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SUMMARY

Having pointed out in a previous work that the adrenal cortex of obese women in basal conditions shows a greater activity with respect to normal women, the authors have tested the functional response of this gland to stimulus with minimal effective doses of corticotropin. It was shown that, while in control subjects only the metabolites of cortisol were significantly increased, in obese women all mineralocorticoids and particularly glucocorticoids respond in a statistically significant way. Also the indices of enzyme activities (hydrogenase and particularly 21-hydroxylase) have confirmed the functional hyperactivity of the adrenal cortex in obesity.

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Cytogenetics of cervical dysplasias

by
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Dysplasias of the uterine cervix are difficult to classify cytogenetically for the following reasons: the most interesting and useful study method by far is the one involving direct hypotonic « squash » which, more than cultures, follows the real karyotypic arrangement of the cell.

However, it is well known that in relation to the tissues, this method has various

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limitations because of the variety in multiplicational rhythm and because of the differences in the fragmentation of the biopsy samples.

The direct « squash » method also presupposes more energetic treatments, which is why we believe that the relevant data in the literature should be considered merely as a guideline.

It is well known that diploid karyotypes are commonly found in benign neoformations. In contrast to malignant neoformations, dysplastic states have received little attention.

Recent studies have given increasing importance to forms which, on the basis of extensive analyses, have been found to represent in chromosomal terms transition forms between stable diploidy and unstable aneuploidy of dysplasia first, and then of carcinoma in situ.

Statistic obtained by various investigators ([1, 2, 3]) suggest the possibility that cytogenetic findings in dysplasia of the cervix correspond to the severity of the histological situation. In view of the fact that this same cytogenetic date cannot be applied to dysplastic or neoplastic histological findings of heterogeneous origin, it is also hazardous to attribute prognostic significance to the comparison of the result obtained from combined studies (histological, cytological, cytogenetic) carried out along the same lines.

Indeed, it happens only rarely that the multiplicity of clones and the technical results agree with the biological behaviour of the neoplasia or displasia in question. Only repeated or multiple examinations and biopsy samples taken from various places in the lesion will allow us to come to an independent cytogenetic assessment in regard to the prognosis which, it must be emphasised once again, does not always agree with the histological assessment.

The majority of investigators ([1, 2, 3, 4]) agree in attributing a peridiploid or peritetraploid karyological type to dysplasia. Sometimes the only difference is in the manner of distribution of the peridiploid karyotype, which is percentually more limited to a particular number (usually diploid) in dysplasia and is more extensive in the forms in situ (pseudomonomodal and pseudopolymodal behaviour).

What is the significance of these findings? In general, the greater the number of mitoses, the higher the probability of « controlling » the nuclear activity. All the mitoses are important, but from a biological point of view the mitoses which are richer in nuclear material will have a higher chromosomal content. Indeed, although it is true that they do not always express a certain prognostic value, they are nevertheless the products of extensive nuclear changes; a typical example are cases of sarcoma, which ordinarily have high ploidy.

These rarely have marker chromosomes, but when it does happen, the presence of a carcinoma can no longer be excluded, because the marker chromosome is produced by the nuclear disorder involved in neoplasia. Secondly, the karyotypes which are steadily repeated, in a greater number than the diploid karyotype, are also characteristic of tumours, in the same way as those in inferior numbers may be related to the presence of dominant clones. When this possibility is not confirmed, if only a few metaphases are produced, perhaps not very clearly (as occurs in a not inconsiderable number of cases) one must recur of necessity to the synthesis of all the available data, and to the removal of a good sample. It is probable that the cervical tissue under examination will not produce mitosis; if so, the cytokaryology method described by Delle Piane may be useful.

On the other hand, it is also likely that cytogenetics will be able to deal with problems relating to histologically confirmed carcinoma in situ.

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Discussion in the literature suggests that this lesion differs from the preceding one. Indeed, in the latter we find a greater frequency of peridiploid metaphases and also cell units with a higher chromosomal number (triploidy, tetraploidy, heteroploidy). We may even find elements relating to nuclear manipolations, such as marker chromosomes.

In our opinion, fragmentation and disorderly recombinations are highly suspect elements; where they occur even a reasonable reconstruction of any karyotype is impossible.

In the opinion of Wakonig-Vaartaja and Hughes ([4]), the more highly polyploid metaphases of carcinoma in situ (tetraploidy) are incapable of maintaining this multiplicational rhythm and are eliminated from the context of the neoplastic tissue. But it would seem that in proximity to the natural evolution of carcinoma in situ towards the invasive form there occurs a restriction in the number from the ploidy class, and a predominance of peridiploid and peritriploid elements.

We merely wish to stress that this view is in better agreement with the concept of natural selection of pathological clones than with that of the multiplicational rhythm in geometric progression.

It would thus seem that in the context of carcinoma there is a balance of opposing forces, which is not produced by progressive and rapid « polimerisation » of the haploid number, but to a kind of progressive homoestasis which is controlled from time to time while the new karyotype is becoming stabilised. In this way clonal development is slower and momentarily controlled.

In contrast, experimental oncological findings indicate that higher the ploidy of the form, the greater is the tendency towards an invasive nature on the part of the tumour. In human pathology the most outstanding examples are sarcoma and mitotic endoreduplication.

MATERIALS AND METHODS

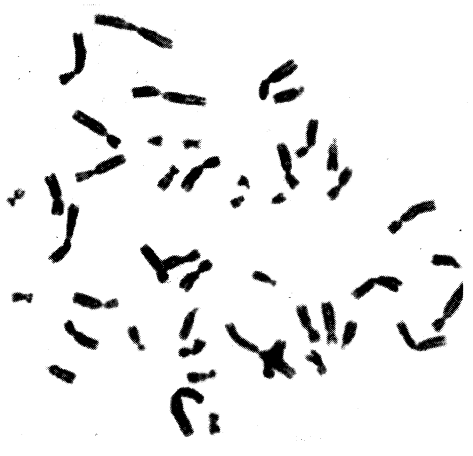
For our hypotonie « squash » studies we used biopsy fragments from cervical dysplasia and invasive carcinoma of the cervix. Karyotypes were analysed from 22 cases of low-grade dysplasia, 11 cases of high-grade dysplasia and 2 cases of invasive carcinoma. The total of 25 cases of cell metaphase were distributed as shown in table 1.

Table 1.

Form	No. chromosomes		
	45	46	46
Low-grade dysplasia	12	3	—
High-grade dysplasia	4	2	—
Invasive cancer	—	1	3

Examples of the metaphases found are shown in figures 1 and 2.

As can be seen from the distribution, the most significant difference is between dysplasia and invasive cancer, rather than between the two types of dysplasia. Characteristic of the latter lesions is the variation in the chromosome number around the diploidy, rather than true diploidy, and no signs of evident morphological changes.



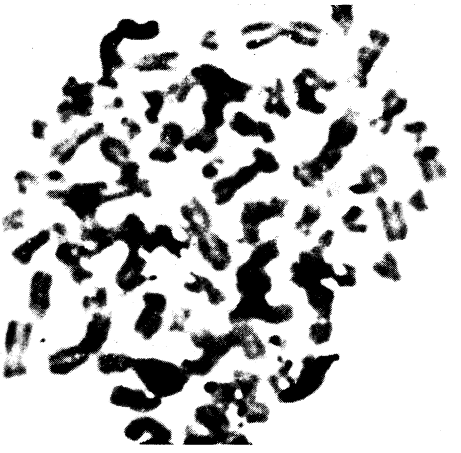


FIG. 1 FIG. 2

FIG. 1 - Metaphase in a case of high-grade dysplasia of the portio.

FIG. 2 - Metaphase in a case of invasive cancer of the cervix.

Is this oscillation an indication of development towards the in situ form, and is it the intrinsic characteristic of dysplasia or is it a technical artefact?

Are there possibly more advanced developmental stages which would indicate the progression of the form more clearly?

SUMMARY

The author analyse and discuss karyotypes obtained form cases of dysplasia and invasive carcinoma of the cervix.

Significant cytogenetic difference were found between dysplasia and carcinoma, but not between the two types of dysplasia.

The karyotypic composition of dysplasia is not consistent, and the interpretation of the authors' own findings and those reported in the literature is therefore uncertain.

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