

Brief Communications

The pattern of peripheral blood chromosomal abnormalities in Northern Jordan

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Chromosomal abnormalities constitute one of the 3 major categories of genetic disorders. Changes in the number or the structure of chromosomes are major causes of mental retardation, multiple malformations, cancer, infertility and spontaneous abortions.^{1,2} One in every one-hundred liveborn children will have a chromosomal abnormality and half of the first trimester spontaneous abortions are due to chromosomal abnormalities.³ Recognizing these facts, the cytogenetics laboratory at Jordan University of Science and Technology was established in 1993 aiming at providing a diagnostic service for the northern sector of Jordan. The laboratory provides primarily karyotyping of peripheral blood specimens for a variety of indications. However, occasional consultations on peripheral blood, amniotic fluid, chorionic villus sampling (CVS), bone marrow and products of conception specimens are provided for other laboratories. We provide here, a description of the function of the laboratory, the methodology used and an analysis of the results over a period of 7 years. We discuss the implications of referral of cases to the laboratory and some aspects of the expansion of the service to include new and updated technologies.

The methodology employed in the laboratory for Giemsa-banding (G-banding) is conventional.⁴ Other staining techniques, such as centromere-banding (C-banding), Nucleolar Organizing Region (NOR) staining and reverse-banding (R-banding) are employed when the need arises.⁴ A detailed report, using the ISCN (International System for Human Cytogenetic Nomenclature; 1995),⁵ is generated in triplicate, one for the patient's file, one for the patient or the legal guardian and one for the referring physician. Cultures that fail to grow are repeated at a later date, except if the repeating was not feasible, such as death of the child or refusal for repeating the test at our laboratory (18/803 cases; 2.2%). Referrals to the laboratory fall under one of the following categories: 1. Couples (sometimes only one member is referred) with recurrent fetal wastage or infertility. 2. An individual with dysmorphism or a pattern of malformations. Referrals to rule out Downs, Turner or Klinefelter syndromes or other known chromosomal abnormality syndromes fall under this

Table 1 - The total number of cases received in each category; the number of abnormal chromosomal complement and the percentage.

Indication	Received	Failed culture	Abnormal
Recurrent fetal waste or infertility	223	0	7
MCA	396	16	143
Delayed puberty	38	0	1
Relative with MCA	71	0	7
Special tests	19	2	4
Total	747	18	152
MCA - multiple congenital anomalies			

Table 2 - List of the detected chromosomal abnormalities in children with MCA.

Chromosomal abnormality	Syndrome
46,XY,del(18)(q23)	18q-
47,XX,+del(12)(q13.2q24.32)	Partial trisomy 12
46,XX,t(13q13q)	Trisomy 13; Patau
46,XX,t(17;20)(q25.3;p11.2)	Balanced
46,XY,t(1;8)(p22.3;q13)	Balanced
46,XX,der(11)ins(11;18)915.1;q12.2q21.31)	Partial trisomy 18
46,XY,t(3;14)(p14.2;q24.1)	Balanced
46,XY,del(7)(q33q34)	Partial monosomy 7
47,XX,+der(X)t(X;?)	-
47,XY,+18	Trisomy 18; Edwards
46,XY,del(5)(p15.3)	Cri du chat
46,XX,t(5;6)(q12;q24)	Balanced
46,XX,inv(21)(q21q22)	Balanced
47,XXX	Triple X syndrome
MCA - multiple congenital anomalies, del - deletion, inv - inversions, der - derivative	

category. 3. Females (occasionally males) with delayed puberty. 4. Parents or relatives of a child with dysmorphism (category number 2) whether the child had a laboratory proven chromosomal abnormality or not. 5. A child with ambiguous genitalia. 6. Special tests to rule out Fanconi anemia (breakage studies), ataxia telangiectasia (sister chromatid exchange) and fragile X-syndrome.

During the 7 year period that started from the establishment of the laboratory through till the end of the year 2000, 803 peripheral blood specimens were received and only 785 reports were generated, since 18 cultures failed to grow and were not repeated. **Table 1** shows the total number of cases received in each category with the exception of the category of a child with ambiguous genitalia, abnormal chromosomal complement and the percentage. Out of 147 samples that were karyotyped to rule out Downs syndrome, 105 were trisomic for chromosome 21 (71.4%). The majority of the cases (101/105; 96%) were due to non-disjunction, while only 4 cases were due to de-novo Robertsonian translocation involving chromosomes 14 and 21 [2 (14; 21) and 2 (21; 21)]. Out of the 42 samples karyotyped to rule out Turner syndrome 10 were abnormal (23.8%), 3 were monosomic for the X-chromosome (45,X), 2 were mosaic for a monosomic cell line and a normal cell line (45,X/46,XX), one was mosaic for a monosomic cell line and a cell line with Xq duplication (45,X/46,X,dup(X)(q12,q25) and 4 had a deletion of the short arm of the X. Only 6 out of the 25 samples received to rule out Klinefelter syndrome turned out to be abnormal (24%). One hundred and 65 samples were received that carried the diagnosis of multiple congenital anomalies other than Downs, Turner or Klinefelter syndromes. Twenty-two samples were abnormal (13.3%) and **Table 2** shows a list of the detected chromosomal abnormalities. A balanced pericentric inversion of chromosome 16, involving bands other than the heterochromatic region was found in one female referred due to delayed puberty. Forty-three cases referred for chromosomal sex assignment were received and in all the chromosomal sex was determined. There were 13 samples received with no clinical data or diagnostic indication, all of which turned out normal.

One of the primary indications for peripheral blood karyotyping is for couples that suffer from infertility or recurrent fetal loss. In our experience, it constitutes almost a quarter of the service. The percentage of abnormal chromosomal complement in our series is 3%. Although, this is less than other reported series, it is probably a small and insufficient number for drawing conclusions. However, it might point to other factors playing more important roles in the etiology of infertility and recurrent fetal wastage in a country like Jordan. Almost half of the received samples constitute a part of a work up of a child with a recognizable or unrecognizable pattern of dysmorphism. In this category, karyotyping is quite rewarding, as it was diagnostic in over one third of

the cases. This category includes referrals to rule out Downs syndrome in which over 70% of the cases had Trisomy 21. This high percentage reflects the adequate clinical skills of pediatricians in our area, as well as the recognizable phenotype of the syndrome. This category also includes referrals to rule out sex chromosome abnormalities such as Turner and Klinefelter syndromes. A quarter of these referrals are accurately diagnosed by karyotyping. Only 13.3% of the cases referred to rule out a chromosomal abnormality in a child with multiple congenital anomalies are diagnostically positive. This lower percentage reflects the clinical difficulties associated with this category due to the variability in the phenotype and the rarity of the conditions. Out of the cases referred as part of the work up for delayed puberty, only one had a chromosomal abnormality. This chromosomal abnormality (pericentric inversion of chromosome 16) is probably non-contributory to the presentation of delayed puberty, although this is not certain. There is room for expansion in our laboratory, and currently we are performing trial experiments to start a prenatal diagnostic service based on karyotyping amniotic fluid cells or CVS, or both. The introduction of new technologies that utilize molecular cytogenetic techniques (in situ hybridization) is also underway which should help in the diagnosis of microdeletion syndromes and cryptic chromosomal rearrangement. It seems that in general terms the karyotyping service has been quite helpful as a diagnostic tool for children with multiple congenital anomalies. Karyotyping is still a part of the work up of couples with recurrent fetal wastage or infertility but due to the low yield and the high expense, it is advised that it is deferred until other causes are excluded. Karyotyping still plays a major role in the gender assignment of children with ambiguous genitalia.

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