

We felt obliged to provide outpatient treatment for all our patients as most had been given some form of treatment from their general practitioner before referral to our rectal clinic. There was no significant difference in the symptomatic response to treatment between the groups, and at 12 months the larger second degree piles did not seem to do any better when treated by rubber band ligation than by photocoagulation. The total number of patients developing side effects was small, but was more significant in those receiving rubber band ligation.

Photocoagulation is undoubtedly a useful form of treatment for first and second degree piles. Side effects are few and usually all three haemorrhoidal swellings may be treated at the first attendance. One further advantage is that a nurse or assistant is not needed during treatment.

Usually only two sites may be treated with ease by band ligation, though others have advocated placing three bands at the first outpatient attendance.³ Despite this, repeated treatment was needed significantly less frequently after band ligation than photocoagulation. Since the long term results of photocoagulation do not differ from rubber band ligation we believe that photocoagulation can be used as primary non-invasive treatment for all new patients with first or second degree haemorrhoids

reserving rubber band ligation for patients who have recurrent symptoms after their initial treatment.

We believe that advice concerning a high fibre diet, prevention of straining,⁴ and perianal hygiene are important factors in reducing recurrent symptoms. These aspects of treatment were mentioned to all our patients.

Agents for photocoagulator in the United Kingdom are: Chilworth Medicals Ltd, 31 Dorking Road, Chilworth, Guildford, Surrey.

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Correlation of persistently high serum amyloid A protein and C-reactive protein concentrations with rapid progression of secondary amyloidosis

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Abstract

The importance of serum amyloid A protein in the progression of renal failure was studied over three years in 28 patients with secondary (amyloid A type) amyloidosis predominantly due to rheumatoid arthritis. Creatinine clearance, the amount of protein in the urine, and serum amyloid A and C-reactive protein concentrations were determined regularly. Linear regression analysis showed a close correlation between the change in creatinine clearance each year and both serum amyloid A concentrations (20 patients: $r = -0.83$, $p < 0.001$) and C-reactive protein concentrations (28 patients: $r = -0.80$, $p < 0.001$). The correlation between serum amyloid A and C-reactive protein concentrations was also significant (317 parallel measurements: $r = 0.81$, $p < 0.001$).

These findings suggest that monitoring serum amyloid A or C-reactive protein concentrations is valuable in assessing the prognosis in secondary amyloidosis and that therapeutic measures that lower serum amyloid A concentrations may reduce the formation of amyloid.

Introduction

The amyloid substance in secondary amyloidosis (amyloid A protein) is believed to be formed from serum amyloid A protein, an acute phase protein.¹⁻³ High serum amyloid A concentrations have been reported in conditions associated with secondary amyloidosis⁴⁻⁶ and are considered to be a prerequisite for the formation of amyloid.⁷ On the basis of this hypothesis it may be assumed that the availability of serum amyloid A protein, the probable substrate, influences the rate of formation of amyloid A protein; some evidence of this has been reported.⁸ We studied the role of serum amyloid A concentrations in secondary amyloidosis by undertaking a three year prospective study of 28 patients with this disease; this is the first long term study to have been carried out.

Patients and methods

We studied 28 patients (20 women, eight men; mean age 52.5 years) with secondary renal amyloidosis proved by biopsy. The underlying disease was rheumatoid arthritis in 24 patients, juvenile chronic polyarthritis in two, ankylosing spondylitis in one, and bronchiectasis in one. At the start of the study the mean time since diagnosis of amyloidosis was 1.6 years.

Twenty-two patients had some degree of renal failure (creatinine clearance under 100 ml/min); the mean creatinine clearance in all the patients was 60.5 ml/min at the beginning and 30.1 ml/min at the end of the study. The mean duration of follow up was 21.6 months (range 12-37 months) and the mean interval between check ups 1.7 months. Renal function was tested, proteinuria measured, and serum acute phase protein concentrations determined on each occasion. A complete series of serum amyloid A concentrations was obtained in 20 cases and of C-reactive protein concentrations in all 28 cases (determination of serum amyloid A concentration was not available during the first

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year of the study). Serum amyloid A concentrations were measured by a radial immunodiffusion method using antiserum against amyloid A protein (Atlantic Antibodies, Scarborough, Maine, USA) and purified tissue amyloid A protein as standard. The change—that is, the decrease or, in three cases, the increase—each year in creatinine clearance and in the amount of protein in the urine each day was calculated. The correlation between serum amyloid A and C-reactive protein concentrations was established from 317 parallel measurements in 37 patients with secondary amyloidosis. Linear regression analysis was used to assess the significance of the correlations.

Results

The correlation between serum amyloid A and C-reactive protein concentrations was significant in secondary amyloidosis ($r=0.81$, $p<0.001$; fig 1). The same correlation was $r=0.88$ ($p<0.001$) when only one pair of values for each patient (the first one ever taken) was used, which shows that replicate values in the same patients did not raise the coefficient. The correlations between the change in creatinine clearance each year and the median serum amyloid A and C-reactive

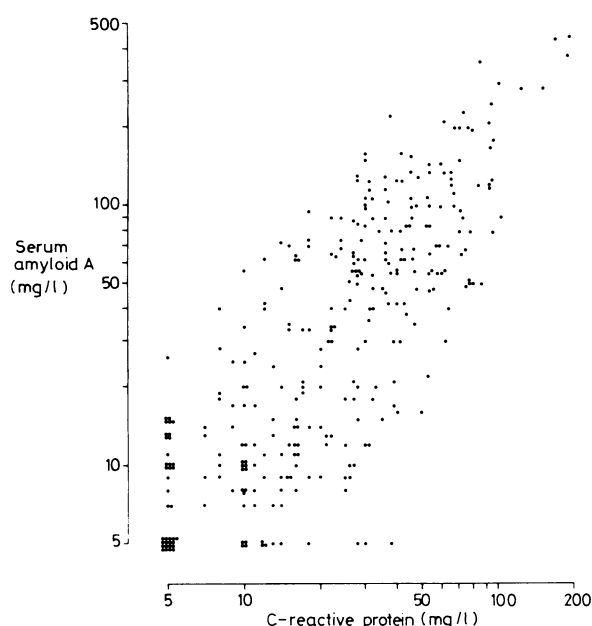


FIG 1—Correlation between 317 parallel measurements of serum amyloid A and C-reactive protein concentrations in 37 patients with secondary amyloidosis ($r=0.81$, $p<0.001$).

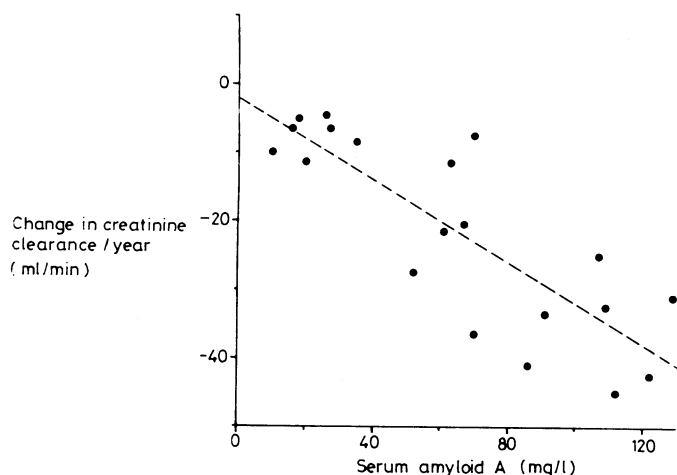


FIG 2—Correlation between change in creatinine clearance each year and "mean" (see text) serum amyloid A protein concentration in 20 patients with secondary amyloidosis ($r=-0.83$, $p<0.001$).

protein concentrations were significant ($r=-0.78$ and $r=-0.74$ respectively). Even better correlations were found to exist between the change in creatinine clearance each year and "mean" values of serum amyloid A and C-reactive protein concentrations, which were calculated from the area confined by the concentration curve and the x axis in a concentration/time coordinate system (see stippled areas in fig 4). The coefficients were $r=-0.83$ for serum amyloid A concentrations (20 patients, $p<0.001$) and $r=-0.80$ for C-reactive protein concentrations (28 patients, $p<0.001$) (figs 2 and 3).

Serum amyloid A and C-reactive protein concentrations were not influenced by the degree of renal failure; there was no correlation between creatinine clearance and either concentration. Figure 4 shows individual curves in four patients representing two average cases and two extremes. The curves in case 1 show that a concentration peak,

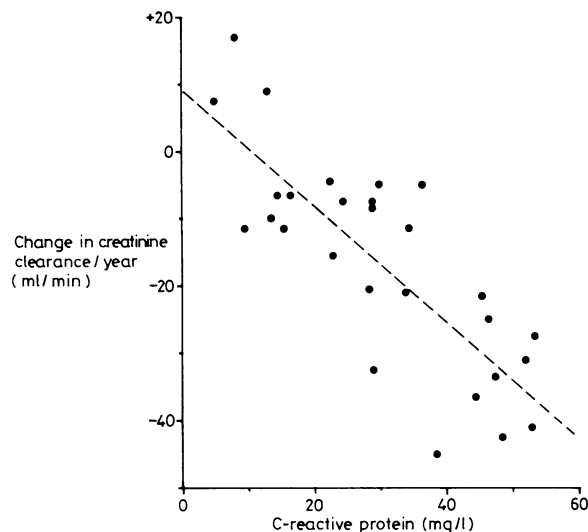


FIG 3—Correlation between change in creatinine clearance each year and "mean" (see text) concentration of C-reactive protein in 28 patients with secondary amyloidosis ($r=-0.80$, $p<0.001$).

even when very high (in this instance due to erysipelas), is not followed by any appreciable change in renal function when it is narrow—that is, of short duration. The same phenomenon was noted in two other patients. The opposite—that is, that high concentration peaks of longer duration are followed by accelerated deterioration of renal function—was seen in several cases (see cases 2 and 3).

The amount of protein in the urine increased in 17 cases, decreased in four, and remained unchanged in seven during follow up. The rate of change correlated positively with the "mean" serum amyloid A or C-reactive protein concentrations ($r=0.41$).

Discussion

This study shows that the rate of deterioration of renal function in secondary amyloidosis correlates with the amount of serum amyloid A protein available over a given time. Although other factors such as interstitial fibrosis and tubular atrophy are partly responsible for the renal failure in amyloidosis, the main cause seems to be deposition of amyloid in the kidney.⁹⁻¹¹ Hence our results add indirect evidence for the hypothesis that amyloid A protein is formed from serum amyloid A protein. Our findings also agree with those of van Rijswijk,⁸ who reported that patients with amyloid A type amyloidosis and higher serum amyloid A concentrations tended to progress to uraemia whereas patients with lower concentrations tended to have stable renal function. He did not, however, report such a close correlation as was found in the present, long term study.

Although C-reactive protein is neither structurally related to nor considered to be a precursor of amyloid A protein, it parallels serum amyloid A protein fairly closely in various conditions.¹²⁻¹⁶ The present study indicates that a similar close

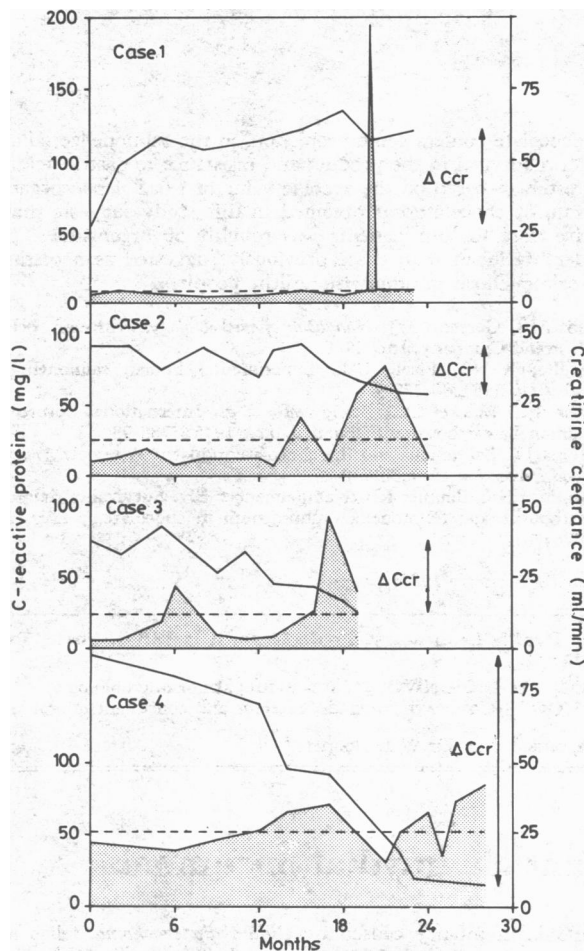


FIG 4—C-reactive protein concentration and creatinine clearance in four patients with secondary amyloidosis. Broken horizontal line indicates "mean" concentration of C-reactive protein calculated from stippled area. Δ Ccr = Total change in creatinine clearance during follow up. Case 1: Increase in creatinine clearance in patient with low mean C-reactive protein concentration. Cases 2 and 3: Moderate decrease in creatinine clearance in patients with medium to high mean C-reactive protein concentration. Case 4: Rapid decrease in creatinine clearance in patient with very high mean C-reactive protein concentration.

correlation exists in secondary amyloidosis. Hence, C-reactive protein concentrations seem to give information on the serum amyloid A concentrations and may be used when determinations of serum amyloid A concentrations are not available.

This study also shows that monitoring serum amyloid A concentrations (or C-reactive protein concentrations) gives valuable information for the assessment of the prognosis and the need for treatment in secondary amyloidosis. Seemingly, therapeutic efforts should be directed towards reducing the inflammatory activity of the underlying disease. Therapeutic measures that lower the serum amyloid A concentration may reduce formation of amyloid.

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WOODBINE, OR HONEY-SUCKLES flower in June, and the fruit is ripe in August.

Doctor Tradition, that grand introducer of errors, that hater of truth, lover of folly, and the mortal foe to Dr Reason, hath taught the common people to use the leaves or flowers of this plant in mouth-water, and by long continuance of time, hath so grounded it in the brains of the vulgar, that you cannot beat it out with a beetle: All mouth-waters ought to be cooling and drying, but Honey Suckles are cleansing, consuming and digesting, and therefore fit for inflammations; thus Dr Reason. Again if you please, we will leave Dr Reason a while, and come to Dr Experience, a learned gentleman, and his brother. Take a leaf and chew it in your mouth, and you will quickly find it likelier to cause a sore mouth and throat than to cure it. Well then, if it be not good for this, What is it good for? It is good for something, for God and nature made nothing in vain. It is an herb of Mercury, and appropriated to the lungs; neither is it Crab claims dominion over it; neither is it a foe to the Lion; if the lungs be afflicted by Jupiter, this is your cure: It is fitting a conserve made of the

flowers of it were kept in every gentlewoman's house; I know no better cure for an asthma than this: besides, it takes away the evil of the spleen, provokes urine, procures speedy delivery of women in travail, helps cramps, convulsions, and palsies, and whatsoever griefs come of cold or stopping; if you please to make use of it as an ointment, it will clear your skin of morpew, freckles, and sun-burnings, or whatsoever else discolours it, and then the maids will love it. Authors say, The flowers are of more effect than the leaves, and that is true; but they say the seeds are least effectual of all. But Dr Reason told me, That there was a vital spirit in every seed to beget its like; and Dr Experience told me, That there was a greater heat in the seed than there was in any other part of the plant: and withal, That heat was the mother of action, and then judge if old Dr Tradition (who may well be honoured for his age, but not for his goodness) hath not so poisoned the world with errors before I was born, that it was never well in its wits since, and there is a great fear it will die mad. (Nicholas Culpeper (1616-54) *The Complete Herbal*, 1850.)