ASSOCIATION OF RESPIRATORY TECHNICIANS AND PHYSIOLOGISTS

VOLUME NO 35 NOVEMBER 1988

BREATH

CONTENTS

ASSOCIATION OF RESPIRATORY TECHNICIANS AND PHYSIOLOGISTS

SPRING MEETING

Saturday 8th April 1989

ST. THOMAS' HOSPITAL, LONDON SE1

Abstracts by 3rd February to:

Dr. P. M. Tweeddale
Respiratory Function Laboratory
City Hospital
Edinburgh EH10 5SB

CHAIRMAN'S REPORT 1987 – 1988

S. L. Hill
The General Hospital, Birmingham

This year has seen the two annual meetings move away from the traditional hospital site. This has happened mainly because of the facilities we now require to hold a scientific meeting and a trade exhibition in close proximity to each other. Additionally the current financial climate in the NHS has meant that many post-graduate medical centres are now charging for the use of facilities, particularly when meetings are held at weekends. The Spring meeting was therefore held at the Kensington Town Hall in London, the usual venue of the Winter meeting of the British Thoracic Society. The facilities and catering were excellent, a venue we shall certainly be using again in the future. In view, however, of the cost of overnight accommodation in London, the use of this venue may be restricted to the one-day Spring meeting. Since the AGM has been held over two days for the past few years, we looked further afield for the venue for this year's meeting, and in particular towards hotels with conference facilities. The Griffin Hotel in Leeds has allowed us to combine our AGM with a large trade exhibition and provided us with the opportunity for members to socialise in very comfortable surroundings.

This format is likely to be repeated although it is anticipated that our AGM and scientific meeting in 1989 will be held as part of a two-day FAMT meeting. At this meeting it is hoped that member societies will hold their own meetings in the form of parallel sessions, with all societies coming together for joint sessions on matters of common interest. A very large trade exhibition is proposed for this event and details are currently being discussed for a proposed date of the first weekend in November. This could potentially set the scene for the future, in bringing all disciplines together without losing autonomy, but in doing so generally improving the profile of FAMT amongst members of all societies.

Of even greater importance to the ARTP is the possibility of a parallel session at a summer meeting of the British Thoracic Society, specifically aimed at technical presentations and discussions. It is hoped that this could be incorporated into the programme of their 1990 summer meeting, which is scheduled to be held on campus at Birmingham University. At present we are unsure if this should be an additional meeting in our annual programme, or if it should replace the Spring meeting. Comments from members of the ARTP would be appreciated.

The scientific programmes for both of our meetings this year have been varied and given us an insight into other areas of thoracic medicine, and more unusual aspects of clinical respiratory physiology which are usually reserved for textbooks. This has included lung immunology, emphysema and alpha-1-antitrypsin deficiency, respiratory adaptations for flying and diving, and respiratory function testing and speech therapy. In addition during the programme of the AGM we learnt how a vital piece of equipment which we all take for granted in the respiratory laboratory is made, namely the special gas cylinder. The Association is grateful to all of our presenters this year. The dates of our forthcoming meetings and abstract submission deadlines will be published well in advance from now on, so plan to be part of the programme in the future.

Discussions with the British Thoracic Society continue. Apart from looking at the possibility of holding parallel sessions as part of their overall meeting programme we are also looking at increasing awareness amongst clinicians, who are responsible for respiratory physiology laboratories. To this end an article is currently being prepared for inclusion in the winter newsletter of the BTS. It is also hoped that this newsletter will in the future carry notices of ARTP meetings, seminars and items of interest. We have been discussing the possibility of running training seminars in conjunction with the Education Committee of the BTS. This has important implications since the BTS may be able to help not only with relevant speakers but also in the financing of any such seminars. We shall continue to encourage clinicians to allow technical staff study leave to attend meetings, particularly if they are held during a weekday. In order to discuss these and many other areas of concern we hope for an extended meeting with our BTS colleagues in the near future.

From the financial point of view the Association is maintaining a yearly profit. We are currently looking at ways of using money for charitable purposes and we hope in the forthcoming year to offer travelling fellowships for members of the Association to attend medical conferences both in this country and abroad. Additionally we may be able to give financial help to members to attend our own meetings. Any other suggestions that you may have on how this money could be used would be gratefully received.

Over the course of the year there have been two resignations, namely that of Penny Wright, our Public Relations Officer, and Sonia Jackson, the membership secretary. The Association would like to thank these two individuals for the hard work and effort they have contributed to the administration of the Association over the years. Additionally, Dena Muirhead, following her confinement and delivery of a healthy baby girl, has no longer been able to continue in the role of secretary. This post has been taken on by Vanessa Hurt, who has done an excellent job since she took over during the middle of the year. Vanessa has also taken over the role of membership secretary and in the future all queries regarding membership should be directed to Mrs. Vanessa Hurt, Cardiothoracic Measurement Department, Derbyshire Royal Infirmary, Derby. The post of Public Relations Officer initially was given to Cherry West, who, due to personal commitments, was unable to continue. Since this time the duties have been taken on by Patricia Tweeddale in the role of meetings organiser, Sarah Robinson as the job vacancy bulletin organiser and we hope to elect Julie Howells into the position of recruiting advertising for both our meetings and the journal.

To conclude, thanks to all members of the Executive and Education Committees for their continuing commitment to the Association including Patricia Tweeddale, who has done a tremendous job in organising this meeting and also in arranging the forthcoming meetings and programmes; Angela McLeod, whose term of office as treasurer comes to an end and who has put our accounts into a very professional and understandable form; Duncan Hutchison, Adrian Kendrick and Stevens Brothers, the printers, for continuing to keep production of *Breath* up to its excellent standard; and to Gill Manning, who is not only the current examinations secretary, as well as secretary of FAMT, but who has helped to get the advertising for the AGM as well as filling any other gaps that needed to be filled. Thanks

to all of our sponsors, without whom we would not have any meetings and certainly no journal. Finally, I would like to thank Derek Cramer who is retiring from the Executive Committee after serving since the beginning of the Association. Thank you, Derek, for all of your efforts over the years, both as chairman and also as a non-office-holding member of the Executive Committee; your contribution has been greatly appreciated.

Education and FAMT Report

1. IN-SERVICE TRAINING MANUALS

The in-service training manuals have been revised and updated and are now appropriate for both in-service and supernumerary students. There is a similar standard between all physiological measurement disciplines with clearly identifiable learning outcomes. A much greater emphasis is placed on continuous assessment and the manuals are the first steps towards a full competency based training programme to be devised according to guidelines from the National Council for Vocational Qualifications which will be discussed later. They were launched by the DHSS in June 1988 to representatives of all the Regional Health Authorities in England, Wales, Scotland and Northern Ireland. These manuals are currently available either from the Department of Health of from Sue Hill.

2. BTEC NATIONAL CERTIFICATE IN SCIENCE

A clear negotiating link has been established between BTEC and FAMT. This has enabled the new BTEC Science National Certificate (MPPM option) to be linked closely to the revised in-training service manual. There is a core theme throughout of patient handling and interpersonnel skills and the new course brings together common areas and applies basic principles to medical physics and physiological measurement. The human physiology unit is now appropriate to underpin the in-service training manual and it is sufficient that there is no longer a generic medical physics and physiological measurement double unit, but an optional double unit of specialist material based on the foundation section of either the physiological measurement manuals or the medical physics manuals. Many colleagues in the country have submitted the new national units to run courses from this current academic year. We therefore look forward to assessing the results of the revamped course and new in-service training manuals over the forthcoming year.

3. HIGHER POST-BASIC EDUCATION

The BTEC Higher National Certificate programme has been recently considered in detail. A seminar was held in October where representatives of all the colleges offering the Higher National Certificate course together with representatives from the professions attended to discuss the possibility of a national course to lead on from the new BTEC National Certificate programme. There was general agreement that the double optional unit should move towards more specialisation. Although the ideal of single discipline specialisation was considered, it was felt that it may be more appropriate to run joint cardio-respiratory, or audio-neurophysiology double units. The question of repetition from the National Certificate programme was discussed in detail and it was felt that this was totally undesirable. A further meeting of all FAMT representatives, colleges and BTEC is proposed for the New Year, when it is hoped that a national framework for this course will be devised, taking into account the profession's requirements for this programme.

Additionally FAMT has been considering the post-Higher National Certificate education of technicians, in particular through the Credit Accumulation Transfer System (CATS), which can eventually lead to a Council for National Academic Awards (CNAA) validated degree. This is particularly important in the area of vocational training, since discreet units can be prepared which are vocationally relevant and accumulated through the CAT system to eventually add up to the points required for the CNAA validated vocational degree. The ARTP is currently looking at preparing units for CATS rating and the areas being considered are clinical exercise physiology and diseases of the airways, although we will be constantly looking for subjects which require post-HNC education. Eventually units may be devised to be relevant for several physiological measurement disciplines, for example covering management and supervisory skills. Any other suggestions would be gratefully received.

4. INFORMATION LEAFLETS

Several of the information leaflets to accompany the in-service training manual are available. If you require a photocopy please get in touch with the Secretary of the Education Committee, Dr. Patricia Tweeddale, Respiratory Laboratory, City Hospital, Edinburgh. We are currently looking at ways of publishing these information leaflets in the form of a book, particularly since these leaflets represent the compilation of information from many different sources which are often difficult to obtain. It may be that the ARTP itself could finance such a venture. Alternatives are some financial support from the BTS, or even through the DHSS. The DHSS is very interested in using this idea for an accompanying training manual, and we shall pursue this avenue.

5. SEMINARS

To start to provide adequate training seminars to accompany the teaching of the in-service training manual, the ARTP is planning to hold two seminars during 1988/89, on two very important aspects of the training manual which are often covered poorly or are poorly understood, namely gas transfer and skin testing and allergy. It is hoped that these courses will be run in the early part of next year. Details will be circulated as soon as they are available. We hope to offer seminars on all aspects of the complete training manual in the forthcoming years.

6. ARTP NATIONAL ASSESSMENT IN RESPIRATORY PHYSIOLOGY

We have examined three students so far this year. There is one assessment outstanding in Northern Ireland which will be conducted later in October. We are particularly encouraged that Northern Ireland is willing to send students for assessment and we are sending two of the Association's representatives to examine this student. This year's results should then be available shortly after. We are continually looking at the assessment system, particularly to fit in with proposals for FAMT, which requires us to provide a one-year assessment suitable for both the first year's training of in-service students and the end of the specialist option supernumerary period.

7. LABORATORY STANDARDISATION

The laboratory standardisation questionnaire is continuing to be analysed. From the initial results an abstract has been accepted for presentation at the forthcoming winter meeting of the British Thoracic Society. Over the next year the remainder of the tests covered by the questionnaire will be analysed in detail and the results will be available in due course.

FAMT NEWS

FAMT over the past year has extended its remit to cover Scotland and a meeting of the Central Council was held there earlier this year. The question of including its remit as far as Northern Ireland is currently being considered. A seminar was held in September for representatives of all Executive and Education Committees of member societies. At this seminar the FAMT proposals for the future were put forward and discussed. The meeting was very well received and gave member societies the opportunity of commenting on several areas which will be of concern over the next few years. The year has also seen FAMT becoming established as the negotiating body for the professions in medical physics and physiological measurement.

National Council for Vocational Qualifications

The National Council for Vocational Qualifications (NCVQ) was established in October 1986 to reform and rationalise the system of vocational qualifications. New qualifications are being introduced to be known as National Vocational Qualifications (NVQ). NVQs will be classified in the NVQ framework according to level and occupational area. The fundamental characteristic of NVQs is that they are based upon the competence required in employment, as determined by those in employment. The aims of NCVQ are firstly to improve vocational qualifications by basing them on standards of competence required in employment and secondly to establish a national vocational qualification framework which is comprehensible and comprehensive, facilitating access, progress and continued learning. The objectives of the NVQ framework are:

1. To rationalise and update the system of qualifications
2. To enable industry to set the standards of qualifications it needs
3. To provide clearer paths for progression from one qualification to another
4. To open access to qualifications and promote education and training.

The benefits of NVQ for the individual are more motivation to obtain qualifications that are clearly related to employment standards and requirements, and clearer routes for career and qualification progression and lastly the opportunity to obtain qualifications without barriers, such as specified periods of training, or age limits.

This system of vocational training will be required within the National Health Service, and the NHS training authority is currently looking at all professions within the NHS and the move towards competency based training programmes. It is hoped however that physiological measurement will be the first profession within the NHS to be established under the NCVQ framework, which needs to be in place by 1991. Currently the manuals are being rewritten according to the guidance from NCVQ by the NHSTA and the relevant professional bodies. This will mean that every task expected of, in our case a basic grade respiratory physiology technician, will be clearly defined, right from the moment the patient walks into the door until the result is sent to the requesting department. This is quite a departure from the manual that exists today but will clearly define all the performance criteria required and the associated skills and knowledge that need to be attained in order to satisfy the performance criteria. It will mean that the manual you see today will eventually be at least four times greater in size. However it is hoped that this should ensure an even greater uniformity of standard throughout the country.

In connection with the move towards competence based training in the NHS, the NHS training authority has a research project which is funded to look at implementation, particularly in terms of the content and structure of the manual and their acceptability and suitability for full competency based training and assessment. It will also look at the link with the educational qualifications and include both trainers and resource requirements and implications. This form of training will eventually apply to post-basic training so we may well be looking at a training manual to accompany the Higher National Certificate programme in the future.

Education and training will be on the agenda for the foreseeable future with potentially many exciting developments.

TREASURER'S REPORT 1987 – 1988

The accounts for 1987-88 have been audited in accordance with the Charities Commission Constitutional provisions.

The income for the year from all sources amounted to £11,000 with the total expenditure being £7,539. Since our stocks of badges and stationery have been depleted, it left few assets to be accounted for in the audit. In total the excess of income over expenditure this financial year amounted to £2,782.

Three editions of the Journal 'Breath' were published which following printing and postal costs produced an income of £424.81. The 'Job Vacancy Bulletin' which incurred little postage or printing charges showed a handsome profit of £2,691.99. These profits we hope to utilise in the forthcoming year to cover the cost of educational publications and also to sponsor members to attend medical conferences.

ALPHA-1-PROTEASE INHIBITOR DEFICIENCY

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Alpha-1-protease inhibitor (API) deficiency and its association with pulmonary emphysema was first described by Laurell and Eriksson (1) just twenty five years ago. Prior to that date, there was little understanding of the biochemical and cellular events leading to the development of emphysema, though the morbid anatomy and pathophysiology had already been thoroughly studied. The discovery of API deficiency provided a crucial turning point and has stimulated a massive expansion of research in this field.

The circumstances of the discovery are of some interest. The research workers seem in no way to have been engaged in a search for the causes of pulmonary emphysema. They were studying serum protein patterns by electrophoresis, when they observed a number of specimens in which the alpha-1-globulin region was almost completely absent (Fig 1). Study of the patients from whom these sera originated revealed a high incidence of emphysema, with striking clinical features. It was soon established that the abnormality had a hereditary basis and the clinical and biochemical features of the disorder were subsequently described in detail (2).

Biochemical properties of API

API consists of a folded polypeptide chain of 394 amino acids of which the full sequence is now known (3). To this 'primary' chain are attached a number of carbohydrate side-chains, giving a total molecular mass of about 52,000 daltons. The main site of synthesis is the liver, though macrophages can also synthesis the protein in small quantities.

API appears to have an important biological function as an inhibitor of proteolytic enzymes. From its biochemical properties and its situation among the alpha-1-globulins it was originally named alpha-1-antitrypsin. It has subsequently been shown to inhibit a number of other enzymes, and so is now more generally known as API. In this context, the most important enzyme is probably the powerful elastase secreted by the polymorphonuclear leukocytes which is inactivated at a faster rate than any other enzyme. The function of the polymorph elastase is to digest micro-organisms and cell debris and it also participates in a continuous process of breakdown and repair of the lung's structural proteins. Under certain circumstances, including infection and cigarette smoking, polymorphs are stimulated to enter the pulmonary tissues and the secretion rate of elastase is much enhanced. During this process, a significant quantity of the enzyme can leak to the exterior of the cell where it can potentially damage the tissues of the lung. This action should normally be opposed by API and it is now generally believed that the lack of this important protective protein is the main reason for the development of emphysema in API deficient patients.

The concept of a 'balance' between elastase and inhibitor has therefore come into being and on this theory the pulmonary elastin is likely to be degraded if there is an excess of enzyme or a deficit of inhibitor (4, 5). The wide variations in the severity of lung disease both in API deficiency and among cigarette smokers generally, indicate that this simple balance theory cannot be the whole story.

The polymorphs generate powerful oxidising agents which can also damage the tissues (6) and both serum and cells contain a number of antioxidants whose function may be to provide the tissues with a further line of defence. Thus the concept of an 'oxidant—antioxidant' balance also enters the picture.

API is in fact very readily degraded by such oxidants and is rendered vulnerable by the presence of a methionine group in position 358 of the primary chain. This is critically placed at the reactive site of the molecule and it has been shown that oxidisation of this methionine group results in complete loss of the inhibitory function of API.

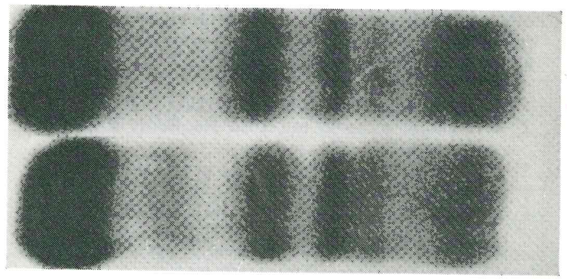

Fig 1. *Paper electrophoretic strip: Below: normal serum. Above: serum in API deficiency. Reproduced from the original publication (1) by courtesy of the author and the editor of Acta Medica Scandinavica.*

It has been postulated that oxidation of API could be in part responsible for the occurrence of emphysema in patients with normal serum levels of API (7). API can be identified in broncho-alveolar lavage fluid, but in patients with chronic bronchitis, much or all of the API is oxidised or otherwise inactivated (8, 9). It has been suggested that oxidants derived from cigarette smoke could be directly responsible, but it now seems more likely that cigarette smoke acts in an indirect manner, by stimulating the entry of polymorphs into the lung and so increasing the local burden of potentially damaging enzymes and oxidants.

Biochemical variants of API

It is now known that API can exist in over thirty different biochemical forms. These variants are known collectively as the Pi system (for 'protease inhibitor') but only a few of these appear to be of clinical importance. This topic is reviewed in detail by Fagerhol and Cox (10).

The common variant is known as Type M; other important variants are Types S and Z, where the abnormalities arise from errors in genetic coding so that there is an amino acid substitution in the primary chain. Every individual inherits one variant from each parent, the combined pair being known as the 'phenotype'. Thus an individual who inherits

Type M from each parent is described as being a 'homozygote' for this type and as having the phenotype MM. Those who inherit two unlike variants (e.g. MZ) are described as 'heterozygotes' (Fig 2.).

The phenotypes which are of any practical importance are shown in Table 1. Each of the variants forming a given phenotype makes a specific contribution to the total serum API concentration, with the exception of Type 'Null' where no API is produced at all. Thus, if the contribution of the common MM phenotype is represented as 100%, then the ZZ phenotype will contribute about 15% and MZ about 57%, 50% derived from the single M component and 7% from Z.

For any given phenotype, however, the serum API concentration varies considerably about the mean value (Table 1), so that it is not possible to predict the phenotype on this basis. The phenotype should therefore be assessed by the technique of isoelectric focusing in all suspected cases.

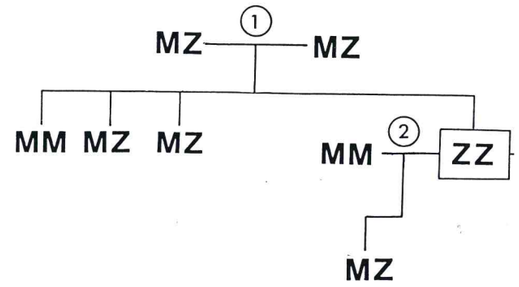

Fig 2. *Theoretical pedigree: 1) Union of two heterozygous MZ carriers; offspring have a one in four chance of being homozygous Type ZZ. 2) ZZ-MM union: MM (85% of population) is most likely spouse, in which case all offspring must be MZ heterozygotes.*

Table 1

Serum API concentration and prevalence associated with various phenotypes.

Phenotype	Serum concentration as % of normal (MM = 100%)		Prevalence in UK population (%)
	Mean	*SD*	
MM	100	25	86
MS	75	16	9
MZ	57	15	3
SS	52	8	0.25
SZ	37	12	0.2
ZZ	15	3	0.03
Null	0	—	Very rare

Prevalence

In the UK, estimates of the prevalence of Type Z homozygotes vary from 1 in 2050 to 1 in 3450. Type S is more common in Spain and Portugal than in the rest of Europe and Type Z is comparatively rare in Black or Asian populations (10).

Clinical features of API deficiency

Homozygotes of Type Z are thought to have a strong tendency to develop pulmonary emphysema. The clinical features were originally described by Eriksson (2) and their findings have been amply confirmed by subsequent authors (11, 12). The main feature is disabling and progressive shortness of breath which may become apparent at any age from 30 onwards. Sputum production is often a feature especially in cigarette smokers. The disorder may progress at a variable pace, but eventually ventilatory failure and cor pulmonale occur. Cigarette smoking has a severe adverse effect upon the course of the disease (13) and survival has been shown to be considerably lower in smokers than among those who have never smoked (14). However, emphysema occuring in a non-smoker should make one suspect API deficiency. The natural history of the condition has been reviewed in detail elsewhere (15).

Lung Function

Tests of lung function reveal abnormalities which are characteristic of emphysema itself, and there are no particular features by which one can definitely distinguish emphysematous patients with API deficiency from those with the normal phenotype. Severe limitation of expiratory flow is a common feature (Table 2) and is related to the airway collapse which results from loss of pulmonary elastic recoil. This can be readily demonstrated using the FEV_1 and the maximal expiratory flow-volume curve may be highly abnormal for the same reason. The vital capacity is usually relatively well preserved but tends to deteriorate in the later stages of the disease; thus there may be a misleading rise in the FEV_1/VC ratio. Little, if any improvement in the FEV_1 follows the administration of a bronchodilator, and on these grounds the condition is often labelled as 'irreversible'. The bronchodilator may, however, lead to a substantial improvement in vital capacity (sometimes as much as one litre) and the increase is related to subjective benefit. Reliance on the FEV_1 alone may mean that the patient is denied beneficial treatment. A marked increase in residual volume is commonly seen, which is usually at the expense of vital capacity.

Reduction in the carbon monoxide transfer factor is another common feature and reflects the reduction in pulmonary surface area for gas exchange. TLCO itself can be reduced by a fall in the vital capacity alone, so a rather better measure of severity is given by the kCO which will have been corrected for volume.

Table 2

Lung function in API deficiency

	Before operation	After operation	Reference values
FEV_1 (litres)	0.4	1.0	2.2
VC (litres)	1.3	1.7	3.0
RV (litres)	—	3.5	1.8
TLC (litres)	—	5.2	4.8
TLCO (SI units)	—	2.1	7.5
$PaCO_2$ (kPa)	—	4.6	4.5 — 6.0
PaO_2 (kPa)	—	8.0	11.0 — 12.5

Values in a 55 year old female patient, (Type ZZ) before and after surgical removal of a large emphysematous bulla. (Figs 3a and 3b).

With regard to arterial blood gases, CO_2 tension remains normal in the earlier stages, and O_2 tension is mildly impaired. Later in the course of the disease, hypoxaemia becomes more severe and finally hypercapnia occurs as a consequence of ventilatory failure.

Radiological findings

The striking feature of the chest radiograph is the localisation of the lesions to the lower zones (Fig 3), in contrast with the upper zone or more uniformly distributed lesions commonly seen in the non-deficient type of emphysema (16). It has been suggested that this is related to the fact that blood flow per unit volume is maximal in the lower zones of the lungs so that the release of elastase from blood borne polymorphs would have the greatest impact at that site.

On occasion, large bullae are seen and these may compress other sections of the lung or cause lateral shift of the mediastinum; such bullae can be removed or decompressed by a thoracic surgeon. Only a small minority of cases, however, present opportunities for imporvement by surgery.

Prognosis

Many of the Type ZZ patients who present to chest clinics are already severely disabled and have a poor long term outlook. The overall prognosis cannot, however, be derived from this selected group, as any Type ZZ subjects with no symptoms may not come to the investigator's attention unless a specific search is made.

In the British Thoracic Society study (12), the majority of Type ZZ subjects were between 45 and 55 years of age, in which age band the UK population is about six million. From the population frequency, (say 1 in 3000) there would be about 2000 ZZ subjects in this age band whereas only about 100 were identified by the chest physicians. The whereabouts of the remainder (some 95% of the total) remains unknown; some no doubt will have died from liver disease in early life and others may have died from emphysema without being notified to the BTS survey. It seems quite possible, however, that the majority of the Type ZZ individuals do not develop any lung disease at all, and if this is true the intriguing question is raised as to why there is such a wide range of susceptibility.

Significance of other phenotypes

After the association of emphysema with the ZZ phenotype had been established, it seemed possible that other phenotypes would behave in a similar manner. This question has aroused considerable controvesy and many studies have been done in attempts to clarify the point.

Type SZ: Heterozygotes of Type SZ have, on average, serum concentrations of about one third of the normal value (Table 1) and thus might appear to have a risk of developing emphysema. In the BTS study (17) only 14 Type SZ index cases were identified whereas 126 ZZ cases were seen during the same time period; the prevalence of Type SZ in the UK population is about seven times that of Type ZZ. The only SZ patients to develop emphysema were, or had been, cigarette smokers and their mean age at the onset of symptoms was about the same as that usually reported by emphysematous patients of normal phenotype and some years later than the age reported by ZZ patients. On the evidence of this study, the SZ phenotype in itself appears to carry little or no extra risk.

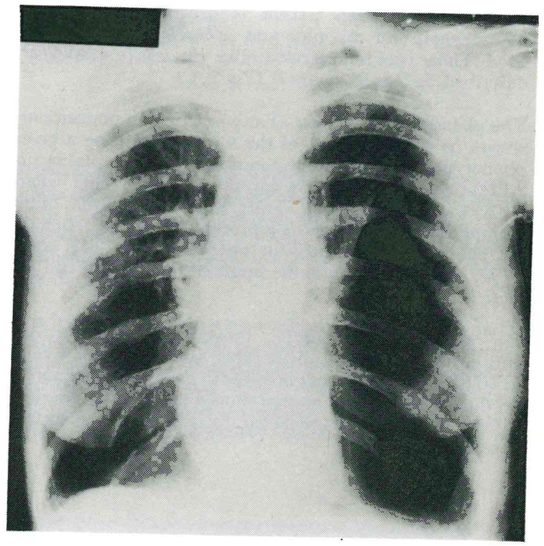

Fig 3a. *Chest radiograph of a woman of 55 years (Type ZZ) showing a large bulla in the left lower zone, causing mediastinal shift (Lung function tests in table 2).*

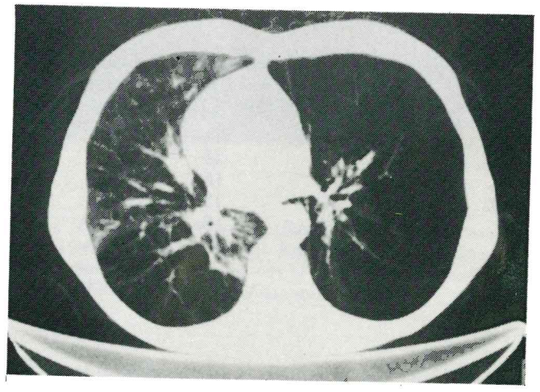

Fig 3b. *CT scan of lower zones (same patient as Fig. 3a).*

Types MS and MZ: Heterozygotes of these phenotypes are much commoner than those of Type SZ, and since they form respectively some 8% and 3% of the UK population, the assessment of any predisposition to lung disease would be of some practical importance. Two types of study have been performed (15); in the first type, the incidence of the heterozygous state has been obtained in patients with emphysema and compared with that of healthy controls. In a number of such studies, Type MZ occurred between two and five times as frequently in patients as controls. No difference between patients and controls, however, has been observed in the incidence of Type MS.

In the second type of study, heterozygotes of Types MS or MZ have been selected from a particular community and their lung function compared with Type MM individuals from the same population. For Type MS no significant differences were observed and any differences between Types MZ and MM were small. The discrepancies between the two types of study in respect of Type MZ can be reasonably explained (18) on the

hypothesis that only a small proportion have a tendency to develop emphysema: statistical tests would then be more likely to yield significant results in studies on patients than in studies based on a normal population.

API deficiency and liver disease

An additional dimension was given to the study of API deficiency with the discovery by Sharp et al (19) of an association between Type ZZ and a severe form of hepatitis in early infancy. Only a minority (some 12%) of ZZ infants develop this syndrome (20, 21) but those that do, present in the first few weeks of life with jaundice and severe liver damage. A minority of those affected may die from liver failure or develop cirrhosis in later childhood with a poor prognosis. The majority seem to recover, but some are left with serum biochemical abnormalities and their long term outlook cannot yet be assessed. There is also a relationship between API deficiency of Type ZZ and the development of cirrhosis in adult life, though again only a minority appear to be so affected (22).

The disorder is brought about by the deposition of API as granular inclusion bodies within the hepatic cells, where it can be demonstrated by specific staining techniques (Fig 4). The abnormality in the primary chain of API is thought to prevent the attachment of the carbohydrate side-chains, a necessary step if the API is to be discharged into the serum from the site of manufacture in the hepatic cell.

Inclusion bodies with similar staining properties (though fewer in number) are also found within the liver cells of patients of Type MZ. An increased prevalence of this phenotype has in fact been observed among patients with hepatic cirrhosis (23).

API deficiency and other diseases

An association between rheumatoid arthritis and Type MZ has been claimed through the evidence is inconsistent. If there were any true relationship, one might have expected a definite association between arthritis and Type ZZ, but no such evidence has yet appeared.

There have been occasional reports in which Type ZZ has been observed in conjunction with disorders of the kidneys, thyroid gland, skin, or other organs, but it seems that these are merely chance associations.

Treatment of API deficiency

Pulmonary emphysema involves irreversible destruction of the lung parenchyma and any treatment short of lung transplantation is therefore of limited value. The severe effects of cigarette smoking in API deficiency indicate that any smoker should immediately abandon this habit and avoidance of any form of atmospheric pollution would be good sense. The administration of a bronchodilator by metered dose inhaler can improve lung function to a modest extent and antibiotics are clearly necessary in the event of an acute infection.

Danazol, a substance related to testosterone but without its hormonal properties can accelerate discharge of API from the liver in subjects of the normal MM phenotype. In Type ZZ homozygotes, however, the response is poor and the serum API concentration is not substantially improved.

Lung transplantation has been carried out in patients with advanced emphysema and can be a life-saving procedure; from the surgeon's point of view double lung and heart transplants offer technical advantages over single lung transplants. Liver transplantation has been carried out in

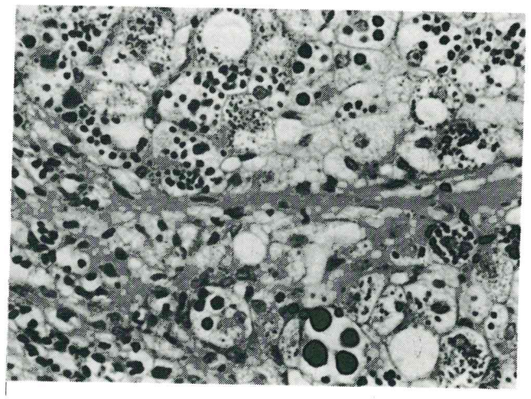

Fig 4. *Liver biopsy from a patient of Type ZZ, stained to show dense globular inclusion bodies in the hepatic cells. (By courtesy of Dr. B. Portmann and William Heinemann Medical Books Ltd).*

a number of patients with advanced hepatic disease; this procedure can rectify the basic genetic disorder and restore the serum API concentration to normal. These demanding procedures together with the powerful immunosuppressor drugs required pose serious problems for the patient and needless to say, may not be successful.

API therapy

Replacement therapy for API deficiency is now available in the UK. API has been extracted from human plasma by Cutter Laboratories in the USA and has been administered to a number of patients by intravenous infusion. It has been shown (24) that this is a safe method of restoring serum API to normal (Fig 5), though the short half-life means that the dose must be given at least monthly (25). A number of low molecular weight elastase inhibitors have been synthesised but none have yet proved safe enough for administration to human subjects. In theory they might prove beneficial when given by mouth and would very probably be cheaper to produce than API.

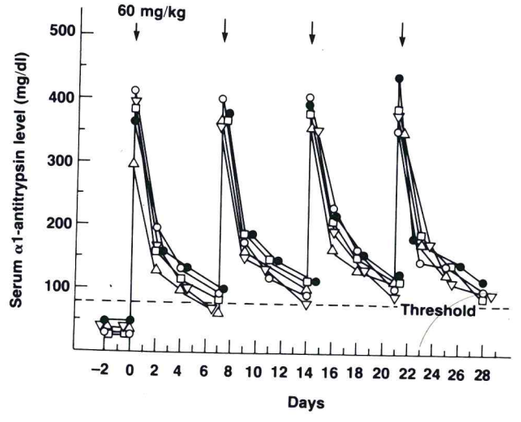

Fig 5. *Serum API concentrations in 5 Type ZZ patients given weekly intravenous infusions of API; samples taken at 30 min, 2, 4 and 7 days after infusion. Modified from Wewers et al (24) by courtesy of the authors and the Editor, N Eng J Med.*

There is at present no evidence on whether this form of treatment is effective in reducing the rate of decline in lung function. Ideally a biochemical marker of elastin breakdown is required and it was originally hoped that urinary turnover of desmosine, an amino acid specific to elastin, would provide a measure of the progress of emphysema; unfortunately, this has not proved sensitive enough to be useful either in cigarette smokers or in patients with API deficiency. The effectiveness of any form of therapy will therefore have to be assessed by measurement of the rate of decline in lung function in a controlled trial; one hundred or more patients would be required, raising considerable economic and organisational problems.

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ANNUAL GENERAL MEETING

The Annual General Meeting of the Association took place at the Griffin Hotel, Leeds on the 14th and 15th October, 1988. We owe grateful thanks to Patricia Tweeddale for organising the meeting, to the speakers for providing a series of varied and interesting papers and to the following firms who generously sponsored the meeting and exhibited their products:

Airspec Ltd*
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* Exhibitor

Seminar: Communication Skills

Verbal presentation — G Manning
Teaching methods in training — K Minty
Writing an original article — D C S Hutchison

Scientific Papers

A longitudinal investigation of cardiorespiratory adaptations to training in elite cyclists. P G Gee, A Norman, S Lal. Bury General Hospital and the General Hospital, St Helier, Jersey.

How a special gas cylinder is made up. J H Scawin, British Oxygen Company (Special Gases).

Respiratory function measurements in speech therapy. A H Kendrick, C Dobson, Bristol Royal Infirmary.

Is the routine screening of lung function useful in detecting the onset of early respiratory disorder? A Parkes, S Sapiano, W Freeman, R M Cayton, East Birmingham Hospital.

Nebulisation: a multi-faceted tool. S L Hill, The General Hospital, Birmingham.

A patient with polycythaemia and right heart failure. M Z Shaheen, W J Windebank, Derbyshire Royal Infirmary.

Abstracts

A longitudinal investigation of cardiorespiratory adaptations to training in elite cyclists

P G Gee, A Norman, S Lal. Bury General Hospital and the General Hospital, St Helier, Jersey.

Evaluation of 12 male cyclists and 6 male 'untrained' controls, equally matched, was undertaken with 4 visits over a 12 month period. The visits correlated to specific points of the cyclists' competitive season, namely pre-, mid-, peak-, and post-season being February, May, August and November respectively.

Several investigations were carried out to establish any changes in cardiorespiratory parameters produced by the training effects of the season. These included static and dynamic lung volumes, carbon monoxide gas transfer (TLCO), carbon dioxide sensitivity (S CO2) and an exercise tst to exhaustion on a bicycle ergometer using a continuously upgraded protocol of 50W increments every 3 minutes, from 50W start and constant pedal rate of 90 rpm.

Comparative differences between the two groups were: (controls v cyclists, ranges) maximum oxygen consumption (VO2/Kg max) 51.7-58.6 v 70.1-83.8 1 min-1Kg-1; maximum carbon dioxide production (VCO2 max) 3.27-3.54 v 4.68-4.86 1 min-1; forced vital capacity (FVC) 6.15-4.8 v 8.2-4.26; forced expiratory volume in 1 second (FEV) 5.23-4.5 v 6.01-3.71; TLCO 48.6-33.3 v 49.6-28.8 m1COmin-1mmHg-1; time to exhaustion 12.8-13.7 v 21.9-23.4 minutes.

There was no significant change in the majority of parameters examined between the four visits. Maximum cardiac output (Qmax) increased in the cyclists from 21.8 to 34.9 1min-1 which was reflected by increased stroke volumes, which was not reflected in the controls.

The physiological adaptations of trained athletes have been shown to be produced to varying levels by short term bouts of training and reversed upon cessation or detraining. These short term fluctuations in cardiorespiratory values were not evident from this study over the evaluation period, however. A follow-up would be required to observe the cyclists after cessation of cycling for a short period before further conclusions can be drawn.

Is the routine screening of lung function useful in detecting the onset of early respiratory disorder?

A Parkes, S Sapiano, W Freeman, R M Cayton, Department of Respiratory Physiology, East Birmingham Hospital, Bordesley Green East, Birmingham, B9 5ST

We were invited by the East Birmingham Community Health Council to a health promotion day and used this opportunity to evaluate the value of lung function screening in the community.

Smoking habits and any known chest disease were noted together with age, height and weight. A wedge bellows spirometer (Vitalograph) and a mini Wright peak flow meter were used to measure forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and peak expiratory flow rate (PEFR). The FEV1/FVC ratio was calculated. The results were compared to predicted values for adults (ECSC 1983, Bull Eur Physiopath Respir.suppl 5:1-93) and children (Cotes 1979, Lung Function. 4th Ed.), and were expressed as % predicted and as standardised residuals (SR). (Thorax 1988;43:265-267).

After assessing 107 people the results from 23 were excluded from the analysis due to known chest disease (16) and poor technique (7). The results from 84 (43M,41F) were evaluated (mean age = 50±15, range = 13-87 years). The mean (×), standard deviation (SD) and range shown for males and females:-

PARAMETER	MALES (n = 43) × ±SD	MALES (n = 43) RANGE	FEMALES (n = 41) × ±SD	FEMALES (n = 41) RANGE
FEVI (1)	3.67±0.82	1.99-4.96	2.63±0.62	1.25-4.10
% PRED	104±16	59-135	110±17	63-140
SR	0.34±1.09	− 2.76-2.52	0.59±1.03	− 2.50-2.10
FVC (1)	4.74±0.98	2.81-6.25	3.24±0.66	1.70-4.39
% PRED	110±18	73-162	115±18	73-151
SR	0.70±1.21	− 1.93-3.46	0.97±1.10	− 1.79-3.04
FEVI/FVC%	77.6±9.2	56-95	81±7.5	63-105
SR	− 0.12±1.23	− 2.60-2.51	0.31±1.00	− 2.01-2.20
PEFR(1/s)	9.88±1.48	6.50-12.50	7.29±1.05	5.00-9.25
% PRED	115±15	78-141	119±16	74-145
SR	1.04±1.09	− 2.60-2.51	1.28±1.07	− 1.92-3.02

14 (17%) were found to be abnormal as defined by either <80% predicted for FEV1, FVC and PEFR and/or>10% below the predicted FEV1/FVC %. Using SR, 11 (13%) individuals were abnormal at the 90% confidence limit, with one or more of the FEV1, FVC, PEFR and FEV1/FVC % lower than − 1.65 SR from the mean.

This study illustrates the influence of criteria used to define normality. Nevertheless using simple screening techniques as many as 13 — 17% of subjects have abnormalities in lung function, thus confirming the value of screening in the community.

Nebulisation — A Multi-Faceted Tool

S L Hill, Pulminory Function Laboratory and Lung Immunobiochemical Research Laboratory, The General Hospital, Steelhouse Lane, Birmingham

Many drugs can be delivered directly to the lung in the form of an acrosol. These include broncho-dilators, humidification and anaesthetic agents and antibiotics. The deposition of these aerosols within the lung is dependent upon three factors:- aerodynamic size of aerosol generated, mode of inhalation and the degree of airway obstruction. The main advantages of delivering drugs to the respiratory surface include the use of a lower therapeutic dose, rapid onset of action and less systemic distribution which reduces the incidence of side effects. This form of therapy has many advantages in the delivery of antibiotics to the lung. The concentration of an oral or systemically administered antibiotic is limited in lung secretions by factors including the chemical properties of the drug and the permeability of the tissue barrier. The delivery of an antibiotic by a nebuliser overcomes many of these limiting factors so that lower doses can result in higher levels of the drug being achieved at the site of infection.

Since the introduction of nebulised antibiotics in 1942 (Am. Rev. Tuberc., 46:268-276), they have been used intermittently in the management of respiratory infections. A whole plethora of antibiotics have been used to treat many conditions but mainly this form of therapy has been used for the treatment of *Pseudomonas* infections in Cystic Fibrosis. Of recent interest is the use of the anti-parasitic agent, Pentamidine, for *Pneumocystis carinii* in AIDS patients. We have recently used nebulised amoxycillin (500 mg b.d. dissolved in 5 ml of sterile water) in patients with bronchiectasis who produce persistently purulent secretions. After 4 months of therapy beneficial effects of PEFR, sputum characteristics and potentially

pathogenic factors including elastase activity and protein transudation into the lung were observed. The nebulisation procedure was both feasible and acceptable to the patients. There were no reported side effects or development of resistant organisms, either in the lung or in the gastro-intestinal tract. The response to this drug in the nebulised form following previous treatment failure with the same drug orally suggests local concentrations are important, particularly when engodenous beta lactamase may be present in the lung secretions.

It is important when antibiotics are used in the form of aerosols that the solutions prepared are isotonic when dissolved in small volumes and are non-toxic, non-irritant and non-allergenic. Solutions should be freshly prepared and the patients instructed to scrupulously clean the nebuliser and attachments. Additionally, to ensure maximum efficiency, compressors should be serviced regularly. In order to monitor the effects of treatment and the development of any side effects patients should be encouraged to keep a daily record and be reviewed regularly with bacterial cultures.

A patient with polycythaemia and right heart failure

M Z Shaheen, W J Windebank, Respiratory Medicine, Derbyshire Royal Infirmary, Derby

This case illustrates the value of respiratory physiology studies in establishing the cause and type of abnormality and implications regarding long term management in a 49 year old lady presenting with mild wheeze and elevated haemoglobin. The patient (a stewardess in a public house) smoked 15 cigarettes/day. She had not received treatment for her wheeze. On examination she was in mild right heart failure, there were no chest signs. Tests included routine pulmonary function tests, response to bronchodilators, right heart pressures, gas exchange studies and arterial blood gas and pH measurements breathing air and various concentrations of oxygen via face-mask and via nasal canula.

The value of these tests in differential diagnosis and the role of long term oxygen therapy will be discussed.

Respiratory Function Measurements in Speech Therapy

A H Kendrick, C Dobinson, Respiratory and Speech Therapy Departments, Bristol Royal Infirmary.

The myoelastic-aerodynamic theory of voice production states that the degree of laryngeal efficiency is dependant on the co-ordinated interplay of two forces — subglottic pressure (Psub) and glottal resistance (GR). These are related according to the equation

$$Psub = MFR \times GR$$

where MRF is the mean flow rate. These measurements of aerodynamic patterns should provide information regarding the efficiency of the laryngeal generator in regulating the translation of air pressure into acoustic signals.

Psub may be measured using an oesophageal balloon, which gives a close approximation with direct tracheal puncture (Lieberman, J Acoust Soc Amer 43, 1157-64 1968). Direct airflow measures may be obtained from either a spirometer or pneumotachograph — Vital Capacity (VC), phonation volume (PV) and phonation time (PT). PV and PT may either be maximal or determined over a preset time.

From these indices, MFR (PV/PT), vocal velocity index (VVI = MFR/VC), the ratio of PV/VC and the maximal predicted phonation time (MPT = 0.67VC/100). Amerman and Williams (Brit J Dis Com 14, 153-9, 1979) have shown the usefulness of these indices in assessing vocal fold pathologies.

One final set of measurements may be the use of breathing patterns (Gordon et al, Folia Phoniat 30, 161-74, 1978), where average values of the various components of the tidal breathing cycle may be used. However, the use of these has not been fully evaluated.

The role of respiratory measurements in the assessment of speech disorders has been shown to be potentially useful. More research is needed to fully evaluate their usefulness.

Editor: Dr. D C S Hutchison, Dept. Thoracic Medicine, King's College Hospital, London SE5

Printed by Stevens Bros., 63 Vyner Street, London, E2 9DQ