and fungi.

Professor Johnston:

Yes, that we've probably never seen. It sounds a bit old hat, that.

Professor Cupples:

I'm sure the students wonder about what was done in the Department of Therapeutics in the '60s and '70s, compared to what's done there today, when you hear about the experiments you've had.

Professor Johnston:

Well, we had a more cavalier approach to studies, which was quite useful. A cavalier approach sometimes produces the goods.

Professor Robin Shanks:

There was no ethical committee in those days, and you could think of an experiment one day and do it the next day.

Professor Johnston:

Yeah, as long as nothing happened.

Professor Robin Shanks:

Nothing happened, no.

Professor Johnston:

Nothing bad happened.

Audience member:

Currently a lot of people are interested in alternative medicines and natural remedies. These are very much high-profile at the minute.

Professor Johnston:

I think people want magic, and there's no way round it. They will always want magic, and they want magic from us, and we can't always provide the magic, so it's partly that, the desire for magic. I was giving a talk at the British Geriatric Society on homeopathy, and there was a lovely quote by the Chief of Homeopathy in America, he said: "There is no evidence for homeopathy", and this was the guru of homeopathy, but they still peddle it, and the reason why it's in the NHS is, Nye Bevan, I think his mother was cured by homeopathy, so it's there, and it's funded to some degree, and the politicians keep voting, so yes, it continues to be funded.

Audience member:

I sometimes wonder if the royal family haven't a lot of sense?

Professor Johnston:

Yes, I mean, the other point is that homeopathy came in at a time when doctors were doing awful things to their patients, and it looked a lot better than the standard bleeding and purging and so on that was going on, so I think there was that aspect to it, the patient didn't get worse.

Audience member:

Safer than digitalis.

Professor Johnston:

Yes, it is, it's safer than digitalis. Nearly anything's safer than digitalis!

Professor Cupples:

Perhaps there's another in the audience? We could keep Dennis talking all evening, but I think perhaps I should say "Thank you" again to him for giving us such an interesting tour of the history of pharmacy. Thank you.

Can I say thank you also everyone for coming. It's great to see the spread of age in the audience, and we would obviously encourage anybody who's here for the first time.

Audience member:

You mean, the advance of age?

Professor Cupples:

We'd encourage anybody who's here for the first time at the Ulster Medical Society, to think about joining us, and I'll stand aside and let you see more of the details of what we do in the Ulster Medical Society, and we do actually encourage people from different disciplines to come and talk and share their experiences, young and old.

Professor Johnston:

So what am I? I am becoming old, or very old?

Professor Cupples:

Tonight we had competition from the younger age group. Many people gave me their apologies, because they had to go and see their children and younger relatives in the Waterfront, because the Methody annual concert was on, but in truth if they'd been here tonight, I'm not quite sure where they

would have sat, so it's great to see you, thanks for coming. We have, as a reward, an attendance certificate, which you may pick up on the table at the door on the way out. We would ask you please to register the fact you're here by signing an attendance sheet, which I think is sitting on the back table, together with the members' book, and I would ask you to join us then for a cup of tea or coffee downstairs in the newly-opened Ulster Medical Society rooms, to explore the nooks and crannies of treasures and to reflect on the refurbished picture of William Whitla himself, and I look forward to seeing you downstairs.

Lastly, can I say also, those attendance certificates may be relevant to those of us who are still working, and keen to gather points for revalidation. Next week Sir Peter Ruben is coming to speak to us, to tell us about the GMC, past, present, and its role in medical education, so again I would welcome all of you back to hear what he has to say next week. Thank you.