Short communications

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A chromosome supplement to the London Dysmorphology Database

SUMMARY A supplement to the computerised database for the diagnosis of rare dysmorphic syndromes described by Winter *et al*[1] is presented, which includes a list of syndromes occurring in patients with unbalanced chromosome aberrations. The extension of the original programme is based on Schinzel's *Catalogue of unbalanced chromosome aberrations in man*.[2]

In 1984, the London Dysmorphology Database was reported in this journal.[1] As pointed out by the authors, this is a computer based data bank, which comprises more than 900 syndromes and 1200 symptoms of non-chromosomal malformation syndromes. The programme is able to select the syndromes characterised by up to three symptoms entered by the user and was therefore regarded as a helpful tool in genetic counselling. After a thorough test in practice, in the Würzburg genetic counselling service among others, it was found to be very useful, but the omission of chromosomal syndromes was thought to be a disadvantage. Therefore an attempt was made to incorporate chromosomal syndromes into an extended version of the London programme. This extension was based on Schinzel's *Catalogue of unbalanced chromosome aberrations in man*.[2]

Existing software

As we were mainly interested in merging cytogenetic data with the information already available in the London Dysmorphology Database, the operating programmes (written in dBase II (tm Ashton-Tate)) were left unchanged except for minor modifications. The amount of data stored, however, was greatly increased. The supplemented version lists in excess of 1500 different syndromes and more than 3500 relevant references. The choice of symptoms contains more than 1400 items.

Programme objectives and data selection

As mentioned above, the main purpose of the extension of the programme was to create a database that included a comprehensive spectrum of most of the malformation syndromes defined at present for use in genetic counselling. Completeness in an area which changes as quickly as human genetics is hardly ever possible, however. On the other hand, the software is fairly easy to use, so that only a very limited knowledge of software handling is required to make a personal update. Furthermore, a standardised update is offered regularly by the London Dysmorphology Database. For reasons of speed of retrieval and compatibility with the London Dysmorphology Database, we continued with the limitation of 28 symptoms per syndrome. Our entries relied on the clinical descriptions given by Schinzel[2]; additional rare abnormalities were completed by consulting the more recent cytogenetic publications. If chromosomal aberrations exhibited more than 28 symptoms, we made our choice of symptoms to be entered on the basis of concordance between at least three major references. Wherever percentages for symptoms were given, they were incorporated in this decision. Our choice of data represents a compromise between common but non-specific symptoms and rare but highly diagnostic symptoms.

Programme extensions

In order to match the description of chromosomal syndromes with the existing data, we had to incorporate a number of new symptoms in the existing list. This was done in consultation with Dr Robin Winter, London, and Professor Albert Schinzel, Zürich.

Conclusion

In our experience, the system presented proves a valuable addition to the other diagnostic tools used in genetic counselling. We would like to stress the point that a diagnosis by the computer is neither possible nor desirable; the decision of which symptoms to include and how to weigh the selection

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criteria has to be made by the user. The performance of the system therefore depends largely on the skill and experience of the user. It should also be emphasised that use of the computerised cytogenetics database should always go hand in hand with the original data source, the Schinzel catalogue, since weighing of choices and comparison with photographs of patients are important steps in the diagnostic process.

Nevertheless, computer aided syndrome searching helps to ease the routine workload in a busy genetic counselling service. One of the major benefits of this approach, we feel, is in the initial stages of student training under the supervision of an experienced geneticist. Regular updates will certainly increase the value of the system for any potential user.

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References

[1] Winter RM, Baraitser M, Douglas JM. A computerised data base for the diagnosis of rare dysmorphic syndromes. *J Med Genet* 1984;**21**:121–3.
[2] Schinzel A. *Catalogue of unbalanced chromosome aberrations in man*. Berlin, New York: de Gruyter, 1983.

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Drs Winter and Baraitser comment on this paper on page 509 of this issue.

Detection of centromeric regions of chromosomes by immunofluorescence: procedure and application

Conventional techniques for the identification of centromeric regions can be time consuming and often produce inconsistent and variable results. The recent description of autoantibodies to centromere antigen in patients with the CREST variant of progressive systemic sclerosis[1] has prompted us to use this antibody as a probe for identifying centromeric chromatin of chromosomes. We describe here a simple and rapid technique for the identification of centromeric regions of chromosomes by immunofluorescence microscopy. The clinical use of this technique is demonstrated by a case study.

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Method

The anticentromere autoantibody used in this study was obtained from the frozen serum bank at E W Sparrow Hospital. The titre of the antibody was 1:5120 as determined by routine ANA screening on a Hep-2 cell substrate (Kallestad Laboratories, Austin, Texas). Chromosome spreads were prepared from peripheral blood cultures by the method of Yunis.[2] Briefly, methotrexate synchronised cultures were harvested, fixed, and dropped onto clean glass slides. The chromosome spreads were flooded with a 1:200 dilution of anticentromere antibody in phosphate buffered saline (PBS, pH 7·2) and incubated in a humidified chamber for 30 minutes at room temperature. The slides were then rinsed in two changes of PBS for five minutes each, then flooded with a 1:80 dilution of fluorescein conjugated antihuman IgG, Fab'2 (Kallestad), and incubated for 30 minutes at room temperature. The slides were washed twice in five minute changes of PBS and examined by fluorescence microscopy on a Zeiss epifluorescence microscope equipped with a 50 watt mercury-arc lamp.

Case report

A 38 year old couple was referred to this laboratory

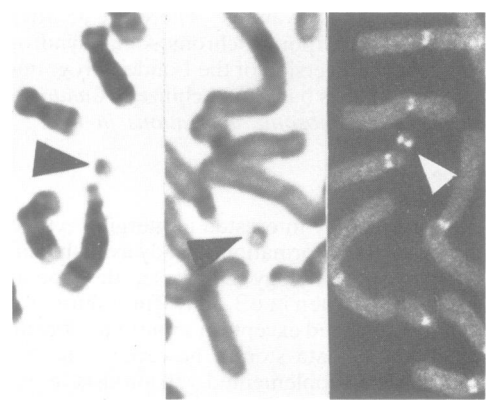

FIGURE *(Left) G banded microchromosome, (middle) C banded microchromosome, (right) anticentromere (AC) banded microchromosome. Note the individual chromatid centromeres in the AC banded photograph.*