GUIDELINES

Recognising and diagnosing autism in children and young people: summary of NICE guidance

Gillian Baird,1 Hannah Rose Douglas,2 M Stephen Murphy2

Autism affects children, young people, and adults and describes qualitative difference and impairments in reciprocal social interaction and communication behaviours combined with a restricted range of interests and rigid or repetitive behaviours. Autism is diagnosed when features meet the criteria defined in the ICD-10 (international classification of diseases, 10th revision)3 and the DSM-IV-TR (diagnostic and statistical manual of mental disorders, fourth edition, revised)4 for “pervasive developmental disorder” and have a considerable impact on function. Core autism behaviours are typically present in early childhood, but are not always apparent until the circumstances of the child or young person change—for example, when the child goes to nursery or primary school or moves to secondary school. Autism is also associated with several coexisting conditions including neurodevelopmental, medical, and mental health problems. Autism was once thought to be an uncommon developmental disorder, but recent studies have reported increased prevalence and the condition is now thought to occur in at least 1% of children.5,6 This has increased demand for diagnostic services for children and young people of all ages in the health service. This article summarises the most recent recommendations from the National Institute for Health and Clinical Excellence (NICE) on how to recognise and diagnose autism in children and young people up to the age of 19 years.6 This summary focuses on recommendations for the non-specialist on how to recognise the condition and when to refer to a specialist autism team.

Recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Development Group’s experience and opinion of what constitutes good practice. Evidence levels for the recommendations are in the full version of this article on bmj.com.

Recognition of autism

• Whenever concerns are raised by parents or by the child or young person, always take the concerns seriously, even if these are not shared by others.
• Consult the NICE guideline’s tables of signs and symptoms for autism if there are any concerns raised by parents, professionals, or the child or young person. The tables are intended to alert professionals to the possibility of autism in a child or young person about whom concerns have been raised. They are not intended to be used alone, but to help professionals recognise a pattern of impairments in reciprocal social and communication skills, together with unusual restricted and repetitive behaviours. The table relating to preschool children (or equivalent mental age) is included here as box 1, but see the full version of this article on bmj.com for the other two tables (boxes 2 and 3), which relate to older children.
• When considering the possibility of autism, be aware that:
  - Signs and symptoms should be seen in the context of the child’s or young person’s overall development
  - When older children or young people present for the first time with possible autism, signs or symptoms may have previously been masked by the child or young person’s coping mechanisms and/or a supportive environment
  - It is necessary to take account of cultural variation, but do not assume that language delay is accounted for by early hearing difficulties or because English is not the family’s first language; ask about the child or young person’s use and understanding of their first language
  - Autism may be missed in those with an intellectual disability
  - Autism may be missed in those who are verbally able
  - Autism may be underdiagnosed in girls
  - Signs and symptoms may not be accounted for by disruptive home experiences or a parent’s or carer’s mental or physical illness.
• Do not rule out autism because of:
  - Good eye contact, smiling, and showing affection to family members
  - Reported pretend play or normal language milestones
  - Difficulties seeming to resolve after a needs based intervention (such as a supportive structured learning environment)
  - A previous assessment that concluded that there was no autism, if new information becomes available.
Box 1 | Signs and symptoms of possible autism in preschool children (or equivalent mental age)

<table>
<thead>
<tr>
<th>Social interaction and reciprocal communication behaviours</th>
<th>Eye contact, pointing, and other gestures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spoken language</td>
<td>• Reduced or absent use of gestures and facial expressions to communicate (although may place an adult’s hand on objects)</td>
</tr>
<tr>
<td>• Language delay (in babble or words—for example, using fewer than 10 words by the age of 2 years)</td>
<td>• Reduced and poorly integrated gestures, facial expressions, body orientation, eye contact (looking at people’s eyes when speaking), and speech used in social communication</td>
</tr>
<tr>
<td>• Regression in or loss of use of speech</td>
<td>• Reduced or absent social use of eye contact (assuming adequate vision)</td>
</tr>
<tr>
<td>• Spoken language (if present) may include unusual features, such as: vocalisations that are not speech-like; odd or flat intonation; frequent repetition of set words and phrases (echolalia); reference to self by name or “you” or “she” or “he” beyond age 3 years</td>
<td>• Reduced or absent “joint attention” (when one person alerts another to something by means of gazing, finger pointing, or other verbal or non-verbal indication for the purpose of sharing interest). This would be evident in the child from lack of:</td>
</tr>
<tr>
<td>Reduced and/or infrequent use of language for communication—for example, use of single words, although able to speak in sentences</td>
<td>-Gaze switching</td>
</tr>
<tr>
<td>Responding to others</td>
<td>-Following a point (looking where the other person points to)—may look at hand)</td>
</tr>
<tr>
<td>• Absent or delayed response to name being called, despite normal hearing</td>
<td>-Using pointing at or showing objects to share interest</td>
</tr>
<tr>
<td>• Reduced or absent responsive social smiling</td>
<td>Ideas and imagination</td>
</tr>
<tr>
<td>• Reduced or absent responsiveness to other people’s facial expressions or feelings</td>
<td>• Reduced or absent imagination and variety of pretend play</td>
</tr>
<tr>
<td>• Unusually negative response to the requests of others (“demand avoidance” behaviour)</td>
<td>Unusual or restricted interests and/or rigid and repetitive behaviours</td>
</tr>
<tr>
<td>• Rejection of cuddles initiated by parent or carer, although the child himself or herself may initiate cuddles</td>
<td>• Repetitive “stereotypical” movements such as hand flapping; body rocking while standing; spinning; finger flicking</td>
</tr>
<tr>
<td>Interacting with others</td>
<td>• Repetitive or stereotyped play—for example, opening and closing doors</td>
</tr>
<tr>
<td>• Reduced or absent awareness of personal space, or unusually intolerant of people entering their personal space</td>
<td>• Overfocussed or unusual interests</td>
</tr>
<tr>
<td>• Reduced or absent social interest in others, including children of his or her own age—may reject others; if interested in others, he or she may approach others inappropriately, seeming to be aggressive or disruptive</td>
<td>• Excessive insistence on following own agenda</td>
</tr>
<tr>
<td>• Reduced or absent imitation of others’ actions</td>
<td>• Extremes of emotional reactivity to change or new situations; insistence on things being “the same”</td>
</tr>
<tr>
<td>• Reduced or absent initiation of social play with others, plays alone</td>
<td>• Over-reaction or under-reaction to sensory stimuli, such as textures, sounds, smells</td>
</tr>
<tr>
<td>• Reduced or absent enjoyment of situations that most children like—for example, birthday parties</td>
<td>• Excessive reaction to the taste, smell, texture, or appearance of food, or having extreme food fads</td>
</tr>
</tbody>
</table>

-Be aware that tools to identify children and young people with an increased likelihood of autism (secondary screening) may be useful in gathering information about signs and symptoms of autism in a structured way but are not essential and should not be used to make or rule out a diagnosis of autism.

-Be aware that if parents or carers or the child or young person have not suspected a developmental or behavioural condition, raising the possibility may cause distress, and that:
  - It may take time for them to come to terms with the concern
  - They may not share the concern.

Referring children and young people to the autism team

• Consider referral to the autism team if you are concerned about possible autism on the basis of reported or observed signs and/or symptoms. Take account of:
  - The severity and duration of the signs and/or symptoms
  - The extent to which the signs and/or symptoms are present across different settings (for example, home and school)
  - The impact of the signs and/or symptoms on the child or young person and on their family
  - The level of parental or carer’s concern and, if appropriate, the concerns of the child or young person
  - Factors associated with an increased prevalence of autism (box 2)
  - The likelihood of an alternative diagnosis.

• If you have concerns about development or behaviour but are not sure whether the signs and/or symptoms suggest autism, consider consulting a member of the autism team.

• Refer children younger than 3 years to the autism team if there is regression in language or social skills.

• Refer first to a paediatrician or paediatric neurologist (who can refer to the autism team if necessary) children and young people who are:
  - Older than three years with regression in language
  - Of any age with regression in motor skills.

• Discuss referral with the parent carer and where appropriate the child or young person.

• When referring to the autism team, include in the referral letter the following information:
Box 2 | Factors associated with an increased prevalence of autism

- A sibling with autism
- Birth defects associated with central nervous system malformation and/or dysfunction, including cerebral palsy
- Gestational age < 35 weeks
- Parental schizophrenia-like psychosis or affective disorder
- Maternal use of sodium valproate in pregnancy
- Intellectual disability
- Neonatal encephalopathy or epileptic encephalopathy, including infantile spasms
- Chromosomal disorders such as Down’s syndrome
- Genetic disorders such as fragile X
- Muscular dystrophy
- Neurofibromatosis
- Tuberous sclerosis

- Reported information from parents, carers, and professionals about signs and/or symptoms of concern
- Your own observations of the signs and/or symptoms
- Additional information (if you consider it is needed), such as information from school or nursery (gain consent)
- If available, antenatal and perinatal history, developmental milestones, factors associated with an increased prevalence of autism (box 2), relevant medical history and investigations, information from previous assessments.

- If you do not think concerns are sufficient to prompt a referral, consider a period of watchful waiting.
- If a concern about possible autism has been raised but there are no signs, symptoms, or other reasons to suspect autism, use professional judgment to decide what to do next.
- Be self critical about your professional competence and seek advice if in doubt about the next step.

Overcoming barriers

Many pathways for diagnosing autism in children and young people exist but often do not include the whole population up to age 19 years. In particular, there is a lack of services for those children and young people of all ages who have a coexisting intellectual disability. The guideline recommends that in each area a multidisciplinary group (the autism team) should be set up. The team, which should include professionals competent to diagnose autism, should consider the differential diagnosis and either have the skills (or have access to professionals with the skills) needed to carry out a diagnostic assessment for autism in children and young people with special circumstances (including coexisting conditions such as severe visual and hearing impairments; motor disorders including cerebral palsy; severe intellectual disability; complex language disorders; and complex mental health disorders). The diagnostic assessment should enable development of a profile of the child’s or young person’s strengths, skills, impairments and needs that can be used to create a needs based management plan, taking into account family and educational context.

Identifying a group of professionals to join the autism team who are able to assess groups of all ages and intellectual abilities, recognise coexisting physical and mental health conditions, and complete the profile may be challenging for some current services and has training implications. But by working and planning across agencies this should be achievable—for example, by minimising the current repetition of assessments.

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How best to diagnose urinary tract infection in preschool children in primary care?

Alastair D Hay,1 Penny Whiting,2 Christopher C Butler3

Accurate and timely diagnosis of urinary tract infection (UTI) in young children presenting to primary care is important because appropriate treatment may alleviate suffering and help prevent long term sequelae such as renal scarring, poor renal growth, recurrent pyelonephritis, impaired glomerular function, hypertension, end stage renal disease, and pre-eclampsia.1 2 The prevalence of renal scarring in the general population is unknown, but a systematic review of studies, largely conducted in secondary care, showed 15% of children with an initial episode of UTI had evidence of renal scarring on follow-up dimercaptosuccinic acid (DMSA) scanning, and there was an 8% incidence of UTI recurrence per year.3

Among consultations for illness episodes in children aged under 5 years in the UK, approximately 40% comprise infectious diseases and respiratory episodes, while about 10% of presentations comprise non-specific symptoms. Thus identifying which children have a significant UTI (which often also presents with non-specific symptoms) is a key challenge for primary care clinicians.

The diagnosis is further hampered because young children cannot clearly articulate symptoms; when children wear nappies, parents are not aware of the classic dysuria and frequency symptoms as experienced by adults; and obtaining an adequate urine sample can be frustrating, time consuming, and costly.

The precise prevalence of UTI among all acutely unwell children presenting to primary care is unclear. One systematic review of 10 studies, eight of which were conducted in hospital emergency departments, one in US paediatricians’ offices, and one in an army medical centre, estimated UTI prevalence at 7%.4 A large Australian emergency department study published in 2010 found a prevalence of 3.4% in children presenting with a febrile illness.5 We identified only one small exploratory study conducted in general practitioner/family physician practices, which found a prevalence of 4%.6

It is not surprising then that the diagnosis of UTI is often delayed and may be missed in up to 50% of children presenting to primary care,7 sometimes due to symptoms being incorrectly attributed to other causes (such as otitis media). The pressure to reduce antibiotic prescribing may reduce the serendipitous treatment of undiagnosed UTI and the consequent prevention of renal sequelae, making accurate diagnosis now even more important than ever.

What is the evidence of the uncertainty?
The 2007 guidelines on the diagnosis, treatment, and long term management of UTI in children by the National Institute for Health and Clinical Excellence (NICE)8 concluded, after a systematic review, that there is uncertainty regarding the following questions on the diagnosis of UTI in children aged less than 5 years in primary care:

1) What is the accuracy of clinical symptoms and signs?
2) What is the accuracy of the combination of nitrite and leucocyte esterase (LE) dipstick test?
3) How do nappy pad or urine bag sample contamination rates compare to supra-pubic aspiration (SPA) or catheter samples?

To address these uncertainties, we considered relevant studies from our 2006 Health Technology Assessment (HTA) funded systematic review of tests for diagnosing UTI in children,7 the NICE guidelines,8 and a systematic literature search of Medline from 2002 (the end date of the HTA review searches) to April 2011. We used a sensitive search strategy combining terms related to UTI with terms relating to “clinical signs and symptoms,” “dipstick testing,” or “urine sampling,” to identify studies published since these reports. We included primary studies or systematic reviews that addressed one of the above questions, used urine culture as the reference standard, enrolled children aged 5 years or less, and were conducted in a primary care or emergency department setting in the Western world.

Clinical symptoms and signs
We found one systematic review9 that included eight primary studies in children aged less than 5 years (n=7892) and three additional primary studies (n=17 462) that fulfilled our inclusion criteria.10 11 12 Of these 11 studies, nine were conducted in hospital emergency departments, and two in paediatricians’ offices; none was conducted in general practices or family physician practices. The web table13 shows positive and negative likelihood ratios for each clinical sign and symptom together with estimates of the post-test probability of disease for the presence and absence of each symptom based on the prevalences (pre-test probabilities) of UTI of 4% seen in the study by O’Brien14 and 7% in the study by Shaikh.15

The data found show that no individual symptom or sign, or any combination of symptoms or signs, was sufficient to rule in a diagnosis of UTI, though some post-test probabilities (such as 25% for increased capillary refill time, no fluid intake, and supra-pubic tenderness) appear high enough to mandate urine testing and empirical treatment while awaiting culture confirmation. A number of symptoms and signs did not appear to have diagnostic value, including some that were recommended for the diagnosis of UTI by NICE8 (for example, poor feeding and vomiting). Some symptoms, signs (for example, respiratory), and proposed clinical prediction rules did reduce the probability of UTI to below 2% (given a pre-test probability of 4%) and these may be considered low enough to rule out UTI and avoid the need to obtain urine. These are summarised in table 1.

The largest study, which included almost 16 000 children,5 derived a clinical prediction rule based on a combination of
Symptoms and signs and dipstick test results helpful for ruling out urinary tract infection in children <5 years

<table>
<thead>
<tr>
<th>Clinical signs or symptoms</th>
<th>Age (years)</th>
<th>No of studies</th>
<th>No of children</th>
<th>Prevalence of sign or symptom (%) *</th>
<th>Likelihood ratio (95% CI)</th>
<th>Post-test probability (%) #</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥2 of: ≤12 months old; white race; temp ≥39°C; no apparent source of fever; fever for ≥48 hours</td>
<td>0-2</td>
<td>2 15</td>
<td>1681</td>
<td>NA</td>
<td>0.15 (0.05 to 0.46) 18; 0.17 (0.10 to 0.46) 18</td>
<td>0.6; 0.7</td>
</tr>
<tr>
<td>Stridor</td>
<td>0-5</td>
<td>1 17</td>
<td>15 781</td>
<td>1.8</td>
<td>0.20 (0.05 to 0.81)</td>
<td>0.8</td>
</tr>
<tr>
<td>Audible wheeze</td>
<td>0-5</td>
<td>1 17</td>
<td>15 781</td>
<td>6.4</td>
<td>0.25 (0.13 to 0.48)</td>
<td>1.0</td>
</tr>
<tr>
<td>Circumcised males</td>
<td>0-2</td>
<td>1 17</td>
<td>6835</td>
<td>NA</td>
<td>0.33 (0.18 to 0.63)</td>
<td>1.4</td>
</tr>
<tr>
<td>Temp ≥39°C with a potential source of fever</td>
<td>0-1</td>
<td>1 17</td>
<td>945</td>
<td>NA</td>
<td>0.37 (0.16 to 0.85)</td>
<td>1.5</td>
</tr>
<tr>
<td>Abnormal chest sounds</td>
<td>0-5</td>
<td>1 17</td>
<td>15 781</td>
<td>15.7</td>
<td>0.43 (0.31 to 0.58)</td>
<td>1.8</td>
</tr>
<tr>
<td>Chest crackles</td>
<td>0-5</td>
<td>1 17</td>
<td>15 781</td>
<td>8.3</td>
<td>0.46 (0.30 to 0.70)</td>
<td>1.9</td>
</tr>
<tr>
<td>Age ≤3 years</td>
<td>0-5</td>
<td>1 17</td>
<td>15 781</td>
<td>78.5</td>
<td>0.47 (0.37 to 0.61)</td>
<td>1.9</td>
</tr>
<tr>
<td>Did not feel hot</td>
<td>0-5</td>
<td>1 17</td>
<td>15 781</td>
<td>7.7</td>
<td>0.47 (0.31 to 0.73)</td>
<td>1.9</td>
</tr>
<tr>
<td>Breathing difficulty</td>
<td>0-5</td>
<td>1 17</td>
<td>15 781</td>
<td>13.7</td>
<td>0.48 (0.35 to 0.66)</td>
<td>2.0</td>
</tr>
<tr>
<td>Dipstick: leucocyte esterase or nitrite negative</td>
<td>0-12</td>
<td>1 17</td>
<td>246</td>
<td>NA</td>
<td>0.88 (0.71 to 1.1)</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td>0-18</td>
<td>1 17</td>
<td>243</td>
<td></td>
<td>0.11 (0.04 to 0.28)</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>0-24</td>
<td>1 17</td>
<td>491</td>
<td></td>
<td>0.72 (0.55 to 0.94)</td>
<td>2.9</td>
</tr>
</tbody>
</table>

*Data on the prevalence of individual features are taken from the study by Craig et al., which enrolled children presenting to an emergency department with fever. Data on the prevalence of features not assessed in this study were not available. Prevalence of these features is likely to vary according to setting.

†The further the likelihood ratio is away from 1 the stronger the evidence for the absence of disease. A likelihood ratio of <0.1 is considered to provide strong evidence to rule out a UTI.

‡Pre-test probabilities (prevalence) selected based on O’Brien et al (4%) and Shaikh et al (7%).

§Studies included in the systematic review by Shaikh et al.

27 signs and symptoms. Results were not reported for specific thresholds, but the model was found to have an area under the receiver operating characteristic curve of 0.80 (95% confidence interval 0.78 to 0.82) leading the authors to conclude that a computer assisted diagnostic decision tool based on this model could improve decision making in the emergency department.

Dipstick testing

We identified five primary studies conducted in children aged less than 5 years that assessed nitrite and leucocyte esterase dipstick testing in an emergency department setting,13-17 all of which were included in our previous HTA review,6 though our published analysis was not stratified by age <5 years. The age stratified results presented in the web table suggest that nitrite and/or leucocyte esterase positivity are useful for identifying children in whom urine should be cultured to confirm the presence of a UTI with post-test probabilities of between 20% and 84%. If both nitrite and leucocyte esterase are negative, the post-test probability ranged from 1% to 2% (based on pre-test probably of 4% to 7%) and this may be sufficient to rule out UTI without urine culture (table).

Urine sampling

The NICE guidelines found “insufficient data to draw conclusions about urine collection bags and urine collection pads” and “low-level evidence that showed that the accuracy of urine collection pads was greatly improved if the pads were not used for longer than 30 minutes.” 16 We identified one study published since these recommendations that reported a sensitivity of 88% and a specificity of 80% for bag samples compared to the recommended (reference) standard of catheter samples in non-toilet trained children.18 No further studies addressing nappy pads were identified.

Is ongoing research likely to provide relevant evidence?

We searched (8 September 2011) the UK Clinical Research Network Study Portfolio (http://public.ukcrn.org.uk/search) for diagnostic studies of UTI in children and identified the Diagnosis of Urinary Tract Infection in Young children (DUTY) study (www.dutystudy.org.uk) and the Epidemiology of Urinary Tract Infection (UTI) in Children with Acute Illness in Primary Care (EURICA) study. DUTY is a diagnostic cohort study designed to derive, validate, and test the efficiency of a diagnostic algorithm (that includes symptoms, signs, and dipstick urinalysis) for UTI in acutely unwell preschool children presenting to primary care. The study will also compare contamination rates between pad and clean catch urine sampling methods and is due to report at the end of 2012. EURICA is designed to estimate the prevalence of UTI in acutely unwell children aged less than 5 years presenting to primary care.

What should we do in the light of the uncertainty?

Many primary care clinicians will question the relatively high prevalence of UTI of 4% and 7% reported in the studies by O’Brien1 and Shaikh,4 since prevalences of this level might suggest more children develop complications than we currently appear to observe. There are a number of possible reasons for this high prevalence, including: (1) false positive results due to contamination; (2) false positive results due to asymptomatic bacteriuria15; (3) poor recognition of complications due to the limitations of existing tests (such as ultrasound and dimeric penicillin (DMSA) scans to detect renal scarring); and (4) uncertainty regarding the natural history of, and the development of complications from, UTI in children.

As with many decisions about who to test in primary care, acutely unwell children can be divided into three broad groups; those who on clinical grounds almost certainly do not have a clinically important UTI (no test); those who almost certainly do (test and treat); and the group in the middle for whom there is ongoing uncertainty. Data presented here suggest we may be able to identify some children in the first group (see table), but until studies conducted in family physician and general practice settings report both UTI
prevalence and the diagnostic value of symptoms and signs, we recommend primary care clinicians adopt a low threshold for urine testing and the use of immediate antibiotics for children testing positive for nitrites or leucocyte esterase, while awaiting culture confirmation.

As to how urine should be sampled, a clean catch approach is always best, especially after cleaning the perineum. Given the absence of clear advantage of the so called pad over bag methods in terms of the risk of contamination, carer or clinician preference and availability and costs of pad or bag should guide the method.

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ANSWERS TO ENDGAMES, p 911. For long answers go to the Education channel on bmj.com

ANATOMY QUIZ

Magnetic resonance study of the abdomen
A Stomach
B Common bile duct
C Second part of duodenum
D Head of pancreas
E Ascending colon

STATISTICAL QUESTION

Odds ratios and adjusting for confounding
Answers a, b, and d are true, whereas c is false.

CASE REPORT

An umbilical nodule with cyclical changes

1 Umbilical endometriosis.
2 Primary or metastatic malignant umbilical tumour, lipoma, lipoleiomyoma, abscess, cyst, hernia, granuloma, keloid, or a congenital malformation of the omphalomesenteric duct or urachus.
3 Inspection, palpation, ultrasound, computed tomography, magnetic resonance imaging, and biopsy with histopathological analysis.
4 Surgical excision and medical treatment.