

Otorhinolaryngology Research Society Abstracts

The following are the abstracts of the meeting held in Freeman Hospital, Newcastle upon Tyne, UK, 7 April 2000

Idiopathic and allergic rhinitis show a similar inflammatory response

D.G. POWE,* R.S. HISKISSON,* A.S. CARNEY,†
D. JENKINS* & N.S. JONES† (*Department of Clinical
Laboratory Sciences and †Department of Otorhinolaryngol-
ogy, Queen's Medical Centre, Nottingham, UK)

Hypothesis. Idiopathic and allergic rhinitis have similar mucosal mast cell and IgE+ cell distribution.

Introduction. The pathophysiology of idiopathic rhinitis (IR) is unknown but patients differ from those with allergic rhinitis (AR) in that they do not express IgE. Our study is novel because we investigated: (1) three study groups chosen prospectively using strict selection criteria over a 4-year period; and (2) mast cell and IgE+ cell counts were on full-thickness, full-length inferior turbinate mucosa.

Methods. Patient groups: allergic ($n=17$); idiopathic: ($n=16$); and normal controls ($n=9$). Immunohistochemistry: mast cell and IgE+ cell detection using anti-mast cell tryptase and anti-IgE antibodies with an avidin-biotin (peroxidase) complex on paraffin processed tissue. Morphometry: sections were divided into three strata comprising an epithelial layer and two submucosal layers. Statistics: Mann-Whitney non-parametric analysis. $\alpha=0.05$, $\beta=0.2$.

Results. The power of the study was 89%. Mast cells ($P=0.03$) and IgE+ cells ($P<0.05$) were significantly increased in the epithelium of idiopathic and allergic rhinitis mucosa compared to the normal control. More IgE+ cells were counted in the AR and IR groups compared to the controls in all three strata.

Conclusion. Mast cells and IgE+ cells are involved in the pathophysiology of IR. We propose that IR may be a variant form of AR involving a localized IgE-mediated inflammatory response.

Is oestrogen therapy justified in the treatment of hereditary haemorrhagic telangiectasia: a biochemical evaluation

H. PAU,* A.S. CARNEY,* R. WALKER† & G.E. MURTY*
(*ENT Department, Leicester Royal Infirmary and †The Breast Cancer Research Unit, Glenfield General Hospital, Leicester, UK)

Introduction. Systemic and topical oestrogen can provoke squamous metaplasia of epithelium. In Hereditary Haemorrhagic Telangiectasia (HTT) the underlying telangiectasia may be protected from trauma and epistaxis reduced. Oestrogens have been advocated but their efficacy is unclear.¹ Recent advances have now identified two oestrogen and one progesterone receptors. The aim of this study is to analyse the sex receptor status of HTT nasal mucosa to determine if oestrogen therapy is biochemically justified.

Method. Five HTT patients (three men, two women) and eight controls (four men, four women) underwent nasal mucosa biopsy. Samples were fixed in formalin and paraffin embedded. Alpha oestrogen (ER α), beta oestrogen (ER β) and progesterone receptors (PgR) receptors were identified using mouse monoclonal antibodies by the Streptavidin-biotin peroxidase method.

Results. ER β was detected in two HTT patients (one man, one woman) and two control patients. ER α and PgR was absent in HTT patients.

Conclusion. This pilot study demonstrated that a subgroup of HTT patients is ER β positive. Oestrogen therapy therefore has a potential therapeutic role on a biochemical basis in these patients. ER β status should be determined before considering oestrogen therapy.

Reference

- 1 HARRISON D.F.N. (1982) Use of oestrogen in treatment of familial haemorrhagic telangiectasia. *Laryngoscope* 92, 314–320

The influence of prednisolone on the secretion of MUC5AC from TH29-MTX cell culture

N. FERGIE,† L. GUO,* J.P. PEARSON† & J.P. BIRCHALL*
(*Queen's Medical Centre, Nottingham, †Leicester Royal Infirmary and ‡Derby Royal Infirmary, University of Newcastle upon Tyne, Newcastle upon Tyne, UK)

Introduction. Glucocorticoids have been used in the treatment of otitis media with effusion with promising but inconsistent results. The HT29-MTX cell line is a completely differentiated and almost exclusively mucous secreting cell line, which therefore has the potential to act as an ideal model for the study of mucus-secreting epithelia. To assess

this potential of steroids in suppressing mucin secretion we have studied the response of the cell culture to prednisolone.

Methods. Confluent cell cultures were trypsinized, subcultured in six-well plates and incubated with four doses of prednisolone from 10^{-5} M to 10^{-11} M and over varying time courses from 12 to 36 h. ELISA was performed using a monoclonal mouse antibody to human gastric mucin by dot-blot ELISA.

Results. Prednisolone caused a reduction in mucin production from the cell line consistently. Media control values ranged from 3495 to 3559 compared with untreated controls of 18 998–27 176 and steroid treatment values of 12 244–27 792. Increasing concentrations of prednisolone result in increasing suppression of MUC5AC ($P=0.005$). There was no independent time-related effect.

Conclusion. There does appear to be a genuine suppression of mucus production by prednisolone and this appears to be dose-dependent but not time-dependent at the times studied. The effect size was small.

Bone-anchored hearing aid: quality of life assess by Glasgow Benefit Inventory

P.S. ARUNACHALAN, D. KILBY, D. MEIKLE, T. DAVISON & I.J.M. JOHNSON (Department of Audiology and ENT, Freeman Hospital, Newcastle upon Tyne, UK)

Introduction. The bone-anchored hearing aid (BAHA) uses the system of osseointegration described by Branemark. It is a well-established mode of treatment and many studies show the audiological benefit, but none have assessed the benefit to the quality of life of patients who underwent this surgical intervention. This study uses the validated Glasgow Benefit Inventory (GBI) to quantify the changes in quality of life. The GBI is a specific patient-orientated questionnaire designed to look at the changes in health status secondary to an ORL intervention.¹ The GBI gives an overall score, but also subscores of general, social and physical benefits.

Method. Sixty consecutive BAHA patients were enrolled in the study. The male: female ratio was 1:26, with a mean age of 45 years. The most common indication was hearing loss secondary to mastoid disease/surgery followed by congenital atresia and chronically discharging ear. The mean bone conduction of the better ear was 19 dB and the mean conductive loss across the speech frequencies was 58 dB. Only patients who were fitted with the classic model were included in the study.

Results. The response rate was > 70%, which is high and adds weight to the results. The general benefit score was +40 which is comparable to middle ear surgery, but just

below benefit from cochlear implantation. The social benefit was +27 with only +10 for the physical score. This pattern mirrors that reported for other ear interventions.

Conclusion. This paper is the first to demonstrate that there is significant quality of life benefit from BAHA surgical intervention as measured by the GBI.

Reference

- 1 GATEHOUSE S., ROBINSON K. & BROWNING G. (1996) Measuring patient benefit from otorhinolaryngological surgery and therapy. *Ann. Otol. Rhino. Laryngol.* **105**, 415–422

Blood flow in the external auditory canal and tympanic membrane as assessed by laser Doppler Blood Flowmetry

J.A. COOK, M. MULHERAN & H. FAYEZ (Department of Otolaryngology, Leicester Royal Infirmary, Leicester, UK)

Introduction. Procedures within the external meatus and tympanum constitute a large part of otological surgery. Successful healing after procedures on the tympanic membrane will in large part be dependent on the integrity of local blood flow. However, there appear to have been relatively few studies investigating blood flow in the external auditory meatus and tympanum in normal subjects and those with conditions requiring surgery, e.g. tympanoplasty. The aim of this study is to obtain such data using Laser Doppler Blood Flowmetry. **Method.** Control volunteers ($n=30$) and patients requiring tympanoplasty ($n=20$) were recruited for the study. Laser Doppler Blood Flowmetry was performed in all patients using a commercially available system (Peri-flux 5000, Perimed AB, Sweden) at four sites: (1) preauricular skin; (2) cartilaginous ear canal; (3) bony ear canal; and (4) tympanic membrane. Mesotympanic temperature was also measured using a Braun Infrared thermometer. Blood flow (flux) was measured as RBC density 'speed following internal calibration.

Results. Analysis revealed that in both the control subjects and pre-tympanoplasty patients, the ranking of blood flow at the sites was 3, 2, 1 and 4 (highest to lowest). Comparing matched sites, there were no significant differences between the two groups. The amplitude of flow was not found to be correlated with mesotympanic temperature.

Conclusion. Grafts applied to repair perforations of the tympanic membrane are likely to obtain the majority of their blood supply from the bony external auditory meatus rather than that tympanic membrane. Further studies are ongoing to define local blood flow patterns in order to optimize the results of tympanoplasty.

Angiogenic cytokines in serum and plasma of patients with head and neck squamous cell carcinoma

J.J. HOMER, J. GREENMAN & N.D. STAFFORD (Department of Otolaryngology/Head and Neck Surgery, Hull Royal Infirmary, University of Hull, Hull, UK)

Introduction. Angiogenesis is critical for tumour growth and dissemination. Some angiogenic cytokines can be detected in the serum/plasma, including vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), angiogenin (ANG) and endostatin. VEGF, bFGF and ANG are pro-angiogenic cytokines implicated in tumour angiogenesis. Endostatin is antiangiogenic and arises from tumour-induced proteolysis. The purpose of this study was to ascertain whether there are differences between healthy controls and patients head and neck squamous cell carcinoma (HNSCC) for each cytokine; and whether there is any association with clinico-pathological variables or prognosis.

Methods. Serum/plasma was assayed by ELISA in the following numbers of patients and controls: serum VEGF (80:80); plasma VEGF (32:15); serum bFGF and ANG (25:15); and plasma endostatin (26:15).

Results. Serum VEGF is raised in patients with HNSCC ($P < 0.001$) but there were no associations with clinico-pathological variables or outcome. Serum VEGF correlated with platelet count ($P = 0.05$) and plasma VEGF ($P = 0.02$) although the latter is substantially lower ($P < 0.001$). bFGF and ANG were not raised in patients with HNSCC. Plasma endostatin was lower in patients with HNSCC than controls ($P = -0.02$). However, with the HNSCC group endostatin was positively associated with disease recurrence ($P = 0.008$).

Conclusions. These data suggest that plasma endostatin may be a clinically useful prognostic marker in patients with HNSCC. Serum VEGF arises from platelet aggregation and does not reflect tumour load, dissemination or prognosis. bFGF and ANG are not raised in patients with HNSCC.

Dynamic assessment of imbalance in acoustic neuroma patients by sway magnetometry

M.M. COLLINS,* I.J.M. JOHNSON,* E. CLIFFORD,† J.P. BIRCHALL† & G.M. O'DONOGHUE† (Departments of Otolaryngology, *Freeman Hospital, Newcastle upon Tyne and †Queen's Medical Centre, Nottingham, UK)

Introduction. Imbalance may be a significant problem for patients with acoustic neuromas. Prospective data on

patients with acoustic neuromas to establish how the vestibular system performs dynamically, in the perioperative phases, is not available. Posturography is an established method of measuring balance and sway magnetometry has been developed as a reliable technique in this field.

Aims. Prospectively to assess pre- and postoperative dynamic vestibular function in patients with acoustic neuromas using sway magnetometry.

Methods. Sway patterns were recorded on 12 patients with acoustic neuromas tested under two sets of conditions: first, a baseline test for 120 s, repeated after 120 s of vestibular stimulation. After each test a validated questionnaire to assess balance subjectively was completed: before operation and 1, 3 and 6 months after operation.

Results. (1) Patients with acoustic neuromas demonstrate 'overswing' on baseline testing: most exaggerated 1 month postoperatively. After vestibular stimulation the 'recovery' time was prolonged to 50 s postoperatively, 62 s postoperatively (1/12), 43 s (3/12), and 47 s (6/12) postoperatively. (2) Mean path length (normal range, 163–287 mm) was increased in all groups: preoperative = 332 mm, 1 month postoperatively = 358 mm, 3 months postoperatively = 308 and 6 months postoperatively = 343 mm (3) The Dizziness Handicap Inventory scores were elevated at all times of testing and significantly correlated with baseline path length ($r_s = 0.6$, $P = 0.03$) and vestibular stimulation path length ($r_s = 0.7$, $P = 0.01$) preoperatively.

Conclusions. This is the first dynamic, prospective study of balance in patients with acoustic neuromas. Abnormal sway patterns and prolonged recovery times pre- and postoperatively, most marked at 1 month, were demonstrated. A subjective assessment of balance disturbance reflected these abnormal sway measurements confirming its clinical usefulness.

The distribution of the calcium buffer calbindin in the cochlea of the guinea-pig

K. PAPAPOSTAS, C.M. HACKNEY & D.N. FURNESS (MacKay Institute of Communication and Neuroscience, School of Life Sciences, Keele University, Keele, UK)

Introduction. Ca^{2+} is involved in many important functions in the inner ear and its intracellular levels are controlled by extrusion mechanisms and stores, and also by buffers such as calbindin. The latter has been demonstrated previously in hair cells of the organ of Corti using immunofluorescence at the light microscopic level, although its precise intracellular distribution has yet to be determined. One postulated role for calbindin in the brain is protection against hypoxic cell

injury and degeneration, in which Ca^{2+} overload has been implicated.

Methods. We have therefore performed postembedding immunogold labelling for electron microscopy on ultrathin sections of apical and basal turns of the guinea-pig cochlea with anticalbindin (Swant), followed by appropriated gold conjugated secondary antibodies. This technique allows quantitative analysis of the distribution of labelling by counting gold particle densities.

Results. Outer hair cells in the apical turn were significantly more heavily labelled than those in the base ($P < 0.001$). In addition, at the apex there was a progressive reduction across the three rows of outer hair cells towards the modiolus ($P < 0.005$) although at the base no radial gradient was detected.

Conclusions. These results confirm previous reports of gradients of calbindin distribution in the organ of Corti. This distribution corresponds with the pattern of hair cell loss that occurs, e.g. after some forms of ototoxicity and it may therefore contribute to the differential susceptibility of hair cells to damage.

Acknowledgement. This work was supported by the Wellcome Trust.

Thyroid stimulating hormone increases angiogenic growth factor expression in rat thyrocytes

H.C. COCKS, J.D. RAMSDEN, J.C. WATKINSON & M.C. EGGO (Division of Medical Sciences, Queen Elizabeth Hospital, Edgbaston, Birmingham, UK)

Introduction. Goitrogenesis is thought to be due to hyperstimulation of the thyroid stimulating hormone (TSH) receptor and is associated with dramatic angiogenesis within the thyroid. The angiogenic growth factors, fibroblast growth factor (FGF-2) and its receptor (FGFR-1) as well as Tie-2 (the receptor for the angiopoietins) are elevated in both the human goitre and in rat goitre. We have investigated the role of TSH in the expression of FGF-2, FGFR-1 and Tie-2 in FRTL-5 cells, which are a functional rat thyroid cell line.

Methods. Cells were cultured in medium containing 5% serum, insulin and antibodies and exposed to a variety of experimental conditions. Proteins were separated by electrophoresis and analysed by Western blotting using polyclonal antibodies to FGFR-1 (extracellular domain, Santa Cruz), Tie-2 (Santa Cruz) and FGF-2 (Sigma).

Results. TSH increased expression of FGF-2 reaching a maximum at 0.3 mU/ml returning to control levels at higher concentrations. A dominant fragment of its receptor

(FGFR-1) at ≥ 57 kDa was dose-dependently increased by TSH. Tie-2 was thought to be predominantly expressed on endothelial cells but we now show that it is expressed as a full-length receptor on FRTL-5 cells with maximal expression at 0.3 mU/ml. This regulation is mediated by cAMP as forskolin and 8-Bromo-cAMP also increased Tie-2 expression.

Conclusion. Both FGF-2 and its receptor, as well as Tie-2 are increased in rat thyroid cells by elevated TSH. These mechanisms may be central to the angiogenesis that occurs in goitrogenesis, and alteration of these growth factors may lead to new treatments for goitre.

The quality of life impact of snoring and the effect of laser palatoplasty

M. REDA, U. ULLAL & J.A. WILSON (Department of Otolaryngology/Head and Neck Surgery, University of Newcastle and Freeman Hospital, Newcastle upon Tyne, UK)

Introduction. Snoring is a common cause of marital disharmony and social embarrassment. Obstructive sleep apnoea (OSA) have further impact on Quality of Life (QoL).

Aims. First, to compare the impact of snoring and OSA on QoL; second, to assess the impact of laser palatoplasty (LAUP) on QoL in snorers.

Methods. We conducted a prospective cohort comparison of 191 snorers (mean age 46 years; 132 men, 59 women), 57 patients with OSA (mean age 47 years; 49 men, 8 women), and 105 patients, at a mean of 12 months (range, 4–24 months) after LAUP (mean age 45 years; 82 men, 23 women). All completed the Nottingham Health Profile (NHP) and the results were compared with established NHP population norms.

Results. The results are shown in Table 1.

Conclusions. This is the largest QoL study of snorers to date and shows that both snoring and OSA have clear impacts on all six NHP domains. The magnitude of the impact in snoring approaches that for OSA for most parameters. The impact of OSA on the sleep domain in men is significantly higher than that of snoring. Energy and emotional reaction domains are significantly improved by LAUP in both sexes, to levels approaching those in the normal population. Also pain, sleep, social isolation and mobility in habitual snorers was helped by surgery. The NHP generic QoL health status measure is a useful tool for the assessment of sleep disorders.

Table 1. Nottingham Health Profile domains

Population	<i>n</i>	Energy	Pain	Emotional reaction	Sleep	Social isolation	Mobility
Men							
Preop.	132	28.6	12.0	16.7	25.1	9.1	7.8
Postop.	82	13.3*	4.3	10.2*	15.5†	4.6	3.9
Population	8	6	9	8	31		
Women							
Preop.	59	36.6	12.4	16.4	23.9	6.0	10.9
Postop.	23	14.2*	11.5	13.9‡	19.8	7.8	10.2
Population		18	10	15	18	6	5
OSA							
Men	49	38.2	11.9	19.4	34.1§	8.7	7.9
Women	8	39.7	3.8	17.2	30.4	2.8	10.2

* $P < 0.001$; † $P < 0.005$; ‡ $P < 0.005$ (Mann–Whitney vs. same-sex preoperative group); § $P = 0.005$ (Mann–Whitney vs. male preoperative habitual snorers).

Differing expression of bax and bcl-3 may influence the different cure rates in mouth and oropharyngeal cancer

N. ANDREWS,* T. HELLIWELL,† C. WALKER‡ & A.S. JONES* (Departments of *Otolaryngology and †Pathology, Royal Liverpool University Hospital, Liverpool and ‡J.K. Douglas Laboratory, Clatterbridge Centre for Oncology, Clatterbridge, UK)

Aim. To determine the reason for the differing cure rates of cancers between the mouth and oropharynx.

Materials and methods. To achieve our aim we carried out immunohistochemistry on paraffin-embedded tissue from 31 oral and 38 oropharyngeal squamous carcinomas using the streptavidin-biotin/HRP method.

Results. The results from this study revealed the mean percentage of bax and bcl-2 expression was higher in the oropharyngeal samples (56.34% and 97.36%, respectively) than in the oral samples (6.6% and 82.38%, respectively). In the oral carcinomas bcl-2 was expressed in a higher percentage of cells than bax, and a high proportion of cases were bcl-2 positive in the absence of significant bax expression. In contrast the oropharyngeal cases showed a high percentage of cells expressing both bcl-2 and bax.

Conclusion. The predominance of anti-apoptotic bcl-2 over the pro-apoptotic bax may result in a survival advantage of the cells of oral carcinomas over the cells of the oropharynx. Tumours of the oral cavity have been found to be clinically more radioresistant than those of the oropharynx. These findings may have implications for radiotherapy treatment since the cells of oral carcinomas may already have a survival advantage and the carcinomas may be less likely to respond to treatment.

A prospective retrieval study to determine how speaking valve failure is effected by colonization

S.R. ELL,* C.M. DAVIES† & A.J. PARKER‡ (*Department of Otolaryngology, University of Hull, Hull and †Department of Otolaryngology, Royal Hallamshire Hospital, Sheffield, UK)

Introduction. It has been suggested that Groningen Low Resistance (GLR) valve failure is associated with biofouling of the valve's oesophageal surface and hinge areas. However, the valve edges are responsible for efficient valve function.¹ Therefore, valve edge colonization should be the most important factor determining valve failure. The null hypothesis that valve edge colonization was not associated with failure was tested using 106 GLR valves retrieved, after failure, from 41 patients.

Methods. The opening pressures, reverse opening pressures and forward resistances of the new valves were determined using apparatus validated previously.² The pressure/flow parameters were measured again after removal and the changes calculated. The degree of colonization of each valve edge, oesophageal surface, hinge area, tracheal surface and valve lumen was scored using 100-mm linear analogue scales. The changes, in pressure/flow parameters were examined for associated with colonization of the five areas described above.

Results. The increase in the opening pressure and resistance, and decrease in reverse opening pressure, of the retrieved valves was significant compared with new valves. The increase in opening pressure was associated with colonization of the valve edge ($r_s = 0.262$, $P = 0.007$). The decrease in reverse opening pressure was associated with colonization of the valve edge, hinge areas and oesophageal surface ($r_s =$

0.266, $P=0.006$; $r_s=0.271$, $P=0.005$; $r_s=0.271$, $P=0.004$, respectively). The increase in resistance was associated with colonization in all areas ($r_s \geq 0.367$, $P=0.0005$).

Conclusion. This study demonstrated that colonization of the valve edge is associated significantly with the changes, in pressure/flow parameters of failed valves.

References

- 1 ELL S.R., MITCHELL A.J. & PARKER A.J. (1995) Microbial colonization of the Groningen speaking valve and its relationship to valve failure. *Clin. Otolaryngol.* **20**, 555–556
- 2 PARKER A.J., STEVENS J.C., WICKHAM M.H. *et al.* (1992) Characteristics of Groningen tracheo-oesophageal speaking valves prior to insertion and after removal or failure. *J. Laryngol. Otol.* **106**, 521–524

Are p53 and MIB-1 overexpressed in cholesteatoma?

M. MOTAMED,* D. POWE,† L. JONES,† C. KENDALL† & A.R. BANERJEE (*Departments of *Otorhinolaryngology/Head and Neck Surgery and †Pathology, Leicester Royal Infirmary, Leicester and ‡Department of Clinical Laboratory Sciences, Queen's Medical Centre, Nottingham, UK)

Introduction. There is controversy regarding the expression of p53 and MIB-1 in cholesteatoma.¹ This study was instituted to study this. p53 is an intracellular protein which plays a critical role in control of the cell cycle at the G1 check point. MIB-1 is recognized as a marker of cellular proliferation. Using deep meatal skin controls, the question addressed was, 'are p53 and MIB-1 overexpressed in cholesteatoma'?

Method. Immunocytochemistry using the avidin-biotin technique on frozen tissue sections with primary antibody to p53 ($n=17$, controls = 17) and MIB ($n=17$, controls = 7) was performed on cholesteatoma and deep meatal skin control specimens. Appropriate positive and negative controls were employed for each antibody. Slides were analysed in a blind fashion by two independent observers. Statistical analysis was performed using the Mann–Whitney test.

Results. Expression of p53 was minimal or absent in both cholesteatoma and controls. No significant difference in p53 expression was found between the two groups ($P=0.02$). MIB-1 expression was higher in cholesteatoma than in controls, although this was not statistically significant ($P=0.09$).

Conclusion. This study did not demonstrate an increased expression of p53 cholesteatoma, indicating no evidence of a dysfunctional cell cycle. MIB-1 results showed a possible trend towards significance, which requires a more powerful study to evaluate this further. The probability that there is an increased rate of cellular proliferation in cholesteatoma,

when compared to deep meatal skin controls, cannot be excluded.

Reference

- 1 ALBINO P. *et al.* (1998) Expression of p53 in middle ear cholesteatomas: pathogenic implications. *Am. J. Otol.* **19**, 30–36.

Does the bacterial DNA found in middle ear effusions come from viable bacteria?

L. PEIZHONG,* K. WHATMOUGH,* J.P. BIRCHALL,† J.A. WILSON* & J.P. PEARSON* (*Departments of Physiology and ENT, University of Newcastle upon Tyne, Newcastle upon Tyne and †Department of Otorhinolaryngology, University of Nottingham, Nottingham, UK)

Introduction. Between 20% and 50% of middle ear effusions in otitis media with effusion test positive for bacteria, i.e. *H. influenzae*, *M. catarrhalis* and *S. pneumoniae*. In one study 48% of effusions that tested negative by culture were positive by polymerase chain reaction (PCR).¹ This has been advanced as evidence for the presence of bacterial biofilms, as agents leading to the persistence of glue ear. There is, however, the possibility that the DNA detected is the fossilized remains of bacteria from previously cleared infections. If this is the case, then the effusion must in some way be protecting the DNA from breakdown by DNases.

Methods. Here we demonstrate, using a viscosity assay, that middle ear effusions taken from children during myringotomy inhibit the breakdown of DNA in a concentration-dependent manner. Middle ear effusion homogenates 0.5–3.0 ml (1:10 Vol. vol/effusion: PBS) were incubated with 3 ml of DNA (0.5 mg/ml in PBS) plus 0.2 ml of DNase 1 (500 Kunitz) at 37°C for 24 h. Viscosity measurements were taken at regular intervals and the changes in viscosity expressed as a percentage of time 0. DNase activity was inhibited by 1.5 ml and 3.0 ml of effusion 48% and 91%, respectively, after 30 min incubation.

Conclusion. This study demonstrated that effusions have the ability to inhibit nuclease activity, and the reported presence of non-culturable bacteria based on DNA detection by PCR could still represent fossilized remains and not viable bacteria. The same could also be true of recent reports of bacterial mRNA.²

References

- 1 Post *et al.* (1996) *JAMA* **273**, 1598–1604
- 2 Rayner *et al.* (1998) *JAMA* **279**, 296–299

Pharmacological protection of auditory function against noise and hypoxia with MK 801

D.K. SELVADURAI,* S. ETHERIDGE,† P. JONES,‡
M. MULHERAN§ & J.A. COOK* (*Department of ENT Surgery, Leicester Royal Infirmary, Leicester, †Medicine Evaluation and ‡Applied Technology Group, Glaxco-Wellcome and §MRC Centre for Toxicology, Leicester University, Leicester, UK)

Introduction. Pharmacological protection of cochlear function is one of the most exciting goals of inner ear medicine. The selective glutamate antagonist MK 801 may be neuroprotective to the cochlea.¹ This study aims to investigate whether round window administration of MK 801 protects cochlear function against a combination of noise and atmospheric hypoxia.

Methods. Eight guinea-pigs were studied. Round Window E. Catheters (Durect Inc., USA) were implanted through a trans-bulla approach and EcoG thresholds determined at 8, 16, 24 and 30 kHz. Artificial perilymph ($n=4$) or 10 mM MK 801 ($n=4$) was then perfused onto the round window membrane. After 15 min the anaesthetized animals were exposed to 100 dB white noise in 11.5–12.5% atmospheric oxygen. Thresholds were determined before and 15 min after exposure.

Results. The mean threshold shifts from pre-perfusion at 8, 16, 24 and 30 kHz were 40, 33, 35 and 17 dB, respectively (in control animals) and 29, 28, 33 and 41 dB, respectively (in treated animals). A marginal protective effect was demonstrated at 8 kHz ($P=0.06$). The 30-kHz thresholds in the treated group fell by 61 dB before noise exposure compared to <1 dB in the controls ($P=0.0007$), suggesting that at high frequencies, 10 mM MK 801 may itself be ototoxic.

Conclusions. These results partially support existing data suggesting that pharmacological protection against noise/hypoxia is possible. Administration of round window NMDA antagonists may affect normal auditory threshold making detailed evaluation of the toxicity of potential inner ear therapies essential before clinical use is contemplated.

Reference

- 1 LIU Y. & FECHTER L.D. (1995) MK-801 protects against carbon monoxide-induced hearing loss. *Toxicol. Appl. Pharmacol.* **132**, 196–202

Fibroblast growth factor receptor expression in vestibular schwannoma

S.B. NAIR,* H.Y. LEUNG,* P. INCE,† R.T. RAMSDEN‡ & J.A. WILSON* (*Department of Surgery, University of Newcastle, †Department of Neuropathology, Newcastle General Hospital, Newcastle upon Tyne and ‡Department of Otolaryngology/Head and Neck Surgery, Manchester Royal Infirmary, Manchester, UK)

Introduction. The family of fibroblast growth factor (FGF) and their receptors (FGFRs) play a critical role in nervous system development. Aberrant expression or a change in the pattern of their expression may contribute to neural tumour formation. The FGFR expression status in vestibular schwannoma is unknown. **Aim.** To characterize the pattern of FGFR-1, FGFR-3 and FGFR-4 expression in resection vestibular schwannoma.

Method. Fifty paraffin-embedded archival specimens of vestibular schwannomas were immunostained for FGFR-1, FGFR-3 and FGFR-4 using specific rabbit polyclonal antibodies. signals were graded as weak, moderate or strong by two independent observers. Normal tissues and appropriate positive and negative controls were included.

Results. FGFR-1 and FGFR-3 appeared to have similar patterns of immunoreactivity with predominantly membrane and cytoplasmic signals in control tissues. In contrast, in vestibular schwannomas, FGFR-1 and FGFR-3, preferentially localize to the nucleus, with moderate to strong signals in 80% and 76% of the specimens, respectively. FGFR-4 expression was upregulated in 70% of vestibular schwannomas to a moderate level, localizing to the perinuclear and cytoplasmic area. Differential cellular localization of receptor proteins has been demonstrated in vestibular schwannomas.

Conclusion. This is the first comprehensive study characterizing FGFR expression in vestibular schwannoma. The development of vestibular schwannomas is associated with an altered pattern and level of FGFR expression. Our ongoing work aims to examine their significance in the pathogenesis of vestibular schwannomas.