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Contents

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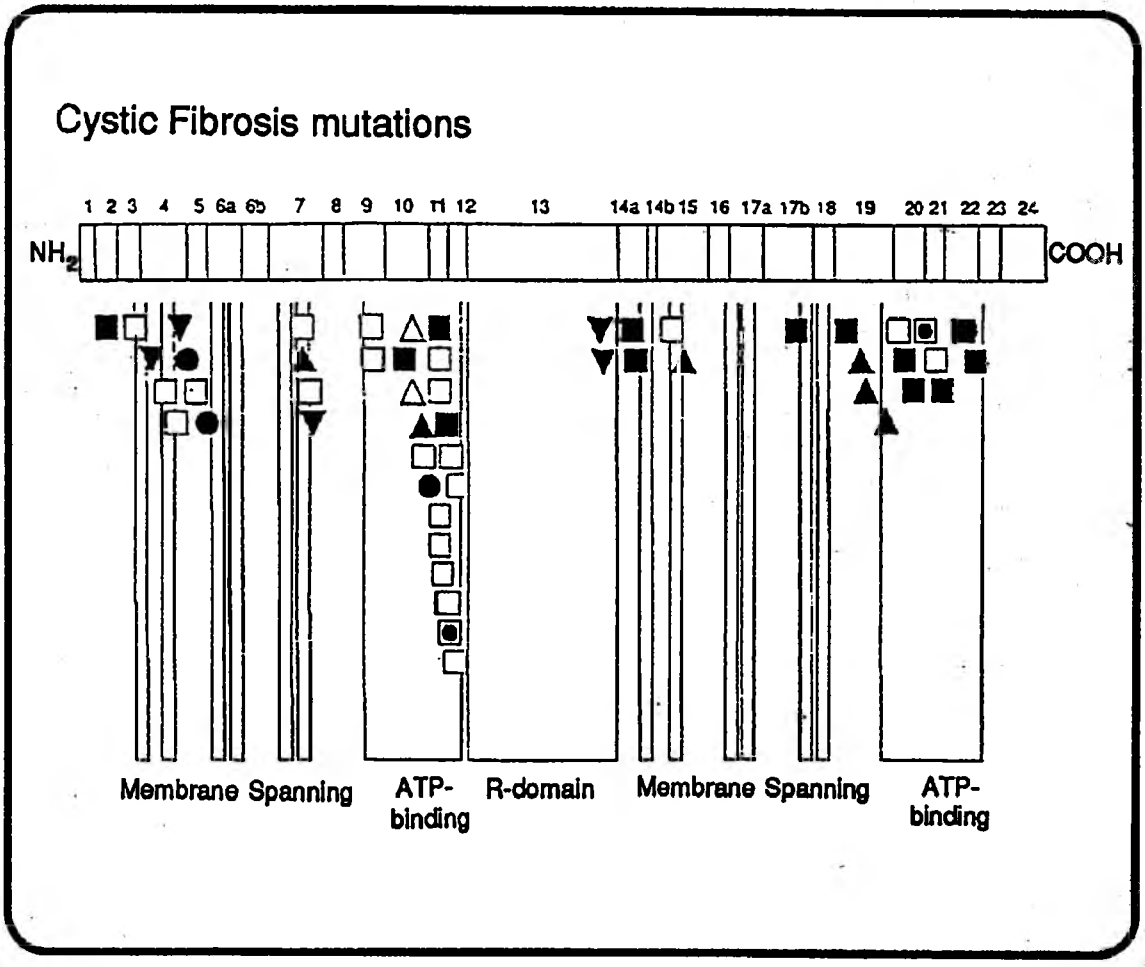

CYSTIC FIBROSIS

Protection in Practice

Founded 1892

The Medical Protection Society

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EDITORIAL

Rapid advances in molecular biology over the last decade has rekindled interest in hereditary diseases such as cystic fibrosis. This particular disease is the most common genetic disorder in Caucasian populations and much effort has gone into determining its biochemical and genetic basis. It was just over a year ago that the cystic fibrosis gene was finally localised and cloned. But has the discovery of the gene provided more questions than answers?

The main article on cystic fibrosis describes the general features of the disease while the accompanying article on the cystic fibrosis gene discusses the significance and implications of its discovery.

Both these articles are written by medical students. We would welcome any contributions from students such as results from honours projects or on any other topics relevant to medical students in general. *Res Medica* is essentially a student medical journal and aims to provide an opportunity for medical students to express themselves.

On a lighter note there is the second instalment of the *Drife Diaries*. Definitely one of the most popular articles in our last issue. Part of its popularity must have been due to the outstanding artwork of Donald Davidson, which does so much to bring the characters to life.

Our thanks also goes to the Medical Sickness Society for providing sponsorship of the inaugural issue of this journal.

We hope you find this issue both entertaining and enlightening.

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Res Medica is the Journal of the Royal Medical Society of Edinburgh.

Royal Medical Society, 5/5 Bristo Square Edinburgh EH8 9AL.

ARTICLE

Cystic Fibrosis

Miss Mary Dolan

Every year members of the Royal Medical Society present dissertations at Private Business Meetings. Traditionally *Res Medica* has published those dissertations of wider interest. We are reintroducing this tradition with an article about cystic fibrosis which was presented last session by one of our current presidents, Miss Mary Dolan. Please note that the information provided in this article, especially with respect to prenatal diagnosis, predates the localisation of the C.F gene.

Cystic fibrosis, a genetic disease with an autosomal recessive mode of inheritance, was first described in 1936 by Fanconi *et al.* He described the disease in a paper entitled *The Coeliac Syndrome with congenital cystic pancreatic fibromatosis and bronchietasis.* Since then the disease has been known by various names such as Cystic Fibrosis of the Pancreas, Mucoviscidoses, fibrosis of the pancreas until it was shortened to Cystic Fibrosis in the 1960s.

Cystic Fibrosis represents the commonest autosomal recessive disorder in Caucasian populations. The mutant gene, recently identified on the long arm of chromosome 7 has a carrier rate equal to 1 in 22 among Caucasians. The overall incidence of the disease in 1 per 2000 live births. However it has a much lower incidence amongst non-Caucasian populations. Amongst the UK population there are 5000 cystic fibrosis sufferers. Slightly more than 300 affected babies are born annually.

Miss Mary Dolan is a final year medical student at the University of Edinburgh.

The disease affects many tissues, especially the endocrine glands. It results in the production of abnormally viscous secretions which cause duct obstruction and are therefore responsible for pancreatic insufficiency, malabsorption syndromes, biliary cirrhosis and male infertility. The lungs of cystic fibrosis patients are found to be normal at birth but are very prone to infection. Recurrent infection is responsible for the irreversible secondary lung damage which is usually responsible for the shortened life-expectancy of cystic fibrosis patients. Death usually results from a severe bacterial pneumonia or is related to the development of cor pulmonale from lung disease.

Clinical presentation occurs before the age of one year in approximately 50% of patients with recurrent respiratory infections, diarrhoea, rectal prolapse, failure to thrive. Tracheal epithelium show increased Na^+ transport with reduced Cl^- absorbance (Knowles 1981). Beta-stimulation of the

Table I. Special characteristics of the salivary glands and blood cells of cystic fibrosis patients

1. Decreased beta-stimulation response in salivary glands
2. ? calcium concentrations in both tissues
3. Erythrocytes: ● no active Ca^{2+} pumps
   ● low rate of passive entry of Ca^{2+}
   ● decreased Na^+/K^+-2Cl transporter
4. Lymphocytes and Granulocytes: decreased response to cAMP stimulation
5. Heterozygotes for the cystic fibrosis gene demonstrated an intermediate response (ie. greater than cystic fibrosis patients but less than normal) to cAMP stimulation

airway results in increased Na^+ absorption but no change in Cl^- secretion. Thus the signals operating via the cAMP system fail to increase chloride permeability. This reduced chloride secretion *has a drying effect on airway surfaces.*

Studies involving the salivary glands and erythrocytes of patients have shown several abnormalities (Table I). It is uncertain whether the viscid mucus secretion results from abnormal ion transport or is due to abnormal secretion. Uncertainties also exist regarding the increased respiratory infections of cystic fibrosis patients. These are either due to abnormal ion composition or mucus accumulation or both.

MANAGEMENT OF THE C.F. CHILD.

Current theories on the management of cystic fibrosis believe that early diagnosis and therefore earlier treatments is important in containing the development of disease complications. Currently it is thought that management of a cystic fibrosis child is improved by having the child's need coordinated by one regional centre. For example in the Victoria state cystic fibrosis centre in Melbourne, 80% of children have a life expectancy of 20 years. (Phelani Hay 1984). Management of the disease centres around pancreatic supplements, antibiotic therapy and physiotherapy. Vaccinations, especially for measles and pertussis and the annual influenza vaccinations are important for preventing the early demise of a cystic fibrosis child. Severe viral infections such as influenza or chicken pox may result in serious deterioration of respiratory function. The dose of influenza vaccine may be halved therefore allowing its use on children under four years. The use of enteric-coated pancreatic supplements has allowed the normal growth and development of cystic fibrosis children. It has also meant the introduction of a normal diet for cystic fibrosis children. They are now advised to take normal calorific values of fat and an excess of this is the suggested managements of some centres. Eventually some cystic fibrosis children will show some signs of slowing of growth and weight loss. This is

generally associated with increased respiratory infection and deteriorating pulmonary function.

Physiotherapy on a routine daily basis forms an important basis for the management of lung disease in children with cystic fibrosis. The aims are to clear the lungs of thickened mucus, irrespective of their infective status. The physiotherapy may involve the patients alone, a form of autogenic drainage. In this technique a form of controlled deep breathing is supplemented by the use of inhalations of moisture, breathing against a positive expiratory pressure and the forced expiratory technique (huffing). Physiotherapy may alternatively involve a therapist or parents and be based on the manual percussion of the chest, postural drainage and again forced expiration by the patients themselves. The autogenic technique allows patients independence and greater flexibility. Most children with cystic fibrosis comply with a physiotherapy routine lasting 20-30 minutes three times a day. Regular exercise programmes provide a means of coughing up secretions but must be a daily activity before they would substitute for physiotherapy.

Continuous antibiotic therapy ins aimed at preventing the development of irreversible lung damage. The antibiotic regime is rationed by continuous monitoring of bacterial pathogens in the sputum at 6 or 12 weekly check ups. Various different organisms culture the lungs at different ages in cystic fibrosis children. Culture of haemophillus influenza exacerbates treatment with amoxycillin and then Augmentin. This is often followed up by *Staphylococcus aureus* infection. The risk of staphylococcus pneumonia is much increased following a viral infection such as measles or chicken pox. Fear of staphylococcal infection precipitates the use of lifelong flucloxacillin therapy. Further infections are with *Pseudomonas Aeruginosa* which after infection cannot be eradicated. Pseudomonas infection can be treated aggressively by three monthly courses of intravenous antibiotics for 10-14 days in any patient in whom Pseudomonas cultures are positive. Training of parents and patients has facilitated the introduction of home intravenous antibiotics. Infections and other sources of Pseudomonas eg. *Pseudomonas Cepacea* are associated with a poor prognosis. This organism is resistant to antibiotic therapy and therefore may be responsible for further declines in respiratory function. One method of dealing with *Pseudomonas cepacea* has been to stop anti-pseudomonas therapy for short periods in the hope that the *P. cepacae* will be replaced by *Pseudomonas aeruginosa.*

PRENATAL DIAGNOSIS.

The prenatal diagnosis of cystic fibrosis involves two techniques. Both methods are best suited to families with a 1 in 4 risk of having an infected child. Chorionic Villous Sampling, occurring 6-8 weeks into pregnancy, involves the use of restriction fragments length polymorphism closely associated with the cystic fibrosis gene. Initially the cystic fibrosis affected family is typed first with the most favoured probe and enzyme. This is followed by establishing the phase relationships between markers and the cystic fibrosis gene. This usually involves examining bands on southern blot of DNA taken from blood of both parents and the already affected child. If the sample from the affected child or the index case is

not available for typing, then it is not possible to proceed with this form of diagnosis. The advantages and disadvantages of chorionic villous sampling is given in Table 2.

The alternative method of prenatal diagnosis involved the use of amniocentesis and the analysis of fetal microvillous enzymes (Glutaryl transpeptidase, aminopeptidase, intestinal alkaline phosphatase). Amniocentesis is carried out at 16-18 weeks and should be reserved for those with a 1 in 4 risk of an affected child. The advantages and disadvantages of aminocentesis are given in Table 3.

PROGNOSIS.

The long term prognosis for the disease has improved greatly over the last thirty years. The life expectancy of many children is now over 20 years, with approximately 25% reaching the age of 30 years. These improvements can be related to:

1. Introduction of antibiotics to treat severe infections and prevent a large decline in respiratory function related to infections.

2. Pancreatic supplements producing an improved diet for cystic fibrosis patients. These allow normal growth and improved quality of life for the patient. They also provide increased resistance to infection.

3. Early diagnosis and treatment of the disease can prevent the early development of complications eg.influenza vaccination prevents serious compromise of respiratory function due to viral infection.

4. Recognition of mild cases - ie. those with later diagnosis has led to improved survival figures.

Future hopes for the disease rest with the use of heart and lung transplantation for severe cor pulmonale; and with genetic research and identifying the defective proteins. Heart and lung transplantation has been used increasingly over the last 5 years as a treatment of severe cor pulmonale, a

Table II. Advantages and Disadvantages of Chorionic Villous Sampling

Advantages

- Increased accuracy of diagnosis.
- Earlier diagnosis allowing a first trimester termination for all affected fetuses

Disadvantages

- Need for blood sample from the 'index' affected child
- Requirements for early workup of nuclear family to assess theinformativeness
- Chance that some will be uninformative or only partially informative for DNA probes

Greater than 5% risk of spontaneous abortion

Table III. Advantages and Disadvantages of amniocentesis

Advantages

- All pregnancies with a 1 in 4 risk of cystic fibrosis can be assessed.
- No prior family workup is required
- Assays may be completed within 1 hour of receipt of the sample

Disadvantages

- Decreased accuracy of diagnosis (cf.CVS). Increased false positives and false negatives
- If termination is required then it will have to be a late termination (18-19 weeks).

major complication of advanced cystic fibrosis. Initially patients had a poor response to transplantation but success rates are now improving. There have been no reports of the epithelial transport defects occurring in the new lung, although the defects are still present above the site of the anastamosis.

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The Cystic Fibrosis Gene

S.J. Louise Smith

It's now well over a year since the cystic fibrosis gene was cloned and there is still much to be done before its localisation can be translated into an improvement in health care for affected people. I'm not going to go into any details on how the gene was located, for this information (which is rather technical) see ref.1. However to put it rather bluntly, despite the fact that the gene has been localised and sequenced has been sequenced, no-one really knows what it does. The cystic fibrosis gene has been named the CFTR gene (cystic fibrosis transmembrane conductance regulator). It is located on the long arm of chromosome 7 and is composed of 27 extrons which code for 1,400 amino-acid residues. There seem to be several different final products of the CFTR gene which result from the removal of exons from the first nucleotide binding fold. The functional significance of these products is not known.

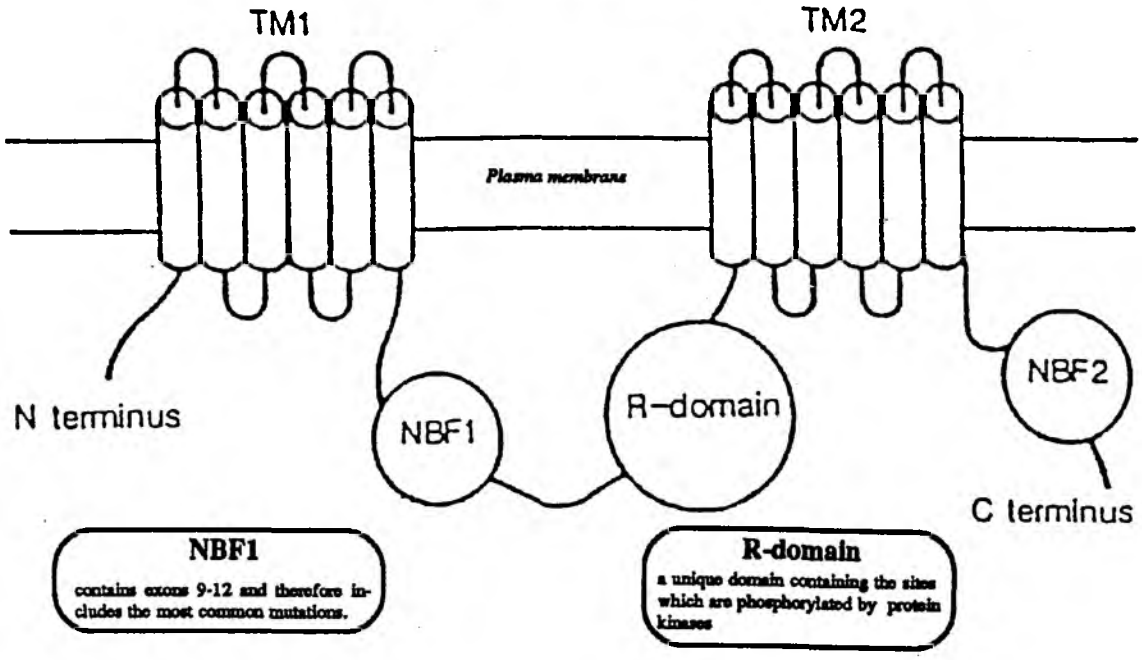

Fig.1. Schematic model of the Cystic Fibrosis gene product (CFTR). TM =Transmembrane region. NBF =nucleotide binding folds.

As I have already stated, the actual protein, and its function in man, is not known, however the sequence of the amino-acids forming the gene is known and this can be used. (directly and in comparison to other genes) to predict a structure for the protein. Using this information it is thought that the gene codes for a large trans-membrane protein which is very similar to several transport proteins all of which have in common the coupling of ATP hydrolysis to the pumping of molecule into or out of the cell. A basic diagram of the suggested structure is shown (Fig.1). These findings agree with what was already known about the pathogenesis of cystic fibrosis; that is that the disease seemed to be caused by defective transport of chloride ions across epithelia. Unfortunately the story is not that simple, it is thought that the CFTR gene product is *not* the ion-channel involved. There are several reasons for this;

1) The CFTR-protein is coupled to ATP-hydrolysis whereas the normal ion channels are not.

2) Normal ion channels allow ions to flow across them in both directions while the CFTR-protein has already been shown to be very like a family of transport proteins which only allow active transport in one direction.

3) Chloride channels seem to be different in different tissues but the mutations found in all C.F. patients so far have been defects in a single gene.

4) The CFTR-protein seems to, quite simply, be too big to be a ion channel.

So, what does the protein actually do? It has been suggested that the protein might transport a molecule which regulates the chloride channel; another explanation is that the protein handles a substrate which

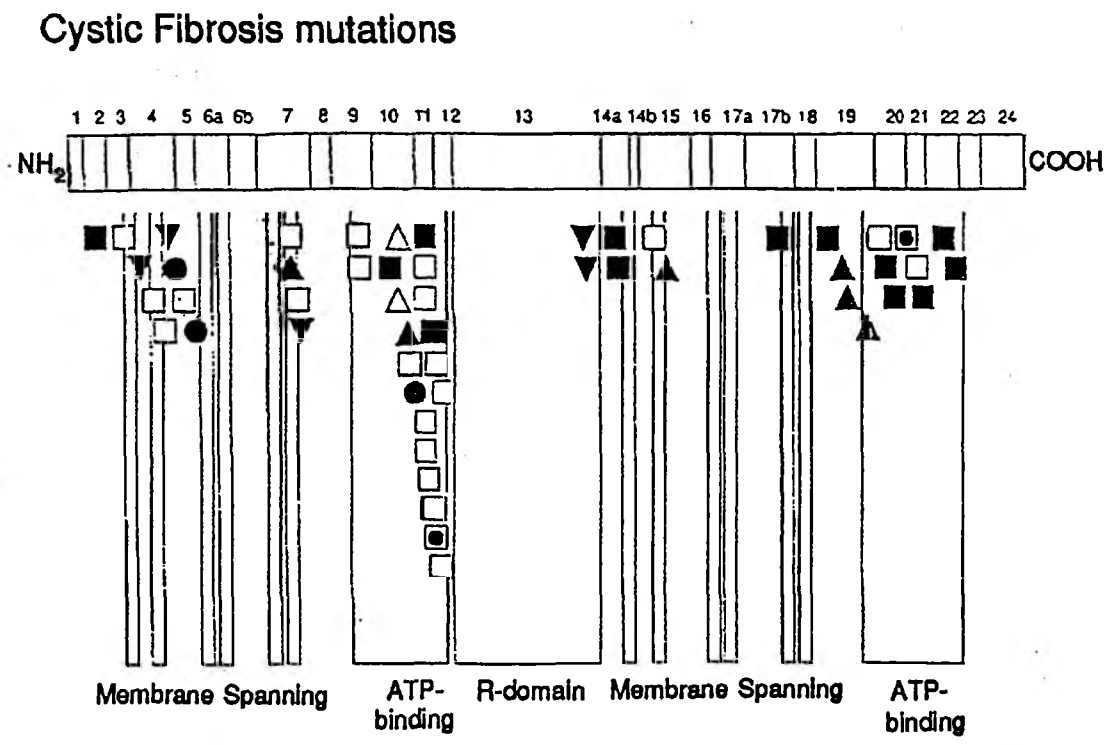

Fig.2. The CFTR gene exons. Each symbol shows the location of one identified mutation.

acts as a regulator on the chloride channel[2]. No doubt more information will be discovered in the near future since this question seems to be central to the whole field of cystic fibrosis.

The finding of the CFTR gene has meant that the exact location of this protein in the tissues of the body can now be determined. This has been done by raising antibodies to the CFTR protein and examining where these antibodies attach to tissues. Preliminary results show that the antibodies attach to sweat glands and to a subset of T-cells but not, as would be expected bearing in mind the clincal observations, to the pancreatic cells. Furthermore it is thought that the antibodies bind specifically to the reabsorptive and not the secretory side of the sweat glands. Further studies are, of course, needed to confirm the exact location of CFTR and these surprising results need to be explained with respect to the clinical disease.

A lot of work has been going on all over the world in an attempt to explain what has gone wrong with the CFTR gene in patients with cystic fibrosis; in others words the identification of the mutations in the gene. This has been found to be more complicated than would have been wished, at present well over 60 different mutations have been found in the gene. The most common of these is the deletion of a phenylalanine residue in about 70% of all patients. In Scotland this is the most common mutation also, and accounts for about 73% of the mutations in this group of patients; the next two commonest mutations between them acount

for a further 11.4% of patients. These two mutations both involve a glycine residue, in the first instance glycine is changed to an aspartine residue, in the second mutation the code for glycine is changed to a "STOP" code which terminates the synthesis of the protein. The information on all mutations when it is collected together shows a rather unusual pattern: it seems the the largest number of mutations are clustered together in the area of the first nuclear binding fold (NBF_1). (Fig.2.) The reason for this, again, is not really known but the second NBF has cetainly been examined for mutations exhaustively. It has also been observed that there are no large deletions or rearrangements anywhere in the gene which is surprising given that the CFTR gene is very large.

Attempts have been made to match the muations in the gene (remember that it is a recessive disorder so there are two mutant copies) to the observed clinical situation in the patient, for example the most common mutation described as a "severe" mutation while other mutations found in the exons 1,9 and 12 are "mild". Surprisingly two patients with both genes containing the common and severe mutation have been found to have pancreatic sufficiency which confounds the above hypothesis. Such attempts to match the patient's symptoms to the genetic cause of the disease will probably only be successful once the molecular basis of the disease is actually understood.

All that I've written so far seems rather negative however some progress has been made; one of the most exciting developments in the last year has been the sucess of correcting abnormal chloride channel permeability in cultured CF cell by getting them to express normal CFTR [3]. This sounds promising but it must be remembered that there is a huge jump from gene insertion into the genome of a cultured cell *in vitro* to possible gene therapy in patients with cystic fibrosis. This is the situation in all aspects of gene therapy, for all different diseases despite the optimism of many people. It has been suggested that it could be possible to deliver a normal CFTR gene to the airway epithelial cells by use of an aerosol delivery, this kind of treatment depends on the use of retroviruses to get the new gene inserted into the patient's DNA. These techniques of retroviral therapy *in-vivo* are sadly not yet adequately developed, but who knows what will happen in the future?

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Acknowledgements

I would like to thank Cheryl Jones and Iain McIntosh from the Human Genetics Department, Western General Hospital, Edinburgh, for all their help with this article.

THE DRIFE DIARIES

Artwork by Donald Davidson

As readers will be aware, Teviot Row is alive with rumours that an ex-Edinburgh medical student is threatening to publish the diaries he kept during his undergraduate days in the "Swinging Sixties". His former colleagues, now distinguished medical men, are said to have offered large sums as "hush money" to "Docter X", and several Edinburgh Publishing Houses have experienced burglaries and arson attacks, as well as telephone calls hinting at complications should the publisher ever need medical treatment. Undaunted, in what must be journalism's coup of the decade, ***Res Medica*** *has secured exclusive rights to these manuscripts, and after consultation with our lawyers (who advise us that their authorship must remain a closely guarded secret) we now present the second instalment of the first extracts from* ***The Drife Diaries.***

JUNE 16th

Got up. Had breakfast. Nev. has graciously lent me his Damon Runyon book - says it was made into a very successful musical, and I should try the style. (Nev reckons if my autobiog is blockbuster he'll be famous: little does he know I intend to change all names, sexes, towns of origin and perversions to protect my royalties.) Anyway here goes ..

This fine evening I am sitting with a group of prominent citizens on the steps of the Royal Infirmary, speaking of this and that and watching the broads with the bedpans going about their business, when all of a sudden I notice four guys approaching me on the sidewalk. They are four very well known characters up and down Lauriston Place, and one is a very tall and very obnoxious guy known to one and all as Andrex. Andrex is giving me a cold stare which suggests strongly that he is sorer than a prolapsed haemorrhoid at me for running against him for the Moderatorship, and the three fellow citizens with him are wearing expressions of such sorrowful reproachfulness that I begin to feel distinctly nervous. Andrex raises his voice above the sound of knuckle-cracking and tries the diplomatic approach:

"Listen, frog-face," he says, "Ever since I am a tiny baby on my mummy's knee I cherish the ambition that some day I will be Moderator Ludorum Laetitiarumque, and I do not care for some greasy schmo to try and blow it away. Furthermore my companions here are so touched by my aspiration that they are investing a substantial number of potatoes on the outcome of the impending election."

They are four very well known characters ...

I think it disrespectful to reply from a sitting position but it is no easy matter to rise when I have Andrex's pal Broncho standing on my left hand and Gertrude the Gorilla standing on my right hand.

"Believe me", say I. "I have no wish to make myself disagreeable to peaceloving citizens such as yourself but my white-haired mother's heart is set on seeing her flesh and blood installed as Moderator and being as I am an only child what else can I do?"

I can see that Gertrude the Gorilla is touched by my filial devotion for he blinks his one good eye and eases the pressure on my right mitt. The fourth member of the deputation, Slit-mouth Charlie, ceases swishing the air in a meaningful fashion with his rolled-up *Evening News* and turns to look at Andrex.

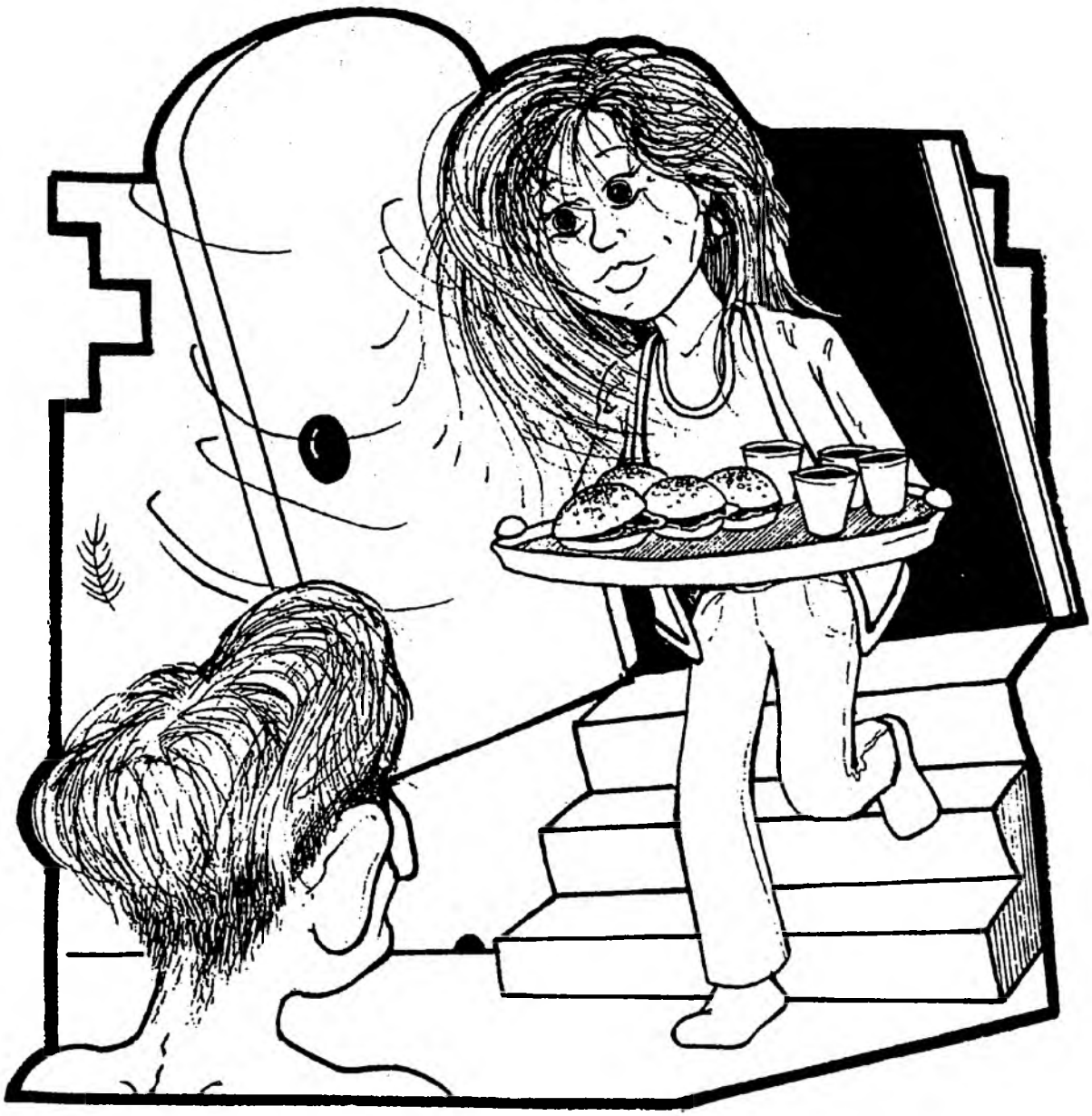
Andrex snaps his fingers and his henchmen back off. "In that case," says he, "I have a proposition. I suggest that we and our advisers meet in equal numbers to discuss our differences. Shall we say Thirlestane and Spottiswoode at midnight?"

Well, five minutes of midnight sees Nev, Tony and me dragging the unwilling Hulk towards the corner of Thirlestane and Spottiswoode. "I am missing my beddy-byes", wails the Hulk. "I am going without my hot chocolate." Rarely am I seeing the Hulk so seriously displeased. "My hotty-bottle will have cooled down by now. Teddy is missing me." Nev and Tony and me smile satisfied smiles at the sound of Hulk working himself into a homicidal frenzy. In the distance we can see strung out across Spottiswoode a line of shadows.

"Two bob says Hulk will not put 'em all in A & E without us doing nothin' but wind him up", whispers Nev.

"You made me miss my bedtime story!" roars Hulk, beating his chest. You see, all week we were putting it about that Hulk is on his elective in Borneo so we figure we have the advantage of surprise. I am therefore more than a little astonished that the shadows do not disappear as soon as Hulk lets off his first yell, and I begin to suspect that Andrex has invited many of his old cronies to join the congregation. Up ahead I hear a high-pitched laugh. "You bums are surrounded!" he shrieks. "This evening my colleagues and I are spreading the word around the neighbourhood that the Marchmont Sharks are planning a surprise attack. The Warrender Jets are somewhat displeased and offer to escort us safely home. Renounce your candidacy, Wimp, or my allies will turn you into an oatmeal porridge."

Behind us we hear the creaking of the leather jackets of a dozen Jimmies. It dawns on me that the Hulk is very silent and when I look at him I see he is now asleep standing up. When this happens nothing west of Krakatoa wakens him, and accordingly I come over somewhat thoughtfully and watch my life floating in front of me. All of a sudden I hear a doll's voice from a nearby doorway. "In here!" says the voice, and figuring and undignified retreat is preferable to three months in traction, we duck up the close, prop the somnolent Hulk against the door, and let the Jets bruise their toecaps kicking the other side.



Her tiny delicate hands trembled ...

JUNE 17th

Got up. Tried to work out what we were all doing asleep in a close. Had breakfast brought down the stairs by the most beautiful girl I've ever seen. This must be love. I may have said that before *(Editor's note: See Jan 5th, Feb 26th, March 4th and 19th, April 28th, etc etc)* but this time it's for real. It's like something out of Mills and Boon.

Her tiny delicate hands trembled as she shyly held out the bacon butty, and for a moment, as I took it from her, out fingertips touched. In that instant a thrill like an electric charge ran through me, and I shivered involuntarily. Her cherry-red lips parted and her clear brow furrowed in a worried little frown. "Are you cold?" she whispered solicitously.

"It's nothing," I laughed, my twinkling blue eyes making fun of her concern.

"Its just that .. I mean, I couldn't help noticing that your friend has taken your cloths," she said, flushing prettily as she averted her gaze.

"Hulk likes to keep warm," I explained, rolling modestly over onto my flat, well-muscled tummy as I tried to unwrap my trousers from around his neck. He had put all three pairs of Y-fronts over his head, and though I desperately wanted to choose her favourite colour I decided it would be quickest to don the outermost pair".

"Can I turn around now?" she whispered tremulously, her eyes screwed up tight and her heart beating wildly in her bosom.

"Just a moment", I answered, deftly flicking my old Cumnockian tie into place. "There!"

She turned and gasped involuntarily as her eyes fell on my broad shoulders, slim hips and long athletic limbs. The little laughter lines crinkled around my piercing blue eyes as I grinned boyishly but tenderly at her. Trembling, she lifted a hand to brush a speck of dust from my lapel.

"Aren't your friends cold?" she asked. "They have gone a funny colour".

"I'll give them back their shirts," I replied and masterfully I ripped the flimsy material from the Hulk's heaving chest. "By the way", I added, "You haven't told me your name".

"It's Edwina", she replied, and as a shaft of sun from the fanlight caught her flame-red hair I thought for the thousandth time how beautiful she was.

"Mine's .."

"I know", she replied. "I've seen your picture on the election posters."

"Then .." I breathed, a wild hope rising in my bosom. "Does this mean .. does this mean I can count on your vote?"

"Oh!" her voice suddenly broke into a wild sob. "O would that it did!" I stared at her, aghast and uncomprehending. "You see," she continued. "I am but a poor Psych and Soc student. Yes, and proud of it too!" Her little jaw lifted and her eyes flashed with spirit. "But a grand gentleman like you would never be seen with

the likes of me. We are two worlds which can never meet. To see each other again would only cause untold pain and suffering, so .. farewell, my love!"

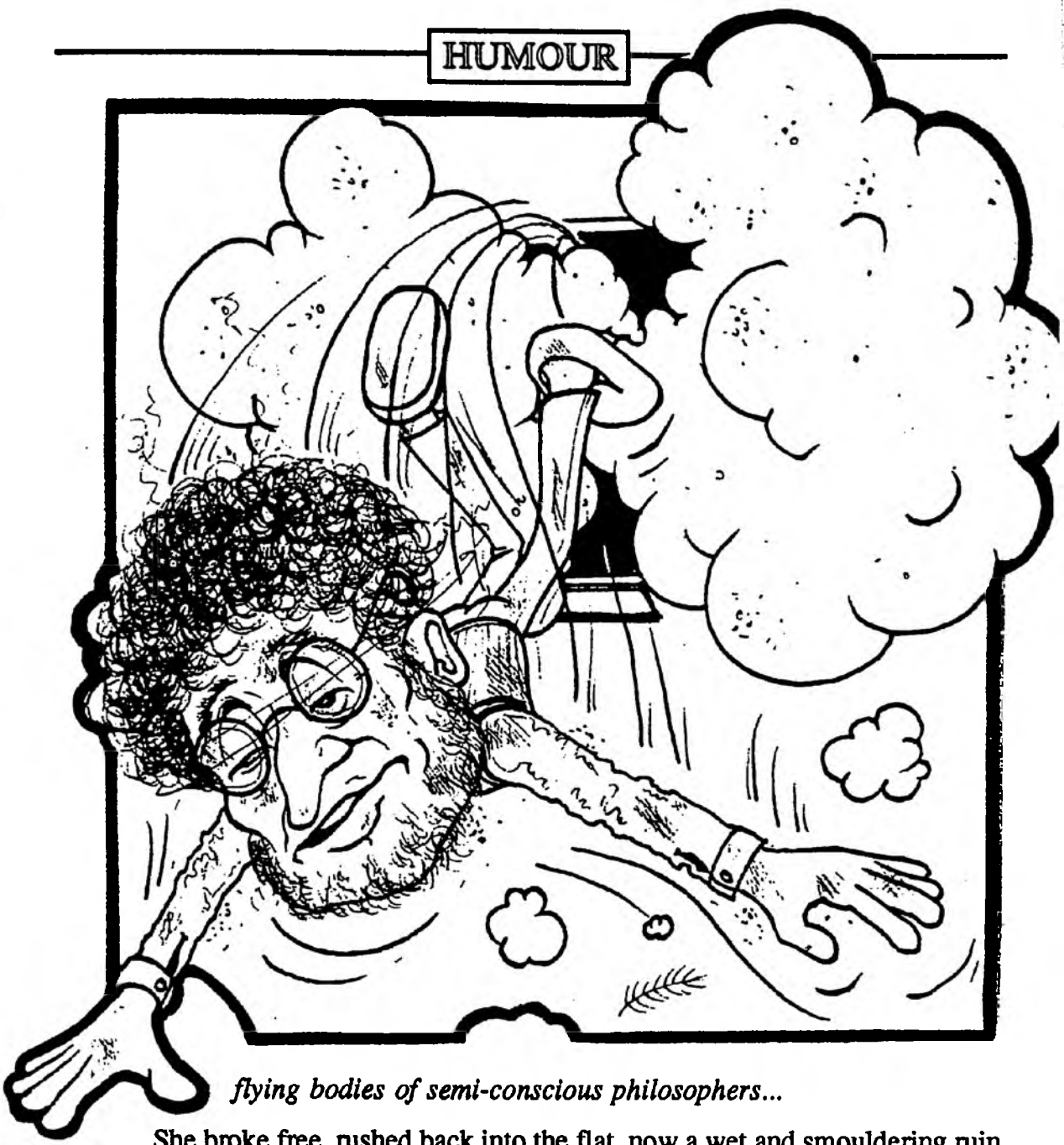
Choking back a sob, she turned and fled like a faerie spirit up the stairs. Ere I could follow, a door slammed above me, and a great weight pressed upon my heart. I knew I could never win her back unless some miracle happened. Wearily I turned back to my recumbent colleagues, squeezed their ear-lobes, rubbed their sternums and waited until they dressed - or in the Hulk's case, undressed. What had Edinburgh to offer me now? The crown of Moderator Ludorum Laetitiarumque - even if I had won it - seems hollow, and as we stumbled into the sunshine of Spottiswoode Road, I realised that without love, life's glittering prizes are but tinsel.

At the corner of the street, I turned for one last glimpse of a happiness that had nearly been mine, but when I did so my heart leapt into my mouth in horror. Smoke! Smoke was drifting in a thin stream from the doorway we had so recently left! My mind was in a whirl as we rushed breathlessly back along the street. Had the poor darling child been so distraught that she had allowed her own bacon butty to burst into flames under the grill? She was a girl of too much spirit to resort to deliberate self-immolation, however deep her despair. We reached the doorway and heedless of our own safety rushed into the smoke-filled close and up the stairs to a door with a dozen hand-written cards stuck to it. My heart went out to the lovely girl forced to live in such squalor, probably with students of politics, philosophy or even, though I shuddered inwardly at the very thought, Eng Lit. Great clouds of smoke billowed under the door and through the letterbox but in a trice the Hulk had put his shoulder to the door and charged into the flames beyond. I tried to follow but I was beaten back by the flying bodies of semi-conscious philosophers as Hulk unceremoniously emptied the flats of its occupants. I waited in an agony of suspense for what seemed like hours and then my heart leapt in my bosom as I saw, dimly through the smoke, the Hulk with Edwina's limp form under his arms. He had somehow found a tap and was dousing the burning walls. "Catch!" he yelled and a deftly threw the elfin child into my outstretched arms. She lay there motionless.

"Is she .. is she ..?" gasped Nev and Tony.

"Are you .. are you ..?" I choked, full of grimmest foreboding.

Edwina stirred and her eyelids fluttered open. "Am I .. am I ..?" she breathed faintly, then her little body began to struggle. "Put me down," she cried. "I must go back to him!"



flying bodies of semi-conscious philosophers...

She broke free, rushed back into the flat, now a wet and smouldering ruin, and threw her arms around Hulk's waist. His snooty anorak was torn, and she reached up shyly to touched the singed hair on his manly chest. "My hero!" she cried, and I could see from the way that she and the Hulk gazed into each other's eyes that there was no place for me now in her life. I turned away, my eyes moist with unshed tears.

"Don't take it hard, man," said Tony, who had experience in these matters. "She's got fat legs."

(to be continued in the next issue of Res Medica)

ANNUAL DINNER

Each year the RMS holds its annual dinner, and this year was no exception. Traditionally the location of this get-together alternates between the Royal College of Physicians in Queen Street and the Royal College of Surgeons at Surgeon's Hall. This year (our 254th session) it was our 'turn' to return to the 'surgeons'.

Although I've now been a member of the RMS for four years this was only my second time at *the* dinner; thus I'd never been inside Surgeons' Hall. As for many people in Edinburgh, all that I'd seen of the famous college was its bus stop. Happily I've now seen the inside and what a fabulous host it was for our dinner.

This year all went exceptionally well and I think it was enjoyed by all present. We were especially pleased to see so many students there, after all it is *our* Society's dinner.

Top row (left to right): Stuart Blake, Aileen McKinley, Simon Hart, Caroline Cobb, Kneale Metcalf. Bottom row (left to right): Emily Cobb, Louise Smith, Mary Dolan, Dr.Ronnie Robertson, Donald Macarthur, Sigrid Wanless, Clare Miles.

Thanks go to all our speakers especially our guest-of-honour Dr. Ronnie Robertson. Any one who's been to his Phase II pathology tutorials in the autopsy suite will remember him (and his comedy act) very well. Other speakers included Professor Alder, Dr. A.Doig, Aileen McKinley (last years senior president) and our current presidents.

The final word of thanks go to Mary Dolan (as Annual Dinner Convener) and our secretary A.P.

Council

Senior President	Donald Macarthur
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2nd Junior President	Louise Smith
3rd Junior President	Sigrid Wanless
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Library Convener	Emily Cobb
Museum Convener	Simon Hart
Entertainments Convener	Agneta Fullarton

As you know this is only the second issue of our 'little baby' and we are still in the early stages of growth. We're trying to set up a mailing list for future issues. If you'd like your name to be added to it then simply send the slip below to the RMS Office.

To: Editor, Res Medica, Royal Medical Society, Students Centre,
5/5 Bristo Square, Edinburgh EH8 9AL.

Please send me ____ copy/copies of RES MEDICA.

Name: _____ Department: _____

_____

_____

_____

Upcoming Events

PUBLIC BUSINESS meetings are held, when appropriate, in the RMS on Wednesday evenings at 8.00pm. These meetings are open to anyone, you don't have to be a member, you don't even have to be a medic. (If you don't have a keycard just ring the doorbell). The speaker is invited to dinner beforehand and anyone is welcome to join the table; just ask to put your name down in the office. A three course meal, wine and coffee is served for the measly sum of £3.50.

PRIVATE BUSINESS meetings are announced weekly and usually start at 9.30pm. On evenings without public business they will start at 8.00pm.

So what's arranged for the next two terms?

Wed 27 February	Private Business
Wed 17 April	Private Business
Wed 24 April	Joint meeting with the Medical Protection Society.
Wed 1 May	Dissertation: Mr. Stuart Blake
Wed 8 May	Annual Extraordinary General Meeting.
Wed 15 May	Private Business
Wed 22 May	Private Business
Friday 31 May	President's valedictory address.

THE FUTURE

*A **History** article about the future seems a bit of an odd idea but we thought it might be 'fun'! This article is the last of three speeches given at the start of the Society's 250th Anniversary Appeal (about four years ago). At the time it was intended to publish a number of articles in a celebration copy of **Res Medica**. Sadly publication was hampered by financial constraints and Res Medica 'slept on' until our first issue last year which featured an historical account of the RMS. This article is about the personal predictions of the future of the RMS by **Dr. Richard Newton**. He was a senior president of the Society and is currently working as a psychiatrist at the Royal Edinburgh Hospital.*

How on earth does one talk about the future of the Royal Medical Society? During these celebrations, however, it is appropriate to wonder what the future might have in store for us and indeed to wonder whether we will still be here in another 250 years time.

To picture the future one really needs to study the past and the present, and I am thankful that this has already been done by the two preceding speakers. It seems to me that the Royal Medical Society stands and has stood for two different things: at any time in the future these two parts of the Society will continue to be important. That is, its historical standpoint and present standpoint.

We have all been around for a long time and that backcloth of history is important to us all. I hope that future members will continue to give us new reasons to be proud of the traditions of excellence to which this Society aspires. Although this background as part of the Royal Medical Society, our members change from year to year and the Society has a "here and now" meaning for each new year of members. What the Society is in "real time" changes from year to year and is dependent on the character of its' membership and on the whims of Council. It seems to me that this "here and now" meaning consists of predominantly two things: The academic side and the social side of belonging to the Royal Medical Society. What changes will the future bring to these aspects of our society?

The Royal Medical Society has rarely placed much emphasis of the importance of being a medical society. A lot of medical students are put off joining because they see us as elitist and a little bit boring. The entry of any medical year hence tends to be a little fragment, with the Medical Students' Coun-

cil doing one thing, the final year clubs organising the odd disco and the Royal Medical Society struggling to present itself as the answer to all social difficulties as well as academic ones.

Last year in Synapse a very strong argument was presented by the editors for the formation of a unified Edinburgh Medical Society with rooms from the University and finances from subscriptions and societies' council grants. It is likely that interest in this from the student body will continue to grow; and in perhaps twenty to thirty years time when the well known phenomenon of student apathy is finally overcome such a medical society will come into being. This inevitably would lead to a sharp drop in our student membership and hence our annual income.

It may be that some time in the future we should address ourselves to this subject. The Royal Medical Society has more facilities than most other student societies and socially they are quite under-used despite the energetic attempts of our Entertainments Conveners. To solve this problem *may* require some changes in our membership and subscription procedures, perhaps with a separate medical society membership, allowing limited access to our facilities, with a much smaller membership taking part in the full academic curriculum and paying higher subscriptions for the privilege. (*At the moment we have no intentions to limit membership, indeed we're open to anyone to join with no increased membership subcription planned -Ed.*)

I see us being faced really with two options: either that we should expand our role and devote much more energy and to becoming a sociable society with the implications that has on our constitution and our financial set up, or alternatively we could contract down on ourselves and stop trying to be everything to all men. Our society is ostensibly devoted to the furtherance of medical excellence and the promotion of medical enquiry. A smaller membership of people genuinely interested in these ideals *may* be the path to the future.

One topic about our social facilities that has persistently been brought up in the past and has been a matter of some debate over my time as an active member whether or not we should have a bar in the rooms (*recently decided against for the time being - Ed*). I am certain that, whatever the future may hold for us, this will remain a matter of some interest well into the future.

What else will we have to offer these drunken but brain-crammed whiz kids of the future? Well, quite a lot, I hope. Our Library is well stocked (*the situation in the library has changed now due to excessive theft -Ed*) and well used by our members. If this Anniversary Appeal is successful then we will be better equipped to maintain these standards in the future. The pattern of education as a whole is changing and even medicine is becoming aware of these changes. It doesn't require a crystal ball to see that computers as tools of learning are going to become absolutely necessary and that we will have to provide these facilities for future members. (*This equipment has been bought and is available in the RMS for all members - Ed.*)

Video demonstrations and tutorials have become invaluable aids to the medical curriculum and our Library in the future will have to include them. I would suggest that with this increasing complexity of the medical school curriculum it will become

important to forge closer ties with the medical faculty. This cooperation will enable us to forge closer ties with the medical faculty. This cooperation will enable us to provide more relevant and up-to-date texts and articles. I hope it would lead to benefits for us in that we could provide better Library facilities, and also benefit the faculty by providing a grounding of extra-curricular discussion of course topics.

The Public and Private Business meetings of the Society have been our raison d'etre over the last 250 years: it is reasonable to suggest that will always be important. It is also likely that attendance at these meetings will always be important. It is also likely that attendance at these meetings will continue to be as sporadic as they have been in the past.

The topics presented at these meetings have always been a reflection of current medical fashion. The large number of presentations on syphilis, heroic surgical procedures, new medical treatments and discoveries bear witness to this. However, the Society has always tended to steer away from discussing socio-political matters. Increasingly health promotion and disease prevention are becoming more pertinent than acute medical treatment. I hope this change in medical fashion will be reflected in our meetings. Throughout the history of medicine environmental and social change have had a great impact on improving quality and quantity of life. However, recognition of this also implies recognition that the business of government is also important in the promotion of health. As doctors and future doctors it is important that we take an interest in the effects of political changes on the health of the populations we care for. Our business meetings would be an ideal forum on which to stimulate discussion of such social and political issues. I think they are important but they are also interesting and of relevance to medical students, particularly in Phase I and Phase II. (*We have regular joint meetings with groups such as the BMA and Medical Protection Society on legal, political and ethical matters*).

I would not suggest, however, that this is done at the expense of the presentation of clinical and scientific papers. It is hoped that part of the revenue generated by this year's Appeal will be used to finance one or two students each year through a BSc. Honours course (*Already in action -Ed*). The research which such a year involves will provide material for original dissertations to be presented, and of course outside speakers will be discussing the new medical advances of the future. I wonder what sort of thing they will be presenting? I'm afraid I have a couple of possibilities for which I take no responsibility: percutaneous aortic Y-grafting - THE END FOR SURGERY?; possibly matter transportation and urethral stricture: post-elective students' viewpoint and remembering the importance of social and political issues: immortality - can the health service afford it?, or perhaps forced diuresis to reduce nephrotoxicity of streptozotocinin the treatment of advanced metastatic insulinoma (BMJ May 1987).

What will medical students be like who are listening to such dissertations? One thing that may occur is that the entrance standards to our medical schools will be lowered and brighter children channelled into pure sciences and research from the beginning of their course at University. Something like the Israeli model. Would this affect our society as it would the whole of medicine or would we actively welcome

A.P. - the permanent secretary of the Royal Medical Society.

bio-medical science students to our membership? We already have a number of non-medics as members, and indeed in the recent past they have played an important role in the running of the Society. Will this trend continue or again will we contract down and define our membership more specifically?

Will, indeed, there be any members coming to our meetings? It doesn't require too large a stretch of the imagination to foresee a time of Home University courses with all preclinical teaching being via some form of audio-visual computer terminal. Perhaps the Royal Medical Society will become an optional computer program available on the Edinburgh Medical School floppy disk. How on earth will A.P. cope with this?

For it is extremely difficult to imagine the Royal Medical Society without our Permanent Secretary. I can see the Society in 100 years time at last having a secretary who can work the electronic typewriter after hours of practice whilst hooked-up to her portable life-support machine. Or perhaps one of the future members could incorporate her into the computer program. Perhaps the last thing the Royal Medical Society will be remembered for is that it had the only personal computer that chain-smoked Benson and Hedges filter tips!

Over the last 250 years the Society has seen many changes in it's rooms, its people and in medicine. I can see similar changes occurring in the future. Medicine and

medical students will change: new treatments, cures for cancers, viral illnesses, dementia, who knows what will be discovered? Technology will become more techno, health I hope will become more healthy. However, over the last 250 years the Royal Medical Society has not changed its fundamental ideals and it's character has remained intact.

This presentation on the future of the Royal Medical Society has been short. This is because I do not believe that any important changes will occur to what actually is the Royal Medical Society. I feel that in the future the Society will continue to provide a forum for exchange of knowledge new and old about medical and paramedical topics. It will continue to be a meeting place where over a video console, a coffee or a beer, ideas about health and medicine will be discussed and where the fellowship involved in belonging to the Society is enhanced.

I am sure that in 250 years time the students then will be as proud of the Society as we are of ours today.

It always interesting to read in retrospect someone's predictions. So how accurate are they? Well the societies' rooms are now extremely well used, especially our coffee lounge at lunchtimes and we certainly don't intend to restrict our membership to medical students only. We're open for all to join. As for the Anniversary Appeal, it has now come to 'fruit' and extra funds are now available for audio-visual equipment, travel and study funds, and bursaries for intercalated years which were awarded for the first time this year.

Journalscan

This is a short collection of interesting items pertinent to medicine and science in general. It gives a taste of some of the current work in hand around the world. We would welcome any contributions of this nature, just a short chatty narrative of an interesting or amusing article that you have seen or read.

Coffee

A recent study[1] of 'healthy' moderate drinkers (consuming 4-6 cups per day; *moderate*? I call that low.) showed that on switching to decaffeinated (in a blind trial) many developed headaches for 2-3 days.

One good reason not to stop? Need another good reason? Here goes ...

A report[2] from Sheffield states that coffee induces a desire to defaecate (by increasing activity in the rectosigmoid) in nearly 30% of people. For some unexplained reason this predominately affects women! - a cheap cure for constipation? Unfortunately the effects of the evil brew doesn't end there; about the same number of people (30% of the population) find that coffee aggravates their symptoms of irritable bowel syndrome.

Will the coffee saga never end?

1. BMJ 1990 No. 6739 Vol.301
2. CIVT 1990, 31, 450-453.

Snoring

Do you snore? Does your old man snore? Did you know that snoring increases your risk of heart attacks? - according to a recent study in Bologna, Italy. The Italians compared patients admitted with their first heart attacks to matched controls (with non-cardiovascular acute illness).

It was found that snorers (as confirmed by the cohabitee) had a significantly increased risk of heart attack. The only question that remains is why? Snoring is associated with sleep apnoea which might put stress on the cardiovascular system. Or snoring *itself* may cause such stress.

1. BMJ 1990; 300:1557

Paurfour du Petit

You've heard about Horners Syndrome, but how about *Paurfour Du Petit* Syndrome? This is a seldom recognised clinical syndrome characterised by a hypersympathetic state following damage to the cervical sympathetic nerves. It was first recognised by a French physician (called, strangely enough, *Paurfour Du Petit!*) in cases of wounds to the neck in the Napoleonic war. This letter[1] details a case of Paurfour Du Petit syndrome following removal of one left parotid gland in a 41 year old male. Post-operatively he

noticed left facial weakness which completely resolved. He also noticed persistent left pupillary dilation, initially associated with some blurring of vision, but this later resolved. On examination six months later, signs of autonomic overactivity on the left side were noticeable ie. lid retraction, pupillary dilation, with direct and consensual light reflexes and a full range of eye movements unaffected. Whilst the possibility of a right sided Horners Syndrome, giving the appearance of a left sided hypersympathetic state was considered, it was deemed unlikely in this surgical procedure. This is believed to be the first reported case of *Paurfour du Petit* syndrome following a surgical procedure.

1. Journal of Neurology, Neurosurgery and Psychiatry. Nov 1990. Byme & Clough.

Policeman's Groin

Sounds nasty, doesn't it? However the lack of safety catches on police revolvers is reported[1] to lead to this unfortunate and thankfully rather unusual occupational injury. At least four incidents have been reported in which police officers have shot *themselves* in the groin while practising drawing their gun when rising from a sitting position. Thankfully at short range the damage caused is minimal and only requires limited surgery.

The same cannot unfortunately be said for a second shooting injury reported in the same issue. A young man was admitted after being shot at close range by a hand gun. One of the bullets had entered his left flank, the wound being very obvious, and the bullet (on X-ray) was shown to be within the flank musculature. Surgical exploration of the area failed to find the bullet and was eventually abandoned to free the operating theatre.

Two days later the bullet had appeared (again on X-ray) to have moved downwards. A second incision was made, and despite using a metal detector this operation was also aborted.

Well to cut a long story short, following a third attempt to remove the bullet and over a week after the incident, X-rays could no longer locate the bullet. It was concluded that the bullet must have penetrated the descending colon and been passed per rectum! The patient made an uneventful recovery. Explaining the whereabouts of this bullet to the police proved difficult.

Finally the authors note that all bullets recovered from patients became their property and should not be released to the police without their proper consent.

1. Injury 1990, 21, 182-192.

Sleeping Genes.

Yet another twin study! This time an American study reported the finding of a genetic factor in the quality of sleep and individual experiences. A general population of about 3000 adult twin pairs were studied (returns from 6000 mailed questionnaires). The authors calculated that genetic factors accounted for at least 33% of the variance in sleep quality and 40% of the variance in sleep pattern. There was no evidence for a decline in the importance of genetic factors with age. As for environmental factors as perhaps expected, short-term environmental fluctuations seemed to account for about 30% of the variance but no effect could be shown for an effect of

shared family environments. At the present genes seem to be implicated in everything.

1. Sleep Vol.13 No.4 1990, 318-335

Dissection v. Prosection

Does dissecting a cadaver really help us to learn anatomy or do we do it because our teachers did? Two groups of first-year students in Nigeria were taught by different methods; the first group in the traditional manner, the second using a programme which excluded dissection by students and used prepared demonstrating samples. In the second group the students were allowed access to the prepared specimens without staff supervision.

The results of this experiment were evaluated by questionnaires, a practical test and a written paper.

The findings? Well ... in both tests the experimental group performed better than the traditional group; significantly better in the theory paper. Furthermore the programme of learning in the experimental form took only 74% of the time taken by the traditional group. The results of the student questionnaire were even less enthusiastic about continuing dissection. Perhaps our anatomy department should take a look ...

1. Medical Education 1990, Vol.24 No.4, 389-395.

Liver Problems

Salmonella, botulism, BSE... Yet another food scare is upon us again. This time it concerns vitamin A which is found in relatively high concentrations in liver.

An excessive intake of vitamin A immediately before or during pregnancy substantially increases the risk of birth defects. Hence the Department of Health's warning to women who are, or are likely to become pregnant to avoid any substance which has a high retinol content such as vitamin tablets and liver.

A recent study showed that the risk of birth defects was highest in women who had taken vitamin supplements (>40000 IU) over the first two months of pregnancy. It also showed that intake under 10000 IU was unlikely to be tetratogenic.

However typical dietary intake of retinol among women of childbearing age is 1400 IU/day and few exceed 10000 IU/day. There has been the odd case of birth defects associated with vitamin A: one woman accidentally ingested 500000 IU during the second month of pregnancy; others consumed over 25000 IU/day over several weeks or months.

It would appear that concern about vitamin A is excessive. Furthermore the liver is a good source of many nutrients required for fetal growth. But until more evidence becomes available the best advice to pregnant women is not to abstain from liver altogether, but to consume only reasonable amounts (<50g/week).

1. BMJ 1990; 301: 1176

Stethoscope?

Which is the odd one out? Opthalmoscope, laryngoscope, gastroscope and stethoscope. Well they are all medical instruments, one of which is used for auscultation while the others are used as visual aids.

The term stethoscope is derived from the Greek *stethos* (chest) and *skopein* (to see). Thus the literal interpretation would be an

instrument for visual inspection of the thorax. The term 'stethophone' from the Greek *phonos* (sound) would clearly been more appropriate.

The misnomer originated in 1816 when the French physician Laennac rolled up a sheet of paper into a tube and used it as an auscultation device. For some unknown reason he named the device a stethoscope. Since then there had been some attempts to correct the mistake but to no avail and the term stethoscope has become ingrained into medical terminology.

1. Journal of the Royal College of Physicians of London. (1990); 24:318.

Head Banging

A report on a study on the phenomenon of head banging, or "a compulsion to rhythmically strike the head against a solid object", was reported in the Lancet.

Apparently head banging occurs in up to 15% of children, particularly during the latter half of the first year of life and more often in boys than girls. Most children are not injured by this unusual pastime which is usually precipitated by temper tantrums. It is not believed that such behaviour is due to underlying emotional disorder although the child's actions can be very disturbing to the parents' involved. Children largely outgrow the behaviour but referral to a psychiatrist may be necessary if the behaviour persists after four years of age.

1. Lancet 1990; 336:1374.

Bellringing

It has recently been revealed that church bell ringing may be damaging to health. Injuries reported include fractures, ropeburns, tooth extraction, a near hanging and a scalping. Bizarre deaths have also occurred such as falling from a bell frame and two suicides, one from jumping from a bell tower and the other a hanging.

It has been suggested that doctors should become more familiar with the injuries associated with bell ringing so that appropriate advice and treatment can be given.

However bell ringing is largely an English pursuit. There are only 15 rings of bells in Scotland and so there is presumably a low incidence of injuries. Of the 140 members of the Scottish Association of Change Ringers only 2.5 will sustain an injury related to bell ringing at the injury rate of 1.8% per year. Bell ringing injuries are therefore not a major concern to doctors in Scotland.

As a final point I would like to say that in ten years of bell ringing I have never sustained a significant injury or seen others injure themselves in a bell tower. bell ringing is much safer than alarmists would have you believe and is almost certainly safer than crossing the road!

1. BMJ 1990; 301:1415-8

Thanks to L.Smith, C.M.Teoh, Clare Miles and Clare Rogers for contributions.

If you have a contribution for Journals*can* send it to the RMS office for the next issue addressed to the Editors, Res Medica and see your name in print.

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From the President ...

A few thoughts on dislocation ... and participation

Now that the new year is here and the Society's President's Annual Dinner is over, there is perhaps a tendency to feel that the high point of the Society's year is passed. I would urge you however to resist such self-indulgent fancies and see that as a Society we have a function throughout the academic year.

From my own point of view, it must be said, the Society's 254th session started quite memorably with the Freshers' Address and Party, at which, as some of you may remember, I pulled off one of the greatest publicity stunts of recent years with a well-timed lateral dislocation of my right patella whilst dancing in the Meeting Hall. The immediate correction of this somewhat painful and rather inconvenient anatomical anomaly necessitated a little trip across to those nice people in the Accident and Emergency Department, at the time undergoing one of their typically pleasant late night Friday sessions. Seeing A&E from under the blankets for a change was rather enlightening. On reflection however I would advise you to be very sceptical of those in the profession who proclaim that a visit to hospital on the receiving end teaches you what it's like to be a patient.

I was seen in an environment that I know, that is not frightening and does not smell strange and unfamiliar. I was seen by medical staff I knew and surely treated differently because of it. Everything done to me was either familiar to me, or could be easily explained to me in medical language that I was conveniently versed. The uncertainty, the unfamiliarity and the fear that must have been the greater part of the average patient's visit to hospital were all absent, and it cannot then be fair to say that I now know how those on the other end of medical care feel.

At any rate after a few weeks of experiencing the fascination of carrying out my 'activities of daily living' with a knee fixed in 3 degrees of flexion, I am pleased to report that the more chronic aspects of the situation and far more instructive with regard to 'how the patient feels'. There would certainly be a case for ensuring that all medical students who haven't had a spell in plaster do so prior to their qualification.

To return to the health of the Society, this has been a good year in terms of membership figures. The perennial complaint, however, that although we have a large number of members, only a small percentage of them are 'active' is as valid as ever. Wednesday evening meeting attendance are on the increase but still don't reflect the potential size of the audience or the quality of the presentations. The Annual Dinner was attended by more students than ever recently, combining to fulfil the hopes of William Cullen over 200 years ago that 'the Professors and students always live in amity together, and sometimes drink wine together.'

The Society has always aimed to provide for the social and educational needs of its members. Many benefit from the existence of our rooms as places of conversation and the worship of soap operas, as places to work, to meet, to worry each other and learn from each other (much in the manner of the Society's original functions). It would be pleasant then to see a little more interest in the Society's Business Meetings - an interest in what has actually kept the Society going for so long and in a sense justified our existence for over 250 years.

Donald Macarthur

PRAESES

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