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ORIGINAL PAPER

# Guidelines and care pathways for genetic diseases: the Scottish collaborative project on tuberous sclerosis

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**In Scotland a national audit project has been undertaken to devise evidence-based guidelines for the clinical management of patients with tuberous sclerosis (TS), a dominantly inherited multisystem disorder. In order to facilitate the audit and use of these guidelines a 'Care Pathway' was devised to form the patient records. We describe the process of guideline development for TS and our TS Care Pathway.**

**Keywords: guidelines; care pathway; audit; tuberous sclerosis**

## Introduction

Clinical genetics services in Scotland are available from four supra-regional centres based in, Aberdeen, Dundee, Edinburgh and Glasgow. Many genetic patients require multidisciplinary care and the precise nature and level of current clinical genetic involvement varies across the centres, often resulting in differing care for individuals, possibly even within a family. Use of accepted multidisciplinary guidelines common to each centre would reduce unnecessary variations in clinical practice and improve communication between professionals involved in patient care.

There is a growing call for audit to be carried out in the field of clinical genetics to ensure a continuing high standard of service. It is important that in such an expanding area of service practical and effective processes are set in place to facilitate the development of audit. One barrier to the introduction of audit in clinical genetic service is the variable quality of patient data held in clinical records. Experience in other areas of hospital practice has shown that 'Integrated Care Pathways' provide a mechanism for the efficient capture of key data for audit purposes and for promoting the use of clinical guidelines in current practice.

In July 1996 a three-year nationwide project was initiated in Scotland. This project aims to establish evidence-based national clinical guidelines and Integrated Care Pathways for five genetic conditions – tuberous sclerosis (TS), myotonic dystrophy (DM), marfan syndrome, Huntington disease (HD) and neurofibromatosis type 1 (NF 1). Together these five conditions account for 20–25% of new referrals, not including cancer, to the Scottish genetics services.

In this article we will briefly describe the experience of the Scottish Clinical Genetics Guidelines Working Group in establishing clinical guidelines and Integrated Care Pathways for the management of five genetic conditions and give details of the guidelines developed for tuberous sclerosis.

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## Development of clinical guidelines in Scotland

The use of guidelines improves the service delivered to the patient and communication between professionals involved in it.[1–3] Professional enquiries and searches of literature revealed there were no evidence-based guidelines published for management of any hereditary conditions. The management of patients in Scotland by the Clinical Genetics Service was known to vary throughout the country and a variety of professionals were involved in patient care. Guidelines were needed to ensure a national level of service based on current levels of evidence.

A three-year grant for the development of guidelines and care pathways was provided from the Clinical Resource and Audit Group (CRAG) of the Scottish Office. As successful completion of the project is dependent on good communication between each of the genetics centres in Scotland, a research assistant, based in Edinburgh, was employed to ensure smooth running and co-ordinate work. Each centre took responsibility for one of the five conditions, Edinburgh for two, and consensus conferences were held every six months to discuss the progress of the project.

In order to develop valid national guidelines for Scotland it is recommended that a certain process of guideline development is adhered to. We applied criteria published by the Scottish Intercollegiate Guidelines Network (SIGN) for the development and appraisal of national guidelines.[4] This method requires a systematic process of identifying and synthesising the evidence, involvement of a multidisciplinary group, including representatives from all key disciplines, and explicit links to be made between the level of evidence and recommendation. (Table 1 and Table 2)

Our experience in Scotland has revealed that for the management of the five selected genetic conditions, limited evidence has come from randomised control trials and thus most recommendations are 'Grade C'. We ensured input from acknowledged experts from allied disciplines in the preparation of draft guidelines. These were then discussed at consensus conferences attended by the guideline developers and representatives from all the Scottish Clinical Genetics Centres (Appendix) before being adapted and agreed as national guidelines. Similar methods of guideline development have also been used by other guideline development groups.[5–6]

**Table 1** Stages in guideline development in Scotland

| |
|---|
| 1 Formation of multidisciplinary team |
| 2 Systematic review of the literature |
| 3 Expert opinions |
| 4 Consensus conference |
| 5 Grading of recommendations |
| 6 Established Scottish guidelines |

## Establishment of Integrated Care Pathways

Integrated Care Pathways (ICPs) are structured multidisciplinary records of care which detail essential steps in the care of patients. Ideally these are devised from guidelines to facilitate their use and improve ease of audit.[7] It has been shown that the use of evidence-based clinical guidelines[1] and of Integrated Care Pathways[8–9] can improve patient care and reduce unnecessary variations in clinical practice across different centres.

Care pathways take the form of simply structured records of care that document each step and type of intervention during a care episode. Any variations from the care pathway are recorded for further analysis. This will provide information on the cause and frequency of variations in patient care that can then be used for audit purposes.

It is important to determine the cause of any variation from the care pathway. Variations that are potentially avoidable can be identified and appropriate measures taken to remedy the situation. If it is found that unavoidable variations occur frequently, there may be underlying problems which also need to be addressed. As care pathways should reflect best current practice it is likely that changes will be made representing improvements in clinical care. These may be identified through the analysis of variations or by medical advances.

**Table 2** Grading of recommendations

| *Grade* | *Recommendation* |
|---|---|
| A | Requires at least one random controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation |
| B | Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation |
| C | Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality |

In order to allow patients more involvement and control over their care and treatment, a summary sheet detailing steps in their anticipated pathway of care is made available to patients. Patients are encouraged to take an active interest in their future care.

We carried out a note review at the four regional clinical genetics centres in Scotland. This found a lack of detail on key clinical data in the clinical records and highlighted important variations in practice between centres. (Figure 1) By studying formats of care pathways already in use and applying these to the agreed Scottish Guidelines for Tuberous Sclerosis we constructed our TS Care Pathway.

Selected pages from the TS Care Pathway are shown. (Figure 2) The care path takes the form of a coloured booklet with a structure consisting of tick boxes and spaces to be filled in. The Scottish Guidelines for TS are printed on facing pages and a variation sheet at the back of the booklet gives space for recording any variations from the path and the reasons for these variations. A page is included for clinical notes. The care path should be signed and dated by the clinician and the patients name and date of consultation should be at the top of each page.

We propose to implement care pathways throughout Scotland for each of the five conditions. These pathways will augment current clinical records and provide a basis for audit of actual practice against the agreed guidelines for best practice. An initial audit will be conducted on the first year of use of each care pathway in each of the four clinical genetics centre in Scotland.

## Audit in Clinical Genetics

Clinical genetics is a relatively new and fast growing area of health care. Advances in this area are of great interest to members of the general public and the media. It is necessary to ensure that audit procedures are implemented now which will assure the public and the health authorities of the high quality of services available.

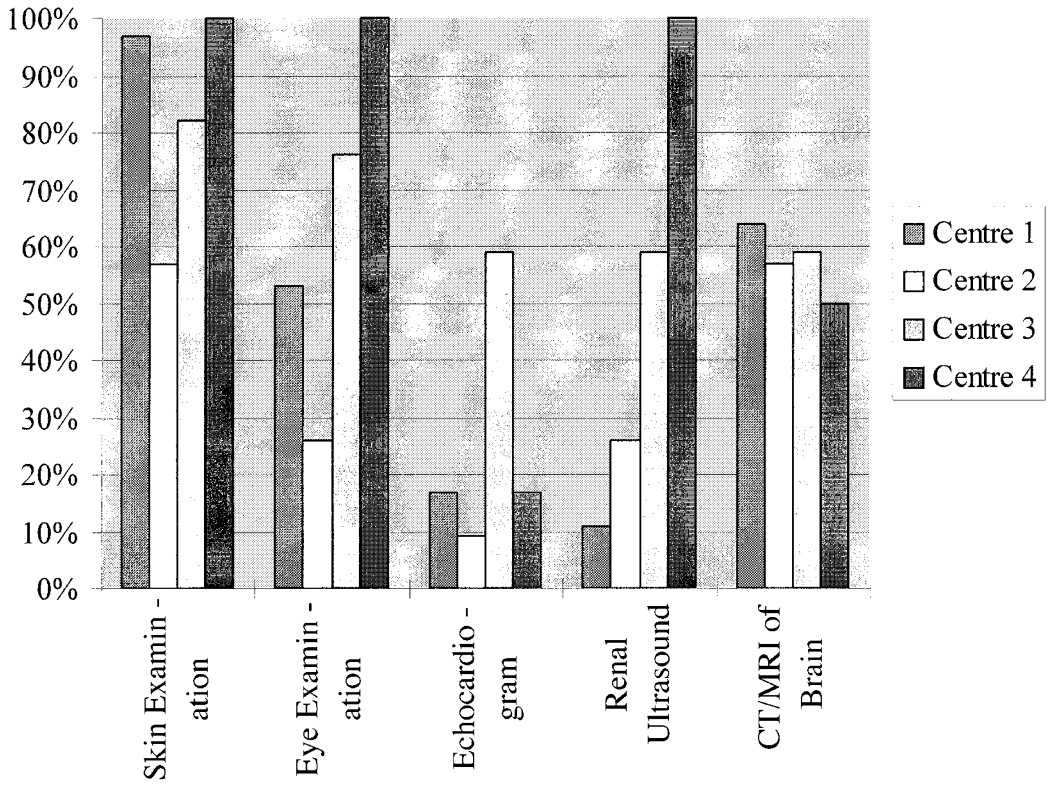


**Figure 1** *Investigations conducted on affected individuals (1971–1996)* (CT = computed tomography; MRI = magnetic resonance imaging.)

**Date** _____

**Name** _____
**Date of Birth** _____
**Pedigree No** _____

## TUBEROUS SCLEROSIS : CARE PATHWAY

| | YES | NO | COMMENTS |
|---|---|---|---|
| Pedigree drawn/confirmed | ☐ | ☐ | _____ |

Reason for referral/Questions _____

_____

_____

| **Seizures** | YES | NO | DON'T KNOW | | |
|---|---|---|---|---|---|
| | ☐ | ☐ | ☐ | | |
| If yes :- | | | | Frequency | Age of Onset |
| Tonic/Clonic | ☐ | ☐ | ☐ | _____ | _____ |
| Partial | ☐ | ☐ | ☐ | _____ | _____ |
| Myoclonic | ☐ | ☐ | ☐ | _____ | _____ |
| Infantile Spasms | ☐ | ☐ | ☐ | _____ | _____ |
| Absence | ☐ | ☐ | ☐ | _____ | _____ |
| Other | _____ | | | _____ | _____ |
| Abnormal EEG | ☐ | ☐ | ☐ | | |
| Medication | ☐ | ☐ | ☐ | Type/Details _____ | |

_____

_____

_____

Prescribed by _____

Needs Further Control ☐ ☐ If yes, referred to _____

Other CNS symptoms ☐ ☐ Details _____

_____

Changes in CNS Symptoms ☐ ☐ Details _____

_____

If yes refer for scan ☐CT ☐MRI Refer to _____

COMMENTS _____

_____

_____

**Figure 2** *Tuberous Sclerosis Care Path form.*

**Date** _____

**Name** _____

**Date of Birth** _____
**Pedigree No** _____

| **Learning Disability** | YES | NO |
|---|---|---|
| | ☐ | ☐ |

If yes- Mild/Moderate/Severe

| **Autism** | YES | NO | COMMENTS |
|---|---|---|---|
| (i) communication difficulties | ☐ | ☐ | _____ |
| (ii) socialisation difficulties | ☐ | ☐ | _____ |
| (iii) obsessive/ritualistic/stereotyped behaviours | ☐ | ☐ | _____ |

COMMENTS _____

_____

_____

**Attention Deficit Hyperactivity Disorder**

| | | | |
|---|---|---|---|
| (i) attention/concentration difficulties | ☐ | ☐ | _____ |
| (ii) hyperactivity | ☐ | ☐ | _____ |
| (iii) impulsivity | ☐ | ☐ | _____ |

COMMENTS _____

_____

_____

**Sleep disturbance**

| | | | |
|---|---|---|---|
| (i) settling at night | ☐ | ☐ | _____ |
| (ii) early waking | ☐ | ☐ | _____ |
| (iii) disturbance during night | ☐ | ☐ | _____ |
| (iv) no of hours of sleep | ☐ | | _____ |

COMMENTS _____

_____

_____

**Other behaviour difficulties**

| | | | |
|---|---|---|---|
| (i) aggressive behaviour | ☐ | ☐ | _____ |
| (ii) violent/destructive behaviour | ☐ | ☐ | _____ |
| (iii) self-injurious behaviour | ☐ | ☐ | _____ |
| (iv) inappropriate sexual behaviour | ☐ | ☐ | _____ |
| (v) withdrawn/overly passive behaviour | ☐ | ☐ | _____ |

(vi) other _____

_____

**Figure 2** *Continued.*

**Date** _____

**Name** _____
**Date of Birth** _____
**Pedigree No** _____

**Renal**

Date of Renal Ultrasound _____
Ultrasound Results

| | YES | NO | |
|---|---|---|---|
| Abnormalities detected | ☐ | ☐ | |
| Presence of warning signs (eg haematuria, flank pain, unexplained fevers or UTI's or anaemia) | ☐ | ☐ | Details _____ |
| If abnormalities detected- | | | |
| Angiomyolipoma <4cm | ☐ | ☐ | Details _____ |
| Angiomyolipoma >4cm | ☐ | ☐ | Details _____ |
| Renal Cysts | ☐ | ☐ | Details _____ |
| Renal Cell Carcinoma | ☐ | ☐ | Details _____ |
| Other | | | _____ |

BP ☐ Comments _____

Creatinine YES ☐ NO ☐ ☐ Comments _____

Refer to a Renal Physician ☐ ☐ Details _____

**Next ultrasound due** (date)

**Intracranial**

| | | YES | NO | |
|---|---|---|---|---|
| Baseline previous | CT | ☐ | ☐ | Date _____ |
| | MRI | ☐ | ☐ | Date _____ |
| If neither refer for scan | ☐ CT | | ☐ MRI | To _____ |

Reason for choice if CT conducted/ referred for?

_____

_____

Findings

| | YES | NO | COMMENTS |
|---|---|---|---|
| Cortical Tubers | ☐ | ☐ | _____ |
| Subependymal Nodules | ☐ | ☐ | _____ |
| Giant Cell Astrocytoma | ☐ | ☐ | _____ |
| Other _____ | | | |

_____

**Figure 2** *Continued.*

**Date** _____

**Name** _____
**Date of Birth** _____
**Pedigree No** _____

**Clinical Examination**

Dermatological Features

| | YES | NO | NOT EVALUATED | COMMENTS |
|---|---|---|---|---|
| Shagreen Patch | ☐ | ☐ | ☐ | _____ |
| Hypomelanic Macules | ☐ | ☐ | ☐ | Typical No _____ Size _____ |
| | | | | Atypical No _____ Size _____ |
| Ungual/Subungual Fibroma | ☐ | ☐ | ☐ | No _____ Site(s) _____ |
| Angiofibroma | ☐ | ☐ | If yes, Bleeding/Disfiguring/Multiple ↓ | |
| Forehead/Scalp Plaque | ☐ | ☐ | If yes, is it enlarging → ☐ referral to dermatologist _____ (date) details _____ | |

COMMENTS _____

**Cardiology**

| | YES | NO | NOT EVALUATED | COMMENTS |
|---|---|---|---|---|
| Cardiac Rhabdomyoma | ☐ | ☐ | ☐ | _____ |

| | YES OK | YES - ABNORMAL | REQUESTED |
|---|---|---|---|
| Baseline ECG | ☐ | ☐ ↓ refer to cardiology | ☐ |

| | NO PROBLEMS | PROBLEMS | COMMENTS |
|---|---|---|---|
| Clinical Exam | ☐ | ☐ ↓ refer to cardiology | _____ _____ |

| | YES | NO |
|---|---|---|
| Refer to Cardiology | ☐ ↓ To _____ | ☐ |

**Figure 2** *Continued.*

**Date** _____

**Name** _____
**Date of Birth** _____
**Pedigree No** _____

| **Other features** | NOT EVALUATED | FOUND BY OTHER SPECIALIST | COMMENTS |
|---|---|---|---|
| Retinal Phakoma | ☐ | ☐ | _____ |
| Lung Cysts | ☐ | ☐ | _____ |

**Clinical investigation of family members**

| | CT/MRI | | Renal | | Clinical | | CONCLUSION |
|---|---|---|---|---|---|---|---|
| Relative- | Yes | No | Yes | No | Yes | No | |
| _____ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | _____ |
| _____ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | _____ |
| _____ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | _____ |

COMMENTS _____

_____

_____

_____

**OUTCOME** UNAFFECTED/AFFECTED/NOT KNOWN

| | YES | NO | DETAILS |
|---|---|---|---|
| Recurrence Risk Given | ☐ | ☐ | _____ |

_____

Follow Up Arrangement _____

_____

_____

Recall date _____

Signed _____
Name Printed _____
Designation _____
Date _____

Please note that the Care Pathway encompasses recommended guidelines and does not remove the value of the clinicians judgement. However it is important that any variations from the pathway are recorded on the form on the additional variation sheet.

**Figure 2** *Continued.*

Current audit procedures involve extra tasks and work from the clinical genetics team. This can be very frustrating and time consuming. The development of guidelines and care pathways provides a method by which audit can be readily and quickly achieved. Using the care pathway to record clinical consultations facilities transfer of information into audit reports. Analysis of variation allows areas for improvement to be readily identified and acted upon.

## Tuberous Sclerosis Guidelines

A search conducted on Medline identified 849 references on TS from the year 1980 onwards. Reducing the limits on a search may have resulted in missing relevant information or recommendations contained within papers, therefore a manual search was conducted by a clinical geneticist (MP) to identify literature for review; 267 relevant papers were identified and obtained for this purpose. Six additional papers were identified during review.

The literature was split into subtopics such as intracranial scanning, nephrology, cardiology, dermatology, behaviour, epilepsy, the gastrointestinal tract, eyes, teeth, lung involvement, plus any other publications. A team from the Clinical Genetics Department in Edinburgh (MP, DF, CB, NB) with the help of a psychiatrist (FR) and clinical psychologist (GM) reviewed this literature and determined recommendations for guidelines from available evidence.

The results of this literature review indicated that there was no evidence available from randomised control trials; therefore there are no 'Grade A' recommendations for the care of individuals affected with TS. Recommendations for guidelines are therefore based on well conducted published clinical studies and expert opinion from both the literature and the experts in the UK. For this purpose the reviewers met a consultant renal physician (MW), a consultant paediatric neurologist (JS), TS nurses (CF and DS), a mental health nurse (PB) and written comments were obtained from a general practitioner (WT), neurologists (KB and MO'R), a consultant dermatologist (RM) and paediatricians, psychiatrists and clinical geneticists involved with TS clinics. (JO, RM and PB). Contact was maintained throughout this process with the Tuberous Sclerosis Association, and their Scottish organiser (NG) was involved at each stage.

Draft guidelines based on the evidence obtained were compiled by the reviewing team and discussed at a National Consensus Conference in Scotland. Staff from each of the four clinical genetics centres attended this meeting and the arising discussion led to the following agreed national guidelines.

Guidelines are shown in bold print and the letter in brackets refers to the grade of recommendation according to the level of evidence available (Table 2).

## Tuberous Sclerosis

### *How to Investigate Symptomatic Patients to Establish the Diagnosis*

Evidence in the literature recommends that investigations should be offered to parents of affected individuals for genetic counselling purposes. These well conducted studies estimate that 56–69% of cases are sporadic and the remaining cases are familial[10–14] inherited in an autosomal dominant pattern. Criteria to determine diagnosis have been published.[15–16]

*Dermatology* The majority (>87%) of affected individuals have depigmented maculae visible on examination of the skin by Woods Light.[11–13] Ungual fibroma can occur in 3–19% of cases[11,14,17–18] and can be the only presenting sign.[19]

**Conduct a thorough clinical examination of the skin and nails including a Woods Light examination. (B)**

*Intracranial* Evidence suggests a CT or MRI scan of the brain should be offered as an investigation.[12,17–26] Neurological involvement is found in the majority (>67%) of cases of TS.[12,14,18,27–29]

**Perform a CT or MRI scan of the brain. (B)**

*Renal* Recent studies of large groups of individuals with TS indicates that renal involvement can occur in approximately 60% of cases.[30–32] Expert recommendations also support investigation of the kidneys by ultrasound.[12–13,22,25–26]

Asymptomatic hepatic hamartomas were found in 23.5% of children with TS.[33] Case reports[34–35] document their presence in other individuals; although not clinically significant, they may help diagnose asymptomatic individuals.

**Perform a renal and liver ultrasound. (B)**

*Genetic Testing* At the present time genetic testing for diagnosis of TS is not being carried out. When this is possible it will be included as a guideline and in the care pathway which can be easily changed to allow for new developments.

## How to Organise the Follow-up

For the investigation of individuals who have been diagnosed with TS the following are recommendations for the clinical geneticist.

*Behaviour* It has been shown that behaviour and sleep problems can occur in individuals with TS[36–46] and this behaviour can severely disrupt the family.[45] These problems and changes in behaviour may indicate an underlying physical problem.[37–38,47] A behaviour checklist for the purpose of identifying and monitoring behaviour problems was designed by a clinical psychologist (GM) and psychiatrist (FR) and incorporated in the TS pathway.

**(a) Conduct a baseline assessment of an individual's behaviour using the behaviour checklist at an initial consultation. In cases where an individual attends a further session at a genetics clinic the checklist could be completed for comparison purposes. (C)**

**(b) The clinical geneticist should maintain contact with a multidisciplinary team specialising in behavioural management, eg including a psychiatrist and psychologist. (C)**

**(c) Offer patient a referral to the relevant multidisciplinary team or neurologist if any problems exist which require further assessment or management. (C)**

*Epilepsy* The majority (62–97%) of individuals with TS suffer from epilepsy at some point in their lives.[11–12,14,17,18,28,40,48–51] The management of epilepsy is similar to that of individuals without TS but a gap in care was identified during the transition from paediatric to adult care.

**(a) Record the type of medication the patient receives, adequacy of control and the key doctor involved in the control of epilepsy. (C)**

**(b) Refer individuals with epilepsy but no learning difficulty to neurologists for treatment in cases where epilepsy is not adequately controlled. If learning difficulty presents, refer to specialist epilepsy clinic. (C)**

*Renal* Renal involvement occurs in approximately 60% of patients with TS.[30–32] Angiomyolipomas (AMLs) are the commonest lesions occurring in approximately 50% of individuals with TS,[30] followed by renal cysts found in approximately 15–18%.[30,52] There may also be a risk of renal cell carcinoma (RCC).[18]

Regular monitoring of the kidneys is indicated[18,20,52–62] and ultrasound scanning seems to be the most appropriate modality in most cases. CT or MR scans are advocated by some authors either regularly or as baseline investigation. There is no good evidence to support such imaging on a routine basis and therefore it should only be considered if the ultrasound gives cause for concern or is unclear. The value of ultrasounds may be maximised by using the same operator who is familiar with the type of involvement seen in kidneys of persons with TS. Treatment of large, symptomatic tumours should be conservative, eg arterial embolisation.

**(a) A renal ultrasound should be carried out when the patient is 5 years old. Enquire about any warning signs – flank pain, unexpected fevers, unexplained urinary tract infections, and anaemia. (B)**

**(b) Ensure the ultrasound scan is repeated every 5 years. (B)**

**(c) If at any stage results are positive, monitor growth every 2–3 years, ultrasounds, measure blood pressure and creatinine levels. (B)**

**(d) If an angiomyolipoma is over 4 cm, or fast growing, arrange yearly ultrasounds. (C)**

**(e) Ensure that carers are aware of warning signs – flank pain, unexpected fevers, unexplained urinary tract infections, and anaemia. Carers should seek urgent medical attention if haematuria occurs. (C)**

**(f) Refer to a renal physician when renal pathology is found *and* raised blood pressure, creatinine, or any of the warning signs are present. (C)**

*Cardiology* Cardiac rhabdomyoma have been shown to occur in approximately 43–66% of children with TS, but have been shown to regress and are less common in adults.[18,62–66] Symptomatic individuals can present with heart failure/arrhythmia in the neonatal period. When this occurs the child receives appropriate care from a paediatrician and therefore the clinical geneticist is unlikely to have a role.

There is a possibility that individuals with TS may have a higher than population incidence of cardiac conduction pre-excitation (Wolff-Parkinson-White syndrome (WPW)). This can be associated with cardiac

rhabdomyoma's and may have a role in sudden unexplained deaths in TS.[65]

**(a) Offer individuals affected with tuberous sclerosis an ECG at the initial consultation. (C)**

**(b) Perform a clinical examination of the heart on all affected individuals and enquire about cardiac symptoms. (C)**

**(c) Refer to a cardiologist if any positive results are found (ie if ECG, clinical examination or symptom enquiry is positive). (C)**

*Dematological Aspects* The majority of individuals have dermatological involvement. Studies indicate that 3–19% of affected individuals have ungual fibromas,[11,14,17,27] 42–87% have angiofibromas[11,14,17,18,27,28,48–49] and more than 64% have depigmented maculae.[11,14,17,18,27,28,48] Reports of individuals having shagreen patches vary from 18–75%.[11,14,17,18,26] The incidence of forehead plaques has been reported as 25%.[23] Expert opinion indicated that similar scalp plaques also occur and have a tendency to grow in late adolescence.

**The clinical geneticist should refer an individual to a dermatologist if**

**(a) there are significant numbers of periungal fibromas**

**(b) there are multiple angiofibroma lesions, disfiguring angiofibroma or bleeding lesions,**

**(c) there are enlarging scalp plaques (C).**

*Pulmonary Aspects* Lung involvement in the form of lymphangiolyomeiomatosis is rare, less than 1%, in TS.[67–68] Published case reports indicate females are more likely to be affected.[67–73] Lymphangiolyomeiomatosis is generally fatal and there is no good evidence for successful therapy.[71–72] Therefore screening is not justified.

**Patients with TS and dyspnoea or pneumothoraces should be referred to a respiratory specialist for further investigations. (C)**

*Intracranial Involvement* As previously indicated the majority of TS cases can have neurological involvement and there is a risk of developing a giant cell astrocytoma.[21,74–76]

Multidisciplinary discussion agreed that neither CT nor MRI are ideal for patients with TS and, as long as behaviour and fits are monitored for changes which would then lead to further investigation, no regular neuro-radiological follow up is necessary.[74,77] However, each patient should have a CT/MRI carried out for baseline reference.[21] Carers should be made aware of warning signs, eg worsening fits, increased headaches, changes in behaviour, or nausea. Surgical removal may be indicated if lesion is symptomatic.[76–79]

**(a) Ensure all patients with TS have had a CT or MRI scan. (B)**

**(b) Ensure the carer is aware of warning signs. (C)**

**(c) Perform a follow-up scan if there are changes in a patient's symptoms (C).**

*Additional Investigations* Appropriate investigations and referrals will be undertaken for any problems which arise and for which there are no guidelines, eg concern about vision would justify a referral to a specialist. These can be noted in the variations section of the care pathway.

*Follow-up* In the absence of other symptoms, frequency of follow-up should be decided by the guidelines for renal involvement.

*Recurrence Risks* Families have been described where there have been diagnostic problems. Genetic counselling should take into account the possibilities of reduced penetrance, variability, germline mosaicism and screening anomalies.[19,22,23,25,80–81]

**If there are no diagnostic signs of the condition, parents and family members should be counselled that the recurrence risk is low.**

**Siblings of patients with apparently sporadic occurrences should be offered genetic counselling at the age of 18, with screening as previously detailed, if they have features suggestive of the TS gene, eg unexplained learning difficulties or epilepsy. (C)**

**Children of an affected parent should be offered a skin examination, renal and liver ultrasound and cardiac ultrasound at an initial consultation. (C)**

## Future Developments

In order to audit the management of tuberous sclerosis, Marfan syndrome, myotonic dystrophy, neurofibromatosis 1 and Huntington disease at each of the four centres in Scotland, the use of the first year of 'care paths' will be carefully analysed. This analysis, and constant communication between the departments involved, should also indicate if clinicians are finding the guidelines and pathway feasible tools.

Integrated Care Pathways are not envisaged as static tools; continuous monitoring of recorded variations from the pathway will allow improvements to be made. These will be constantly implemented in practice. Similarly, as advances are made in medical research, the guidelines may change and be updated.

The TS path is the first of the five Integrated Care Pathways to be introduced in Scotland. The advent of the Scottish TS Clinic, which began in January 1997 and is based in Edinburgh, made TS the ideal candidate. This pathway has now been in use since May and has been found to be helpful in covering key clinical data, reminding staff of guidelines and improving clinician–patient communication. These have not been a burden to complete and have provided an accurate and concise record of the consultation. Further details about guidelines and ICPs for the other conditions are available on request.

It is hoped that other Clinical Genetics Departments and groups involved in patient management will adopt these evidence-based guidelines and the Integrated Care Pathway approach. We would like the use of these guidelines to extend to a wider area.

## Acknowledgements

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# Appendix

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