Oddly, the authors did not investigate the part played by supply in explaining some of the differences. Variations in the available beds per 1000 population might be a determinant of such differences, particularly as they have remained consistent over 15 years and among most diagnostic groups.⁷ Moreover, in the United States the relative variation of the number of doctors per 1000 population is quite large across regions, and that variation, too, might be partly responsible for the differences.⁸

Ten years ago Maxwell suggested that if France were to adopt the United States length of stay it would require only half as many hospital beds to still treat the same number of patients.⁹ The causes of variations in length of stay are clearly complicated and probably depend on aggregated hospital supply, national norms, local pressures, and individual discretion as well as the characteristics of patients. The Office of Technology Assessment review also looked carefully at publications on the crucial question of health outcome and its relation to length of stay. (The authors stated repeatedly that their goal was to determine standards for length of stay from such research, with which regional or hospital figures could be compared. This seems a naive and slightly misplaced hope, for there are too many imponderables for any standard to be useful as a yardstick.) They found 17 randomised comparisons of the effect of length of stay on health outcome which they rated as methodologically sound. These were restricted to the treatment of myocardial infarction, selected surgical operations, obstetrics, and psychiatry, and the reports were well reviewed. The conclusions were disappointing, however, for it proved impossible to compare with any useful certainty the relative efficacy of short stay against long stay for any of these treatments. Only extremely large effects could be excluded. Of the trials reported, none had more than a 75% chance of detecting a halving of either morbidity rates or mortality by changing length of stay (usually reducing it). On first principles one might generally expect a more modest effect than that.

Why, then, have questions about length of stay not been examined more seriously? Perhaps the answer lies in the nature of the underlying economic arguments. Hospital costs, per head, for a community depend on the product of admission rates with average cost per case. Clearly changing length of stay directly affects only the latter—and since a shortening saves time in hospital when costs are lowest this time saved might be taken up by admission of a new patient for whom the daily costs would be higher. More shorter admissions may well increase the overall costs. In the United States this effect has been forecast as one of the consequences of the new legislation providing for some reimbursement for hospital care according to diagnostic related groups.¹⁰ Reimbursement will no longer depend on hospital stay but exclusively on the 467 diagnostic related groups into which each patient is categorised.

Here in Britain we have the added complication of devolving care to the open ended facilities of the general practitioners, and community services. (Since 1977, according to Metcalfe, each general practitioner has had an extra 710 patient days added to his or her responsibility as a consequence of shorter hospital stays.¹¹) Hence the case for shortening length of stay for care which is at all discretionary in order to reduce expenditure becomes obscured by the need to justify both the extra expenditure on patients who would not be otherwise admitted, at least at that time, and the net costs incurred outside the hospital.

Furthermore, the crucial question of whether shortening length of stay would increase the efficiency of provision of health care must remain open until we can devise (and obtain

funding for) satisfactory research protocols to provide reliable estimates of the relative effectiveness of different lengths of stay on pertinent measures of outcome. At least for most common surgical procedures in the United States, however, variations in admission rates are a stronger determinant of costs per head than are lengths of stay.¹² Moreover, admission rates are no more variable among hospital service areas in the United States than they are in Britain.¹³ The question of efficiency cannot be answered finally, therefore, until we know which admission policy yields greater benefits in terms of health outcome. If our aim is to increase the efficiency of the provision of health care it is this question that deserves the greatest amount of attention.

KLIM MCPHERSON

Lecturer in Medical Statistics,
Department of Community Medicine and
General Practice,
University of Oxford,
Oxford OX2 6HE

¹ Office of Population Censuses and Surveys. *Hospital in-patient enquiry. Main tables. 1980.* London: HMSO, 1980. (Series MB4, No 15.)

² Office of Population Censuses and Surveys. *Hospital in-patient enquiry. Main tables. 1974.* London: HMSO, 1974. (Series MB4, No 2.)

³ National Center for Health Statistics. *Vital and health statistics, series 13.* 1974:No 26. (DHEW publication No (HRA)76-1777.)

⁴ National Center for Health Statistics. *Vital and health statistics, series 13.* 1980:No 64. (DHEW publication No (PHS)82-1725.)

⁵ McPherson K, Strong PM, Epstein A, Jones L. Regional variations in the use of common surgical procedures: within and between England and Wales, Canada and the United States of America. *Soc Sci Med [A]* 1981; 15:273-88.

⁶ Office of Technology Assessment. *Variations in hospital length of stay: their relationship to health outcomes.* Washington: Office of Technology Assessment of the United States Congress, 1983. (Health Technology Case Study 24.)

⁷ Feldstein MS. *Economic analysis for health service efficiency.* Amsterdam: North-Holland Publishing Co, 1968.

⁸ American College of Surgeons. American Surgical Association. *Surgery in the United States. A summary report of the study on surgical services for the United States.* Chicago: American College of Surgeons. American Surgical Association, 1976.

⁹ Maxwell R. *Health care: the growing dilemma.* London: McKinsey and Co, 1974.

¹⁰ Simborg DW, Creep DRG. A new hospital-acquired disease. *N Engl J Med* 1981;304:1602-4.

¹¹ Metcalfe D. Trends in the utilization of the National Health Service. *J R Coll Gen Pract* 1983;33:615-7.

¹² Wennberg JE, Barnes BA, Zubkoff M. Professional uncertainty and the problem of supplier-induced demand. *Soc Sci Med* 1982;16:811-24.

¹³ McPherson K, Wennberg JE, Hovind OB, Clifford P. Small-area variations in the use of common surgical procedures: an international comparison of New England, England, and Norway. *N Engl J Med* 1982; 307:1310-4.

Systemic sclerosis: a collagen or microvascular disease?

The concept of "collagen disease" was introduced by Klemperer and colleagues in 1942 to describe connective tissue disorders such as rheumatoid arthritis, systemic lupus erythematosus, and polyarteritis nodosa.¹ Klemperer observed fibrinoid degeneration in collagen suggesting a basis for development of these disorders. Further study has shown that the structure and metabolism of collagen are largely unaltered in these diseases; the changes that occur in collagen are secondary to other biochemical and immunological events—yet, inappropriate as it may be, the name remains in use.

Systemic sclerosis has remained as the archetypal collagen

disorder. The evidence for disordered and excessive collagen synthesis seems clear cut. Scleroderma is the most obvious feature, with induration and tightness of the skin leading to deformities and disabilities. In some patients extensive changes may make the whole body appear as if encased in a suit of armour. Biopsy specimens show gross proliferation of new collagen fibres with atrophy of the appendages of the skin. Analogous changes occur in viscera such as the oesophagus and the small and large intestines, leading to dysphagia, malabsorption syndrome, and pseudodiverticulosis. Skin fibroblasts show an increased rate of production of collagen² which seems to be most pronounced in cells derived from the deeper layers of the dermis.³ There may be a serological factor that selectively potentiates high collagen clones of fibroblasts producing large amounts of collagen,⁴ or a lymphokine derived from mononuclear cells may stimulate fibroblasts to secrete excess collagen.⁵

Attention has been concentrated on the fibrotic features of systemic sclerosis because of the dramatic skin changes in patients with the diffuse disease. The most common pattern, however, is the so called CREST variant (calcinosis, Raynaud's syndrome, [o]esophageal damage, sclerodactyly, and telangiectasia), in which the tightness and induration of the skin are frequently minimal. Patients with this form of the disease suffer predominantly from vascular problems, mainly in the fingers. As an early feature of the disease Raynaud's phenomenon with reversible peripheral ischaemia is almost universal, but later more permanent evidence of vascular damage may appear, with digital pitting, ulceration, and even gangrene.⁶ Vascular changes may develop in the viscera causing pulmonary hypertension or renal disease.

Pathological studies show changes predominantly in the small arteries and arterioles,^{6,7} with considerable intimal thickening due to proliferation and thickening of endothelial cells and deposition of glycosaminoglycan together with deposits of fibrinogen or fibrin.⁸ A small perivascular cuff of fibrosis and a mononuclear infiltration may be seen. Eventually the lumen of the vessel may become completely blocked and the specific pathological changes replaced by fibrosis and atrophy of the blood vessels. The numbers of capillaries are severely reduced to perhaps only 20% of normal, with consequent profound devascularisation. Those capillaries that remain become dilated and may be seen in the skin as telangiectases and in the nail beds by capillary microscopy.⁹ The pattern of capillary abnormalities correlates with the extent of visceral disease.¹⁰ The remaining capillaries show gross thickening of the basement membrane and the endothelial cells may be swollen or necrotic.

Damage to endothelial cells may be the initial feature of small vessel disease and may lead to increased vascular permeability and the development of fibrosis. Increased concentrations of circulating factor VIII and von Willebrand factor activity indicate endothelial damage,¹¹ and raised concentrations of circulating platelet aggregates and β thromboglobulin suggest platelet activation, which may be both a cause and effect of endothelial damage.¹² There may be a circulating endothelial cell cytotoxic factor,¹³ but the evidence for this is controversial.^{14,15} A deficiency of the circulating protease inhibitors normally present might allow this cytotoxic activity.¹⁶

The blood vessels of patients with systemic sclerosis may be hypersensitive to serotonin, suggesting that this feature may possibly play a part in the pathogenesis of this disease.¹⁷ The principal actions of serotonin are to cause vasoconstriction and to initiate and amplify aggregation of platelets. Injection into the skin produces scleroderma-like changes,¹⁸ and into

the pulmonary arteries the pathological changes of pulmonary hypertension.¹⁹ Scleroderma-like lesions occur in association with carcinoid tumours.²⁰ Patients with systemic sclerosis lack the normal increase of urinary excretion of 5-hydroxy-indoleacetic acid after oral loading with L-tryptophan, suggesting impaired transformation of serotonin to 5-hydroxy-indoleacetic acid due to diminished monoamine oxidase activity leading to raised serotonin concentrations.²¹ There is some evidence of reduced concentrations of monoamine oxidase and some correlation between raised serotonin concentrations and the severity of the disease.²²

When the fibrinolytic activity of the blood is diminished²³ fibrinogen concentrations are raised and blood viscosity increased.^{24,25} The viscosity changes are most definite at low temperatures and low shear rates as in the peripheral microcirculation. Failure to clear deposits of fibrin on vessel walls⁸ may be due to impaired fibrinolytic activity²³ and defective plasminogen activator release (personal observations) and may lead to progressive narrowing of the lumen of the blood vessels.

Complement fixing serological factors²⁶ and deposition of immune complexes²⁷ may also damage the small vessels. A perivascular cuff of chronic inflammatory cells around the small blood vessels is an early feature of this disease.⁶ Antinuclear factors are found in virtually all cases, with an antibody directed against the centromeres of dividing cells specifically associated with the CREST syndrome.²⁸ Circulating immune complexes^{29,30} and a mixed cryoglobulinaemia³¹ do not, however, show much correlation with the clinical pattern.

The microvascular disease may possibly lead to proliferation of collagen. Serotonin may stimulate collagen synthesis,^{32,33} and other platelet derived factors may activate myofibroblasts.³⁴ A decreased supply of oxygen to the tissues may result in excess production of lactic acid, which in turn may stimulate collagen synthesis.³⁵ Immunological investigations indicate that the collagen that proliferates in this disorder is predominantly vascular.^{36,37} Anecdotal reports have appeared of aggressive hypotensive treatment of renal crises in scleroderma causing regression of both the cutaneous features of the disease and the Raynaud's phenomenon.^{38,39} An interesting analogy may be drawn with children with insulin dependent diabetes mellitus who develop skin changes resembling sclerodactyly⁴⁰ associated with microvascular complications of the diabetes.⁴¹

The treatment of systemic sclerosis is not satisfactory. Drugs used to interfere with formation of collagen, including penicillamine and colchicine, have proved of doubtful benefit. The microvascular concept has led to studies of treatment with vasodilators, calcium channel blocking agents, serotonin antagonists, prostaglandins, antiplatelet treatment, and fibrinolytic enhancing agents. Some of these have seemed effective in improving the peripheral microcirculation and the ischaemic features of the disease. Whether they can influence the abnormal fibrosis remains to be determined.

MALCOLM I V JAYSON

Professor of Rheumatology,
Rheumatic Diseases Centre,
University of Manchester,
Hope Hospital,
Salford M6 8HD

¹ Klemperer P, Pollack AD, Baehr G. Diffuse collagen disease. Acute disseminated lupus erythematosus and diffuse scleroderma. *JAMA* 1942;119:331-2.

² LeRoy EC. Increased collagen synthesis by scleroderma skin fibroblasts in vitro. A possible defect in the regulation or activation of the scleroderma fibroblast. *J Clin Invest* 1974;54:880-9.

³ Buckingham RB, Prince RK, Rodnan GP, Taylor F. Increased collagen

- accumulation in dermal fibroblast cultures from patients with progressive systemic sclerosis (scleroderma). *J Lab Clin Med* 1978;**92**:5-21.
- ⁴ Botstein GR, Sherer GK, LeRoy EC. Fibroblast selection in scleroderma. An alternative model of fibrosis. *Arthritis Rheum* 1982;**25**:189-95.
 - ⁵ Johnson RL, Ziff M. Lymphokine stimulation of collagen accumulation. *J Clin Invest* 1976;**58**:240-52.
 - ⁶ Campbell PM, LeRoy EC. Pathogenesis of systemic sclerosis: a vascular hypothesis. *Semin Arthritis Rheum* 1975;**4**:351-68.
 - ⁷ Norton WL, Nardo JM. Vascular disease in progressive systemic sclerosis (scleroderma). *Ann Intern Med* 1970;**73**:317-24.
 - ⁸ Fennell RH Jr, Reddy CRRM, Vazquez JJ. Progressive systemic sclerosis and malignant hypertension. *Archives of Pathology* 1961;**72**:209-15.
 - ⁹ Maricq HR. Widefield capillary microscopy. Technique and rating scale for abnormalities seen in scleroderma and related disorders. *Arthritis Rheum* 1981;**24**:1159-65.
 - ¹⁰ Maricq HR, Spencer-Green G, LeRoy EC. Skin capillary abnormalities as indicators of organ involvement in scleroderma (systemic sclerosis), Raynaud's syndrome and dermatomyositis. *Am J Med* 1976;**61**:862-70.
 - ¹¹ Kahaleh MB, Osborn I, LeRoy EC. Increased factor VIII/von Willebrand factor antigen and von Willebrand factor activity in scleroderma and in Raynaud's phenomenon. *Ann Intern Med* 1981;**94**:482-4.
 - ¹² Kahaleh MB, Osborn I, LeRoy EC. Elevated levels of circulating platelet aggregates and beta-thromboglobulin in scleroderma. *Ann Intern Med* 1982;**96**:610-3.
 - ¹³ Kahaleh MB, Sherer GK, LeRoy EC. Endothelial injury in scleroderma. *J Exp Med* 1979;**149**:1326-35.
 - ¹⁴ Summers GD, Weiss JB, Jayson MIV. Studies of the growth of human endothelial cell in serum from patients with scleroderma and other rheumatic diseases. *Scleroderma symposium* (in press).
 - ¹⁵ Blake DR, Scott DGI, Winyard P, et al. Endothelial cell cytotoxicity and vasculitis: the role of oxidised lipoprotein [Abstract]. *Ann Rheum Dis* (in press).
 - ¹⁶ Kahaleh MB, LeRoy EC. Endothelial injury in scleroderma. A protease mechanism. *J Lab Clin Med* 1983;**101**:553-60.
 - ¹⁷ Winkelmann RK, Goldyne ME, Linscheid RL. Hypersensitivity of scleroderma cutaneous vascular smooth muscle to 5-hydroxytryptamine. *Br J Dermatol* 1976;**95**:51-6.
 - ¹⁸ MacDonald RA, Robbins SL, Mallory GK. Dermal fibrosis following subcutaneous injections of serotonin creatinine sulphate. *Proc Soc Exp Biol Med* 1958;**97**:334-7.
 - ¹⁹ Rossi P, Zamboni L. Pulmonary arteriosclerosis due to serotonin. *Nature* 1958;**181**:1216-7.
 - ²⁰ Fries JF, Lindgren JA, Bull JM. Scleroderma-like lesions and the carcinoid syndrome. *Arch Intern Med* 1973;**131**:550-3.
 - ²¹ Stachow A, Jablonska S, Skiendziecowska A. 5-hydroxytryptamine and tryptamine pathways in scleroderma. *Br J Dermatol* 1977;**97**:147-54.
 - ²² Stachow A, Jablonska S, Skiendziecowska A. Biogenic amines derived from tryptophan in systemic and cutaneous scleroderma. *Acta Derm Venereol (Stockh)* 1979;**59**:1-5.
 - ²³ Jarrett PEM, Morland M, Browne NL. Treatment of Raynaud's phenomenon by fibrinolytic enhancement. *Br Med J* 1978;**ii**:523-5.
 - ²⁴ Goyle KB, Dormandy JA. Abnormal blood viscosity in Raynaud's phenomenon. *Lancet* 1976;**ii**:1317-8.
 - ²⁵ McGrath MA, Peek R, Penny R. Blood hyperviscosity with reduced skin blood flow in scleroderma. *Ann Rheum Dis* 1977;**36**:569-74.
 - ²⁶ Tan EM, Pearson CM. Rheumatic disease sera reactive with capillaries in the mouse kidney. *Arthritis Rheum* 1972;**15**:23-8.
 - ²⁷ Lapenas D, Rodnan GP, Cavallo T. Immunopathology of the renal vascular lesion of progressive systemic sclerosis (scleroderma). *Am J Pathol* 1978;**91**:243-58.
 - ²⁸ Tan EM, Rodnan GP, Carcia I, Morol Y, Fritzler MJ, Peebles C. Diversity of antinuclear antibodies in progressive systemic sclerosis. Anti-centromere antibody and its relationship to CREST syndrome. *Arthritis Rheum* 1980;**23**:617-25.
 - ²⁹ Seibold JR, Medsger TA Jr, Winkelstein A, Kelly RH, Rodnan GP. Immune complexes in progressive systemic sclerosis (scleroderma). *Arthritis Rheum* 1982;**25**:1167-73.
 - ³⁰ Siminovitch K, Klein M, Pruzanski W, et al. Circulating immune complexes in patients with progressive systemic sclerosis. *Arthritis Rheum* 1982;**25**:1174-9.
 - ³¹ Husson JM, Druet P, Contet A, et al. Systemic sclerosis and cryoglobulinemia. *Clin Immunol Immunopathol* 1976;**6**:77-82.
 - ³² Boucek RJ, Speropoulos AJ, Noble NL. Serotonin and ribonucleic acid and collagen metabolism of fibroblasts in vitro. *Proc Soc Exp Biol Med* 1972;**140**:599-603.
 - ³³ Boucek RJ, Noble NL. Histamine, norepinephrine, and bradykinin stimulation of fibroblast growth and modification of serotonin response (37714). *Proc Soc Exp Biol Med* 1973;**144**:929-33.
 - ³⁴ Castor CW, Ritchie JC, Williams CH, et al. Connective tissue activation. XIV. Composition and actions of a human platelet autocoagulant mediator. *Arthritis Rheum* 1979;**22**:260-72.
 - ³⁵ Chvapil M, Ryan JN, Madden JW, Peacock EE. Effect of chelating agents, proline analogs and oxygen tension in vivo and in vitro experiments on hydroxylation, transport, degradation and accumulation of collagen. In: Vogel HG, ed. *Connective tissue and ageing*. Amsterdam: Excerpta Medica, 1973:195-207.
 - ³⁶ Gay RE, Buckingham RB, Prince RK, Gay S, Rodnan GP, Miller EJ. Collagen types synthesized in dermal fibroblast cultures from patients with early progressive systemic sclerosis. *Arthritis Rheum* 1980;**23**:190-6.

- ³⁷ Mackel AM, DeLustro F, Harper FE, LeRoy EC. Antibodies to collagen in scleroderma. *Arthritis Rheum* 1982;**25**:522-31.
- ³⁸ Wanser C, Cooke CR, Fries JF. Successful medical treatment of scleroderma renal crisis. *N Engl J Med* 1978;**299**:873-5.
- ³⁹ Whitman HH III, Case DB, Laragh JH, et al. Variable response to oral angiotensin-converting-enzyme blockade in hypertensive scleroderma patients. *Arthritis Rheum* 1982;**25**:241-8.
- ⁴⁰ Seibold JR. Digital sclerosis in children with insulin-dependent diabetes mellitus. *Arthritis Rheum* 1982;**25**:1357-61.
- ⁴¹ Rosenbloom AL, Silverstein JH, Lezotte DC, Richardson K, McCallum M. Limited joint mobility in childhood diabetes mellitus indicates increased risk for microvascular disease. *N Engl J Med* 1981;**305**:191-4.

Pain in the temporomandibular joint

Pain in the temporomandibular joint is rarely due to organic disease. Patients with rheumatoid arthritis, for example, commonly have radiographic changes in this joint, but pain is rare and, indeed, no more frequent than in a control population.¹ Similarly, degenerative joint disease at this site is usually no more than a chance radiological finding; severe or protracted symptoms are unusual²—though a few examples have been reported in younger patients.^{3,4}

By far the most common cause of pain in the region of the joint is infection and acute inflammation round a partially erupted wisdom tooth—a readily recognisable condition, typically of late adolescence. In the elderly, by contrast, an important cause of periarticular pain is ischaemia of the muscles associated with giant cell arteritis. Symptoms are brought on by mastication—a condition often called “jaw claudication,” even though the jaw cannot by any stretch of the imagination limp.

In young adults the most common cause of pain is the so called pain dysfunction (or myofascial pain dysfunction) syndrome. This should not be but often is confused with Costen's syndrome. In 1934 Costen described 11 patients with a variety of symptoms such as headache, tenderness around the temporomandibular joint, pain in or around the ears, tinnitus, and impairment of hearing, which he ascribed to “overclosure” of the joint.⁵ This in turn was postulated to irritate the chorda tympani, auriculotemporal and other nerves in the vicinity—and even the dura, from erosion of the glenoid fossa. Thus was Costen's syndrome born, but, in spite of having been effectively dismissed by several groups of workers,⁶⁻⁸ it has been a long time a-dying and still appears in the latest and most respected of medical textbooks.

Twenty years after Costen's paper Schwartz, working with a radiologist and a psychiatrist, investigated no fewer than 500 patients with pain in their temporomandibular joints and described the pain dysfunction syndrome.^{9,10} Typically this affects otherwise healthy women between 15 and 40 and causes dull, aching pain, usually unilateral, in front of the ear. The pain is made worse by mastication and associated with limited opening of the mouth or episodes of “locking” of the jaw. Inflammation or radiological signs of joint disease are absent. Movement of the jaw may also produce clicking—a sign that is, however, also common in asymptomatic people.

The most widely held view about the mechanism underlying the pain dysfunction syndrome is that some disturbance of neuromuscular coordination causes spasm and fatigue of the masticatory muscles. Disordered dental occlusion was long believed to be the main aetiological factor, but there is little supporting evidence for this.¹¹

Is there any other relatively common, minor disorder, essentially functional and typically self limiting, which has given