Objective: To determine the prognosis for resolution of abnormal cutaneous photosensitivity in patients with chronic actinic dermatitis (also known as the photosensitivity dermatitis and actinic reticuloid syndrome).

Design: Historical cohort study involving follow-up of patients for up to 24 years from diagnosis.

Setting: A Scottish tertiary referral center for investigation of photodermatosis.

Patients: One hundred seventy-eight patients with chronic actinic dermatitis, 62% of a cohort of 285 living patients identified in the Photobiology Unit database.

Interventions: Recall for repeated clinical assessment and monochromator phototesting. All patients underwent patch testing when initially assessed; this was repeated at follow-up in a subgroup of patients.

Main Outcome Measures: Resolution of abnormal photosensitivity, defined as clinical resolution and return of phototest responses to within normal population limits. In addition, possible prognostic factors for resolution of photosensitivity were examined.

Results: The probability of abnormal photosensitivity resolving by 10 years from diagnosis is 1 in 5. Particularly severe abnormal UV-B photosensitivity (minimal erythema dose at 305±5 nm half-maximum bandwidth, ≤5.6 mJ·cm⁻²) and the identification of separate contact allergens in 2 or more patch test batteries are predictors of a poorer prognosis for resolution. Loss of contact allergies was not associated with a different prognosis for photosensitivity resolution. Our findings probably underestimate the probability of resolution, as those referred to a tertiary referral center and willing to attend for follow-up may include a disproportionate number of severely affected patients.

Conclusions: Newly diagnosed patients can be told that most of them will improve with appropriate UV/visible light and allergen avoidance and that there is hope that their photosensitivity will completely resolve.

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Patients with chronic actinic dermatitis (CAD),¹ also known as the photosensitivity dermatitis and actinic reticuloid syndrome,² are abnormally photosensitive to UV (UV-B and UV-A) and often visible wavelengths. Studies from Europe reported that most patients also have allergic contact dermatitis,³⁴ although this has been detected in a lower proportion in a North American series.⁵⁶ In our experience, this often-disabling condition improves, to a varying degree, in most patients after investigation and appropriate advice. Sustained improvement usually depends on continued careful UV/visible light and allergen avoidance. Marked improvement, including subjective clearance, has been reported.⁷ However, true spontaneous resolution (with the return of photosensitivity to within the normal population range confirmed by phototesting) has not been previously described.

One of the first questions asked by the newly diagnosed CAD patient is “Will I ever get completely better?” To date, we have been unable to provide a satisfactory reply.

The primary aim of this study was to define the prognosis for the abnormal photosensitivity component of this syndrome. Secondary aims were to determine whether there were any identifiable factors at diagnosis that helped to predict prognosis and to find out whether resolution of abnormal photosensitivity was associated with resolution of allergic contact dermatitis.

RESULTS

DESCRIPTION OF PATIENTS FOLLOWED UP

We followed up 178 patients. The majority of patients (147/178 [83%]) had 1 or more contact allergens (Table 1).

All patients had discontinued systemic immunosuppressive therapy for at least 1 month when assessed, but 18 (10%), of whom 2 were from Tayside,
PATIENTS AND METHODS

STUDY DESIGN

Although the ideal study would involve prospective monitoring of all patients, this would be costly, difficult to organize, and, most importantly, would not answer the key question for at least 20 years. Accordingly, this historical follow-up was conducted at the Scottish national photodermatology unit in Dundee, Tayside—a tertiary referral center for the investigation of photodermatosis.

PATIENTS

The number of potential subjects identified by the Photobiology Unit database was 331. Of these, 285 were remaining as potential subjects after exclusion of those found to have died without follow-up. Of the 285 subjects, 178 were able to attend the follow-up assessment. One hundred fifty-six (88%) of the 178 patients were men and 22 (12%) were women. The median age at diagnosis was 60 years (range, 21-88 years). Forty-seven (26%) of the 178 patients had a Tayside home address at last assessment.

Patients diagnosed with CAD and followed up for 1 year or longer after clinical assessment and monochromator phototesting were included and formed a defined inception cohort. As a result of the Photobiology Unit’s long-standing interest in this condition, many patients seen after 1972 were routinely reviewed with repeated phototesting and, as appropriate, patch testing. Only a minority were reinvestigated specifically because of a clinical suspicion of worsening abnormal photosensitivity. For the majority of patients, the purpose of follow-up was education, that is, to keep patients up-to-date with their degree and wavelength of abnormal photosensitivity and their contact allergen profile.

We attempted to reduce selection bias by reassessment of as many patients as possible who had not attended for more than 1 year, regardless of the outcome of the last assessment. Patients’ life/death status was determined by checking with (1) the Community Health Index (for local [Tayside] patients); (2) the patients’ dermatologists; (3) a record search of the New Registry House, Edinburgh; and (4) the medical records department of local hospitals.

To reduce selection bias arising from the fact that those who still had abnormal photosensitivity would be expected to be more likely to reattend than those no longer affected, we emphasized the purposes of the study and offered to reimburse patients’ travel expenses.

had been treated with oral prednisolone, psoralen–UV-A, azathioprine, or cyclosporin between the diagnosis and assessment.

For 96 patients (54%), it was possible to estimate the likely year of onset of photosensitivity, which ranged from 30 years to less than 1 year (median, 2 years) before the diagnosis was established. However, we used the date of diagnosis, rather than the estimated date of onset, as our follow-up start time. This was because of the difficulty in making an accurate diagnosis of abnormal photosensitivity without phototesting and the problem of retrospectively distinguishing the onset of a preceding endogenous or allergic contact dermatitis from onset of the CAD syndrome. Patients were followed up for up to 24 years from diagnosis.

PHOTOBIOLOGY UNIT ASSESSMENT

Clinical

A detailed history was taken and physical examination performed at each assessment. Only those patients no longer aware of abnormal photosensitivity were regarded as having “resolved” or “much reduced” abnormal photosensitivity.

Phototesting

All patients were phototested using a 1600-W high-pressure xenon arc lamp with a diffraction grating monochromator. The same technique, described by Mackenzie and Frain-Bell, has been used since 1972. On the first day of testing, the skin on the patients’ back was irradiated with a series of defined doses of the following wavelengths (± half-maximum bandwidth): 305±5, 335±30, 365±30, 400±30, and 430±30 nm. At each patient’s first assessment, longer visible wavelength (460±30 nm and longer) irradiation was also used and was repeated at subsequent visits if abnormal photosensitivity was detected at visible wavelengths. Irradiation sites were examined for reactions immediately and 7 and 24 hours after irradiation for all patients. To define the minimal erythema dose (MED) at each wavelength with sufficient accuracy to assign the patient to one of the photosensitivity classes defined for this study, further doses were given on a second day of testing to narrow the gap between the MED and the dose producing no response after the first day’s testing.

Patch Testing

All patients underwent patch testing. To avoid the “angry back syndrome,” patch testing was carried out only when the patient’s skin disease was inactive. This sometimes required a period of inpatient dermatitis suppression. Topical corticosteroid application to upper back test sites was avoided for at least 1 week before testing. Patch tests were applied for 48 hours to back skin using Finn chambers on Scanpor tape (Norgesplaster, Kristiansand, Norway). Readings were performed at 72 hours, with reactions recorded as irritant (if strictly confined to site of application with a well-demarcated edge) or allergic, with strength of reaction graded on a 0-to-4 scale (grading scheme for allergic reactions: 0, no response; 0.5, doubtful response; 1, definite but faint erythema; 2, definite erythema; 3, erythema and edema; and 4, erythema, edema, and vesicles).

RESOLUTION OF ABNORMAL PHOTOSENSITIVITY

The probability of resolution of abnormal photosensitivity at varying follow-up duration from diagnosis is shown in Figure 1 and Table 2. Visual inspection of survival curves and log-rank test comparing the probability of resolution of abnor-
Some patients had their patch testing conducted over more than one assessment visit. The lack of suitable skin space (phototesting requiring much of the back), the need to minimize patient discomfort, and the risk of bad back phenomenon precluded completion of patch testing at every patient’s initial assessment. The presence or absence of a positive patch test result (defined as a reaction of grade 2 or higher) was recorded for agents in our European standard, plant (Compositae plants, tars, and balsams), medicament, sunscreen, and corticosteroid series when each of these series was first applied.

Patients attending for follow-up were invited to undergo repeated patch testing for previously identified contact allergens. An extra visit was required for delayed patch test readings. “Lost” patch test reactions (defined below) were documented.

DEFINITIONS

Chronic Actinic Dermatitis

The following diagnostic criteria were used: Dermatitis and/or pseudolymphomatous eruption (confirmed in cases of clinical doubt and all with a reticuloid presentation by histopathological findings) affecting photoexposed sites and monochromator phototesting demonstration of abnormal delayed erythematous responses to UV-B or UV-A; UV-B and UV-A; or UV-B, UV-A, and visible wavelengths with an MED for at least 1 of the wavelengths involved of less than 50% of the lowest normal population value in the absence of photoactive medication. All of our patients showed UV-B photosensitivity, although for consistency with previous definitions, we did not insist on it as a diagnostic criterion.

Degree of Improvement in Abnormal Photosensitivity

Resolved indicates that the patient was, at the last assessment, no longer subjectively aware of abnormal photosensitivity and the results of monochromator phototesting were within normal population limits at all wavelengths tested (305±5, 335±30, 365±30, 400±30, and 430±30 nm and, if appropriate, longer wavelengths).

Much improved (marked improvement) indicates that the condition was not “resolved” but that the patient was no longer subjectively aware of abnormal photosensitivity, and that, at each and every wavelength tested (305±5, 335±30, 365±30, and 400±30 nm), the MED was either above the lowest normal population value or at least double the patient’s previous lowest value and greater than or equal to 60% of the lowest normal population value.

Clinically improved indicates that the patient’s condition was significantly improved on clinical assessment but without objective evidence of a reduction in the severity of abnormal photosensitivity.

Lost Patch Test Reaction

A lost patch test reaction was recorded if, on repeated patch testing for the purposes of follow-up, a patient no longer produced an allergic reaction to a substance to which he or she previously had a reaction of grade 2 or higher.

STATISTICAL ANALYSIS

Data analysis was performed with Stata for Windows (Intercooled Stata for Windows, release 3; Stata Corp, College Station, Tex). Simple descriptive statistics were used to summarize basic demographic data and the proportions with identified contact allergens. The χ² test was used when comparing proportions. Kaplan-Meier survival analysis was used to describe the probability of resolution of abnormal photosensitivity, marked improvement in abnormal photosensitivity, and clinical improvement (as defined) at varying years of follow-up. “Survival time” was censored when the patient died or was otherwise lost to follow-up. We decided to determine the probability of resolution of photosensitivity after 5, 10, and 15 years.

An assumption inherent in Kaplan-Meier survival analysis is that the probability of reaching the end point of interest (eg, resolution of photosensitivity) is the same for those still being followed up and those lost to follow-up. Our suspicion was that this assumption would be closer to the truth for the Tayside patients (who might be more likely to reattend even if no longer affected) than for those patients traveling from further afield. We therefore compared survival curves for Tayside and non-Tayside patients using the log-rank test.

The log-rank test was also used in exploratory analysis to compare the probability of resolution of abnormal photosensitivity according to other variables, including the severity of UV-B photosensitivity at diagnosis, number of different allergens, sex, and age. It was also used to compare the probability of resolution of abnormal photosensitivity in those who had “lost” contact allergens and the rest of the subgroup of patients in whom follow-up patch testing was performed.
ditions in adequate numbers of patients. However, subgroup analysis of the following variables was possible.

Severities of Abnormal Photosensitivity at Diagnosis

Those with severe UV-B photosensitivity (MED at 305±5 nm, ≤5.6 mJ·cm−2) showed a worse prognosis than those with a higher but still abnormally low (≤27 mJ·cm−2) UV-B MED (P=.01) (Figure 2). Neither the presence nor absence of visible wavelength photosensitivity nor the severity of UV-A photosensitivity was a prognostic factor for complete resolution.

Having identified the severity of UV-B photosensitivity at diagnosis as an important prognostic factor, we looked back at the records of the 107 patients (38% of potential subjects) who did not attend follow-up visits. At diagnosis, 59% of those followed up, compared with 51% of those not followed up, had severe UV-B photosensitivity (P=.19).

Number of Patch Test Reactions

The identification of contact allergens in 2 or more patch test batteries (European standard series, plants, steroids, medicaments, and sunscreens) was associated with a worse prognosis than absent allergens or allergens in only 1 of these patch test series (P=.005) (Figure 3).

Sex

Although none of the 22 women followed up showed resolution of their abnormal photosensitivity, the number of women evaluated was small. Nevertheless, the probability of resolution of abnormal photosensitivity for women was significantly worse than for men (P=.046). However, this difference may reflect referral bias. A significant difference was no longer detectable when this analysis was repeated with stratification by severity of UV-B photosensitivity (P=.09).

Age at Diagnosis

Only 11 of the study patients were younger than 40 years old at diagnosis, and the follow-up duration range for this

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### Table 1. Distinct Contact Allergens in 178 Patients Who Underwent Multiple Patch Test Series

<table>
<thead>
<tr>
<th>No. of Allergen Series</th>
<th>No. (%) of Patients Reacting</th>
<th>European Standard Series</th>
<th>Plants</th>
<th>Sunscreens</th>
<th>Medicaments</th>
<th>Steroids</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>31 (17)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>1</td>
<td>61 (34)</td>
<td>34</td>
<td>18</td>
<td>8</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>55 (31)</td>
<td>50</td>
<td>43</td>
<td>14</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>23 (13)</td>
<td>23</td>
<td>21</td>
<td>17</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>7 (4)</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>1 (1)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

*Ellipses indicate no allergies were tested for this group.

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### Table 2. Probabilities of Resolution, Marked Improvement, and Clinical Improvement Only of Abnormal Photosensitivity 5, 10, and 15 Years After Diagnosis

<table>
<thead>
<tr>
<th>Time After Diagnosis, y</th>
<th>Probability (95% CI)</th>
<th>Probability (95% CI)</th>
<th>Probability (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Resolution</td>
<td>Marked Improvement</td>
<td>Clinical Improvement</td>
</tr>
<tr>
<td>5</td>
<td>0.07 (0.04-0.12)</td>
<td>0.13 (0.08-0.20)</td>
<td>0.37 (0.30-0.46)</td>
</tr>
<tr>
<td>10</td>
<td>0.22 (0.14-0.35)</td>
<td>0.24 (0.15-0.35)</td>
<td>0.64 (0.54-0.73)</td>
</tr>
<tr>
<td>15</td>
<td>0.45 (0.27-0.67)</td>
<td>0.30 (0.20-0.44)</td>
<td>0.79 (0.68-0.89)</td>
</tr>
</tbody>
</table>

*CI indicates confidence interval.

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Figure 1. The probability of varying degrees of improvement (defined in the “Patients and Methods” section) of abnormal photosensitivity and time from diagnosis.

Figure 2. The severity of abnormal photosensitivity to UV-B (305±5 nm) wavelength at diagnosis affects the prognosis for resolution of abnormal photosensitivity. MED indicates minimal erythema dose.

Figure 3. The probability of resolution of abnormal photosensitivity to UV-B (305±5 nm) wavelength at diagnosis affects the prognosis for resolution of abnormal photosensitivity. MED indicates minimal erythema dose.
group was 2 to 17 years. With such small numbers, a conclusive prognostication was not possible. Abnormal photosensitivity resolved in 1 case (16 years after diagnosis) and in another 2 was shown to be much improved at the last assessment.

Analysis of follow-up experience of patients stratified into age groups (<40 years [n=11], 40-59 years [n=76], and ≥60 years [n=91]) at diagnosis (Figure 4) showed no significant differences in probability of spontaneous resolution (P=.06).

FOLLOW-UP PATCH TESTING

A subgroup of 55 patients with previously identified contact allergen reactions of grade 2 or higher agreed to undergo patch testing again. Only 1 patient no longer had any demonstrable contact allergens. He was unusual in that all 3 previously identified contact allergens were sunscreen constituents. Nine (16%) of these 55 patients showed complete resolution of their abnormal photosensitivity; 2 lost at least 1 contact allergen. There was no detectable difference in the probability of resolution of abnormal photosensitivity for the 4 patients who had and the 51 who had not lost at least 1 contact allergen (P=.81).

COMMENT

The abnormal photosensitivity component of the CAD syndrome spontaneously resolves in a significant proportion of patients. Clinical improvement not accompanied by objective evidence of a loss of abnormal photosensitivity has been documented before, but this is the first objective report.

The allergic contact dermatitis component of the syndrome persists. Among those patients who agreed to undergo repeated patch testing, there was no difference in prognosis for resolution of abnormal photosensitivity among those who had and those who had not “lost” previously identified contact allergens. We cannot be sure how representative these patients (31% of the cohort) were, selected as those able and willing to attend for the extra visit required. However, our findings are consistent with a previous study that showed that resolution of allergic contact dermatitis in CAD is exceptional.

When interpreting our findings, we need to consider factors that could make the prognosis in our follow-up cohort different from that of other newly diagnosed CAD patients. First, we must assess the possible effects of referral bias. We followed up only those patients whose condition had been recognized as requiring investigation at a tertiary referral center. It is likely that this group of patients included a disproportionate number with severe UV-B photosensitivity, which we found to be a poor prognostic factor for resolution. Also, in a condition often thought of as an “old man’s disease,” referral bias would be expected to lead to our group of patients including particularly severely affected women and young patients. We determined from this information that we may have underestimated the probability of spontaneous resolution in these groups.

Second, selection bias because of loss to follow-up may have led to an apparently worse prognosis than what actually existed. Loss to follow-up because of death or change of address is unlikely to have systematically altered our results. However, we suspect that those we attempted to contact, but who either did not reply or declined our invitation to re-attend for phototesting, included a disproportionate number of patients who were no-longer photosensitive. This selection bias probably has less effect for local (Tayside) patients than for those required to travel further for reassessment. It is reassuring that there was no detectable difference in prognosis for Tayside patients compared with non-Tayside patients. Nor was there a statistically significant greater proportion of patients with severe UV-B photosensitivity in our follow-up cohort compared with those lost to follow-up.

The effect of the above factors raises the possibility that our findings are, if anything, pessimistic regarding the probability of complete resolution of abnormal photosensitivity. Our figures for the proportions of patients expected to achieve photosensitivity resolution should be regarded as minimum estimates.

Chronic actinic dermatitis has been described in European, American, and Asian populations. The absence of diagnostic phototesting facilities in some
regions may lead to CAD not being recognized, with, for example, only the allergic contact dermatitis component being diagnosed. Nevertheless, CAD probably occurs worldwide. Can our findings be used when discussing prognosis with patients in other parts of the world? In the absence of similar studies from other populations and different environments, some caution is called for, but there is no reason to believe that our findings are only relevant to European patients.

What should we now tell newly diagnosed CAD patients about their prognosis? The majority of patients do improve. This may be because of treatment (the avoidance of UV/visible causative wavelengths and contact allergens), but we can give new patients further hope by adding that there is a possibility of complete resolution of abnormal photosensitivity. The "typical" newly diagnosed patient has an almost 1 in 10 chance of resolution of photosensitivity in 5 years, rising to a 1 in 5 chance by 10 years and nearly a 1 in 2 chance after 15 years. Exceptionally severe UV-B photosensitivity or multiple unrelated contact allergens demand a more cautious prognosis. Women and young (\leq 40 years) patients may fare worse but, in view of the relatively small numbers followed up and the possibility of referral bias in our cohort, it is reasonable to give such patients the same prognosis information as the "typical" patient.

Patients who ask, "Will I lose my contact allergies?" must be told that it is highly unlikely, regardless of whether or not the photosensitivity resolves. This is an interesting observation, for if we regard CAD as a state of general heightened activity of the skin's immune system delayed-type hypersensitivity response, we might expect both major components of the syndrome to resolve together.

In summary, the abnormal photosensitivity (but not the allergic contact dermatitis) of CAD completely resolved in a significant proportion of our study patients.

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