

differences are shown for aminopeptidase P ( $p=0.913$ ) or carboxypeptidase N ( $p=0.117$ ). Furthermore, when we repeated blood sampling three times at intervals of 1 month in ten patients, aminopeptidase P and carboxypeptidase N measurements varied by less than 10%.

Our results indicate that an association exists between low plasma activity of aminopeptidase P and previous episodes of angio-oedema. In ACE-inhibitor associated angio-oedema, contrary to what happens in hereditary angio-oedema due to C1-inhibitor deficiency, the high plasma bradykinin concentrations are not accompanied by the presence in plasma of cleavage products of high molecular weight kininogen (the precursor of bradykinin). The pathogenetic mechanism of ACE-inhibitor associated angio-oedema, therefore, probably rests in the catabolic site of bradykinin metabolism.<sup>1</sup> Since aminopeptidase P plays a major part in plasma bradykinin catabolism when ACE is inhibited,<sup>3</sup> the lower plasma concentrations of aminopeptidase P seen in patients who had previously had ACE-inhibitor associated angio-oedema could indicate a predisposition for development of angio-oedema in some patients treated with ACE inhibitors. In view of the fact that 35–40 million individuals are exposed to ACE inhibitors worldwide, a prospective study of the plasma activity of aminopeptidase P as a risk factor of angio-oedema in patients treated with ACE inhibitors is advisable. A difficulty associated with the study of angio-oedema is its manifestation anywhere between a few hours to 10 years after an ACE inhibitor is first taken.<sup>1</sup> For this reason, many physicians fail to recognise the association between treatment with an ACE inhibitor and angio-oedema, despite the fact that the adverse effect is well known and always explained in the information leaflet provided with the drug.

#### Contributors

A Adam, G Molinaro, and M Perez did biochemical analyses and wrote the report; M Cugno and A Agostoni diagnosed and treated patients, obtained samples, and helped to write the report; and Y Lepage did statistical analyses and approved the report.

#### Conflict of interest statement

G Molinaro received a travel grant to present results of this work at the AHA meeting in Anaheim, USA, in November, 2001.

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## The causal links between stress and burnout in a longitudinal study of UK doctors

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**Burnout and stress are common, linked problems in health-care workers. We aimed to clarify their causal associations. We assessed stress and the three components of burnout (emotional exhaustion, depersonalisation, and low personal accomplishment) using structural equation modelling in a 3-year longitudinal study of a representative sample of 331 UK doctors. Emotional exhaustion and stress showed reciprocal causation: high levels of emotional exhaustion caused stress ( $\beta=0.189$ ), and high levels of stress caused emotional exhaustion ( $\beta=0.175$ ). High levels of personal accomplishment increased stress levels ( $\beta=0.080$ ), whereas depersonalisation lowered stress levels ( $\beta=-0.105$ ).**

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Stress and burnout are substantial problems for health-care workers. Maslach and colleagues<sup>1</sup> have described how in burnout, “What started out as important, meaningful and challenging work becomes unpleasant, unfulfilling and meaningless. Energy turns into exhaustion, involvement turns into cynicism, and efficacy turns into ineffectiveness”. Burnout is assessed using the Maslach burnout inventory (MBI), which has subscales of emotional exhaustion, depersonalisation (cynicism), and personal accomplishment (professional efficacy), which is scored in reverse.<sup>1</sup> Stress is generally assessed with the general health questionnaire (GHQ), on which high scores indicate caseness for anxiety disorders and depression (ie, at or above the threshold at which patients have an 80% probability of a formal psychiatric diagnosis).<sup>2</sup> Although often associated with anxiety and depression, burnout is distinct from both, with work-related rather than physical or biological symptoms.<sup>1</sup> Despite being common in health-care workers, the development and causal relations of burnout and stress are unclear, in part due to an absence of adequate longitudinal studies.<sup>1</sup> We assessed stress and burnout in a large-scale, 3-year study of UK doctors, and used path analysis to measure their causal relations.

In November, 1997, we did a postal survey of attitudes of UK doctors to the General Medical Council’s *Performance Procedures*.<sup>3</sup> We randomly selected a stratified sample of 800 doctors from the UK *Medical Directory* (Harlow: Cartermill, 1997) by use of random numbers from the CD-ROM version. We included equal numbers of men and women and hospital doctors and family practitioners, who qualified in equal proportions in 5-year bands between 1950–59 and 1990–94. One in five doctors in each age, sex, and practice type had qualified outside the UK. The four-page questionnaire included the 12-item version of the GHQ (GHQ-12)<sup>3</sup> and an abbreviated nine-item version of the MBI (aMBI). In September, 2000, we presented the same questionnaire to the 551 doctors who had returned the questionnaire on the first occasion. We scored the GHQ-12 in two standard ways: we classed participants with totals of 4 or more, with the four response categories on each item scored as 0–0–1–1, as showing caseness for anxiety disorders and depression; for the remaining analyses we scored the questionnaire as 0–1–2–3, the normal distribution provided more power for multivariate analyses. We coded aMBI items as 0 for “never” to 6 for “every day”; factor analysis confirmed the presence of the three factors: emotional exhaustion, depersonalisation, and personal accomplishment. We used standard statistical methods with SPSS software (version 10.0). We did causal (structural equation) modelling of the results with the maximum likelihood method in LISREL (version 8.30)

|                  | <b>GHQ<sub>2</sub></b> | <b>DP<sub>2</sub></b> | <b>EE<sub>2</sub></b> | <b>PA<sub>2</sub></b> | <b>GHQ<sub>1</sub></b> | <b>DP<sub>1</sub></b> | <b>EE<sub>1</sub></b> | <b>PA<sub>1</sub></b> |
|------------------|------------------------|-----------------------|-----------------------|-----------------------|------------------------|-----------------------|-----------------------|-----------------------|
| GHQ <sub>2</sub> | <b>21.623</b>          | 0.141                 | 0.533                 | 0.014                 | 0.505                  | 0.057                 | 0.382                 | -0.029                |
| DP <sub>2</sub>  | 2.052                  | <b>9.797</b>          | 0.328                 | -0.003                | 0.196                  | 0.668                 | 0.295                 | -0.089                |
| EE <sub>2</sub>  | 10.980                 | 4.548                 | <b>19.625</b>         | 0.060                 | 0.445                  | 0.204                 | 0.624                 | 0.003                 |
| PA <sub>2</sub>  | 0.186                  | -0.027                | 0.760                 | <b>8.180</b>          | -0.061                 | -0.015                | -0.002                | 0.598                 |
| GHQ <sub>1</sub> | 10.614                 | 2.773                 | 8.911                 | -0.789                | <b>20.430</b>          | 0.251                 | 0.535                 | -0.218                |
| DP <sub>1</sub>  | 0.808                  | 6.377                 | 2.756                 | -0.131                | 3.460                  | <b>9.302</b>          | 0.390                 | -0.092                |
| EE <sub>1</sub>  | 7.301                  | 3.795                 | 11.361                | -0.024                | 9.939                  | 4.889                 | <b>16.892</b>         | -0.093                |
| PA <sub>1</sub>  | -0.374                 | -0.772                | 0.037                 | 4.737                 | -2.729                 | -0.777                | -1.059                | <b>7.673</b>          |

**Variances (bold, diagonal), covariances (below diagonal), and correlations (italics, above diagonal) between general health questionnaire (GHQ), depersonalisation (DP), emotional exhaustion (EE), and personal accomplishment (PA), at time<sub>1</sub> (1997) and time<sub>2</sub> (2000)**

applied to the covariance matrix. We replaced missing values with the MVA program of SPSS. We began analysis with a saturated model containing all paths in the  $\Gamma$  matrix between the four variables (general health questionnaire, emotional exhaustion, depersonalisation, personal accomplishment) in 1997 and 2000 then dropped the least significant paths sequentially until all remaining paths were significant.

382 (69%) doctors replied to the second questionnaire. Respondents in 2000 did not differ from non-respondents with respect to their 1997 GHQ or aMBI scores ( $p=0.485$ ,  $0.424$ ,  $0.592$ , and  $0.357$  for GHQ and aMBI), although they had qualified about 2 years later. Complete data were available for 331 participants.<sup>3</sup> 57 (17%) doctors in 1997, and 59 (18%) in 2000 (difference not significant,  $p=0.902$ , McNemar's test) showed caseness for these disorders, 25 (8%) on both occasions. This incidence is fairly low,<sup>4</sup> and no evidence here or in other cross-sectional data<sup>3</sup> suggests that these disorders have increased since 1997. On the aMBI scale, mean scores in 2000 were slightly higher than in 1997 for emotional exhaustion ( $p=0.004$ ), unchanged for depersonalisation ( $p=0.585$ ), and slightly lower for personal accomplishment ( $p=0.034$ ). All measures were significantly correlated ( $p=0.0001$ ) between

1997 and 2000 (GHQ  $r=0.479$ , emotional exhaustion  $0.615$ , depersonalisation  $0.652$ , personal accomplishment  $0.578$ ).

Data from 365 doctors were available for causal modelling (table). The  $\Phi$  and  $\Psi$  matrices were free and symmetrical. The path from personal accomplishment in 1997 to GHQ in 2000 was only of borderline significance, but we kept it in because of its theoretical interest. The figure's top panel is a conventional diagram, of the significant paths in the model, which had excellent fit ( $p=0.579$ ), with a high goodness of fit index ( $0.996$ ) and adjusted goodness of fit index ( $0.980$ ).

The bottom panel of the figure shows the top panel rearranged for clearer display of causal patterns. The largest causal effects in the model show a causal cycle in which emotional exhaustion makes doctors more stressed and stress makes doctors more emotionally exhausted. The other components of burnout also affect stress (although neither is itself caused by stress). Depersonalisation (cynicism) reduces stress, presumably through an ego-defence mechanism. By contrast, personal accomplishment increases stress both directly and also indirectly by increasing emotional exhaustion.

An increasing emphasis on higher professional standards might therefore increase stress and burnout in doctors, whereas depersonalisation could act as a defence against stress. Since the strongest paths in the model include emotional exhaustion, stress reduction programmes should probably concentrate on reducing emotional exhaustion, perhaps through reduced workload. Depersonalisation (cynicism) should also be recognised as adaptive, whereas increased professional efficacy can be maladaptive, increasing future stress and burnout.

**Contributors**

I C McManus designed the study, B C Winder coordinated data collection and analysis, and D Gordon was responsible for managing the study. I C McManus did statistical analyses, and all authors helped to write the report.

**Conflict of interest statement**

None declared.

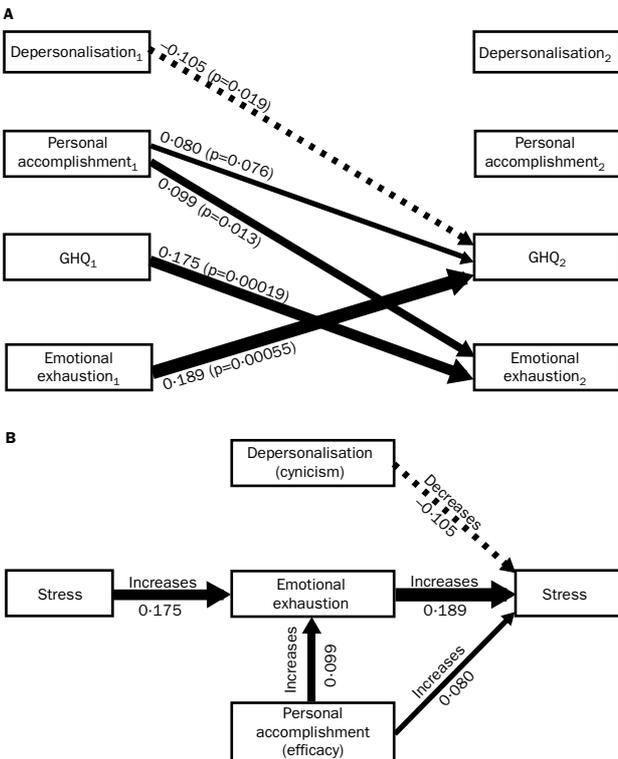
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**Significant causal paths (standardised path coefficients; significance level in parentheses) between variables at time<sub>1</sub> (1997) and time<sub>2</sub> (2000)**

The width of arrows is proportional to the size of the path coefficients. Dotted lines indicate negative values. Auto-correlations have been omitted for clarity.