Disorders of sex development (DSDs), formerly termed ambiguous genitalia, are a group of conditions where the external genitalia appear abnormal. It represents a true medical and social emergency that needs a multidisciplinary team approach for elucidation. The pediatric radiologist plays an important role in defining the genital anatomy that remains one of the most important factors in sex determination, in addition to chromosomal analysis.

**BACKGROUND AND OBJECTIVES:** Disorders of sex development (DSDs), formerly termed ambiguous genitalia, are a group of conditions where the external genitalia appear abnormal. It represents a true medical and social emergency that needs a multidisciplinary team approach for elucidation. The pediatric radiologist plays an important role in defining the genital anatomy that remains one of the most important factors in sex determination, in addition to chromosomal analysis.

**DESIGN AND SETTINGS:** A retrospective study, conducted between January 1995 and December 2010.

**MATERIALS AND METHODS:** Imaging studies (ultrasound, genitogram, and/or magnetic resonance imaging) were performed in patients with ambiguous genitalia, confirmed by chromosomal analysis and appropriate hormonal investigations.

**RESULTS:** The sensitivity of ultrasound is 89.5%, while its specificity reaches 100%. Retrograde genitogram is more invasive and less sensitive, as the yield of determining the presence of a uterus ± vagina is 84.2%. However, magnetic resonance imaging (MRI) is more sensitive for gonadal tissue identification. Its specificity reaches up to 100% and can provide detailed internal structures (uterus, fallopian tubes, and gonads).

**CONCLUSION:** Ultrasound examination is still the main modality of choice for screening patients with ambiguous genitalia. It is cheap and readily available everywhere. In addition to elucidating the uterus in 89.5%, it can also give more information on the adrenal glands. However, genitography is good—84.2% in elucidating genital anatomy—but it gives no information of the gonads and it is time consuming and invasive. MRI is helpful in cases with equivocal ultrasound, reaches 100% in elucidating internal extractor, and therefore could be reserved for that.
modalities (ultrasound, genitogram, and MRI) in the assessment of children with DSD, at the King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia between January 1995 and December 2010.

MATERIALS AND METHODS

Patients with ambiguous genitalia who attended a pediatric endocrine clinic over a period of 15 years between January 1995 and December 2010 were included in this study. Patients included were those with various ambiguous genitalia. A detailed history and clinical examination were performed in all patients followed by chromosomal analysis and appropriate hormonal assays. This research was approved by the Institutional Review Board.

Imaging plays an important role in demonstrating the anatomy and associated anomalies. Ultrasonography is the primary modality for demonstrating internal organs; genitography is used to assess the urethra, vagina, uterus, and any fistulas or complex tracts; and MRI is used as an adjunct modality to detail the anatomy, if necessary.

Ultrasound (US) examinations were performed using real-time sector scanners with either 5 or 7.5 MHz transducers. The aim of the examination was to determine the presence or absence of a uterus. The ovaries were more difficult to identify with certainty than the uterus, and were therefore not relied upon in determining the gender. An attempt was made to identify the uterus in both sagittal and transverse planes in each case. The children were not catheterized in order to fill their bladders, but studies were performed after sufficient urine had been allowed to accumulate.

Genitography is a more invasive procedure involving cannulation of the urethra and urogenital sinus. A preliminary film of the pelvis was obtained in the supine and lateral positions. After sterile cleaning, water-soluble non-ionic contrast medium was injected through a feeding tube into the perineal orifices. When it had filled the vagina, the medium entered the endocervical canal and, in some cases, the uterine cavity, the fallopian tubes, and/or the urethra. All examinations were performed under fluoroscopy in the lateral position with a spot film device. MRI was performed on 1.5 tesla machine in 8 patients (4 female pseudohermaphroditism, 2 male pseudohermaphroditism, and 2 truehermaphroditism).

### Table 1. Etiological diagnosis and radiological studies in 38 patients with female pseudohermaphroditism (46 XX karyotype).

| Etiological diagnosis                                      | Ultrasound +ve uterus | +ve vagina ± uterus | Genitogram Male type urethra | Inc |
|------------------------------------------------------------|-----------------------|---------------------|------------------------------|-----|
| CAH-21 hydroxylase deficiency (34)                         | 30                    | 28                  | 2                            | 1   |
| CAH-11 hydroxylase deficiency (3)                          | 3                     | 3                   | 2                            | 1   |
| CAH-3 hydroxy-steroid dehydrogenase deficiency (1)        | 1                     | 1                   | -                            | -   |
| Total (38)                                                 | 34 (89.5%)            | 32 (84.2%)          | 4 (10.4%)                    | 2 (5.2%) |

CAH: Congenital adrenal hyperplasia, Inc: inconclusive.

### Table 2. Etiological diagnosis and radiological studies in 10 patients with male pseudohermaphroditism (46 XY karyotype).

| Etiological diagnosis                                      | Ultrasound -ve uterus | -ve vagina ± uterus | Genitogram Male type urethra | Inc |
|------------------------------------------------------------|-----------------------|---------------------|------------------------------|-----|
| Complete androgen insensitivity (CAI) (4)                  | 4                     | 4                   | 3                            | 1   |
| 5α-reductase (1)                                           | 1                     | 1                   | 1                            | -   |
| Hypogonadotropic deficiency (1)                            | 1                     | 1                   | 1                            | -   |
| Isolated hypospadias (3)                                   | 3                     | 3                   | 2                            | 1   |
| CAH 3β-hydroxy-steroid dehydrogenase deficiency (1)       | 1                     | 1                   | 1                            | -   |
| Total (10)                                                 | 10 (100%)             | 10 (100%)           | 8 (80%)                      | 2 (20%) |
RESULTS
Fifty patients were evaluated for ambiguous genitalia in the period under review. Their ages ranged from few days to 12 years. There were 38 children with female pseudohermaphroditism (46 XX karyotype) and 10 with male pseudohermaphroditism (46 XY karyotype). Two patients were with true hermaphroditism. Tables 1 and 2 show the genetic sex, etiological diagnosis and radiological investigations. The sensitivity of ultrasound is 89.5%, while its specificity reaches 100%. However, in retrograde genitogram, the yield was less (84.2%). MRI was also performed in 8 patients. It was very sensitive in delineating the internal structures (uterus and fallopian tubes) and picking the gonads in 100%.

DISCUSSION
DSD, former termed ambiguous genitalia, constitutes a major complex medical and social emergency requiring a multidisciplinary team approach. Clinical findings that suggest DSD and serve as indications for further investigation include the following: overt genital ambiguity; an apparent male with bilateral non-palpable testes (full-term infant), micropenis, hypopadias associated with separation of scrotal sac, or an undescended testis with mild hypospadias; an apparent female with clitoral hypertrophy of any degree, a foreshortened vulva with a single opening, or an inguinal labial hernia containing a gonad; a family history of DSD (e.g., complete andro-

Figure 1. A newborn infant with ambiguous genitalia (male-pseudohermaphroditism XY-DSD), showing severe under virilization of the external genitalia who was proven to have 3-hydroxysteroid dehydrogenase deficiency, congenital adrenal hyperplasia.

Figure 2. An ultrasound of a newborn baby with ambiguous genitalia caused by congenital adrenal hyperplasia, 21-hydroxylase deficiency, showing bladder (BL), uterus (UT), and vagina (V).

Figure 3. An ultrasound image showing an enlarged adrenal gland (arrows), which has “cerebriform” appearance in a newborn baby with congenital adrenal hyperplasia due to 21-hydroxylase deficiency.
Figure 4. A retrograde genitography of a newborn baby with ambiguous genitalia, (female-pseudohermaphroditis, XX, DSD proven to have congenital adrenal hyperplasia, 21-hydroxylase deficiency, showing contrast material filling the bladder (BL), vagina (V) and uterus (arrow).

Figure 5. A T2-weighted magnetic resonance image (MRI) of the pelvis, showing no uterus and (B) testicles within the inguinal canals (arrows) in a patient with complete androgen insensitivity (CAI).

gen insensitivity syndrome; and a discordance between genital appearance and a prenatal karyotype.1-5

Imaging plays an important role in determining the internal organs and urogenital anatomy in children with ambiguous genitalia. US is the primary modality for evaluation of internal reproductive organs (Figure 2). It is not invasive and can be performed quickly and does not involve radiation or sedation. An ultrasound examination should include the inguinal, perineal, renal, and adrenal regions. The uterus and ovaries are relatively easy to find out the neonatal period, since these structures are prominent under the influence of maternal hormones.10,11,14-18

Congenital adrenal hyperplasia (CAH) is being the most common cause of ambiguous genitalia,8 it manifests as various degrees of virilization in girls. Most cases are secondary to 21-hydroxylase deficiency associated with elevated 17-hydroxy-progesterone. Adrenal glands with a limb over 20 mm long and 4 mm wide and with normal corticomedullary differentiation are suggestive of CAH12,19 (Figure 3). Al Awain et al20 found that a combination of a limb with greater than 4 mm, a
lobulated surface, and stippled echogenicity had a sensitivity of 92% and a specificity of 100% in making the diagnosis of CAH. However, the presence of normal-sized adrenal glands does not exclude the diagnosis. Male pseudohermaphroditism is suggested by the absence of a uterus in the presence of gonads.

Retrograde genitography demonstrates the uterus or a male or a female type urethral configuration and any fistulous communication with the vagina or rectum (Figure 4). Many patients have persistent urogenital sinus, and an adequate genitograph should help identifying the exact location where the urethra and the vagina are joined. These anatomic characteristics are very essential markers for surgical strategy, and, therefore, should be done in the assessment.

MRI using T1- and T2-weighted MRI sequences with their multiplanar capacity and superior tissue characterization can provide detailed anatomic information. In one study, MRI was found useful in the evaluation of ambiguous genitalia, with the detection of the uterus in 93% of cases, the vagina in 95%, the penis in 100%, the testes in 88%, and an ovary in 74%. MRI is more sensitive than US in the evaluation of the gonads, but is still completely reliable for excluding intra-abdominal gonads. Ectopic gonads, testes, and noncystic immature ovaries have intermediate signal intensity on T1-weighted MRI and high signal intensity with an intermediate-signal-intensity-outer rim on T2-weighted MRI.

In conclusion, it is vital that a child with ambiguous genitalia be evaluated by a multidisciplinary team including, but not limited to, an experienced endocrinologist and radiologist, using a coordinated approach to arrive at a timely diagnosis so that a proper gender assignment can be made early in life. Imaging plays an important role in demonstrating the anatomy and potential effects on other organs. Ultrasoundography is a preferred modality for the initial evaluation. Genitography is used to assess the uterus, urethra, vagina, and any fistulous connection and to plan for surgery. MRI can serve as a problem-solving modality that can clearly depict the genitalia and gonads.

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