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Coexpression of cytokeratins and vimentin in common epithelial tumours of the ovary: an immunocytochemical study of eighty-three cases*

Giuseppe Viale[1], Marcello Gambacorta[2], Patrizia Dell'Orto[1], and Guido Coggi[1]

[1] Second Department of Pathology, University of Milan, School of Medicine, Via Di Rudini 8, I-20142 Milano, Italy
[2] Department of Surgical Pathology, E.O. Ca' Granda, Milan, Italy

Summary. An immunocytochemical investigation has been performed on 83 common epithelial tumours of the ovary, to ascertain their capability of expressing vimentin in addition to cytokeratins. Our results demonstrate that vimentin coexpression is related to the tumour histotype and -to a lesser extent- to the degree of differentiation of malignant variants. Indeed, most serous tumours (80%), some endometrioid adenocarcinomas, and all the clear cell carcinomas investigated exhibited a variable number of neoplastic cells co-synthesizing the two distinct intermediate filament (IF) proteins, whereas only one of 29 mucinous tumours and none of the Brenner tumours displayed vimentin-immunoreactive cells. Moreover, in serous and endometrioid carcinomas, the expression of vimentin was related to the degree of tumour differentiation, being consistently identifiable in the better differentiated cases. The immunocytochemical findings of a parallel investigation on IF expression in the ovarian coelomic epithelium and in the müllerian-derived epithelia of the female genital tract allowed us to ascertain that ovarian epithelial tumours (with the possible exception of poorly differentiated carcinomas) maintain the pattern of IF expression typical of the normal epithelia. This investigation emphasizes the usefulness of IF typing as a tool for the more precise characterization of the origin and differentiation of human neoplasms.

Key words: Cytokeratins – Vimentin – Immunocytochemistry – Ovarian epithelial tumours – Intermediate filament coexpression

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Offprint requests to: G. Viale

Introduction

The immunocytochemical identification of the distinct classes of intermediate filament (IF) proteins expressed by neoplastic cells is widely acknowledged as a valuable diagnostic tool, because tumours retain the capability to synthesize the same IFs as their parent tissues (Gabbiani et al. 1981; Osborn and Weber 1983). Though in most cases individual cell types and their derived tumours express a single class of IFs, a growing number of reports illustrate normal and neoplastic tissues coexpressing two or more distinct IF proteins (Miettinen et al. 1984a; Gould 1985; McNutt et al. 1985). This peculiar feature of some human tumours may be particularly useful as an adjunct for a better understanding of their biology and for a more precise identification of their histogenesis.

In many instances, however, reports of IF coexpression in normal and neoplastic human tissues have provided contradictory results, invalidating the reliability of IF coexpression as a marker in diagnostic pathology. This holds true for several different neoplasms, including tumours of the thyroid gland (Miettinen et al. 1984b; Schröder et al. 1986; Buley et al. 1987; Henzen-Logmans et al. 1987), of the choroid plexus (Coffin et al. 1986; Miettinen et al. 1986; Doglioni et al. 1987) and of the neuroendocrine system (Lehto et al. 1983, 1984; Blobel et al. 1985; Broers et al. 1985).

Contrasting findings on the coexpression of cytokeratins and vimentin have also been reported for some normal epithelia and epithelial tumours of the female genital tract. Indeed, while some investigations have documented coexpression of

these IF proteins in the ovarian coelomic epithelium (Miettinen et al. 1983; Moll et al. 1983; Czernobilsky et al. 1985), in some ovarian neoplasms (Miettinen et al. 1983; Gown and Vogel 1985; McNutt et al. 1985; Puts et al. 1987), in the endometrial epithelium and in endometrial carcinomas (Bonazzi del Poggetto et al. 1983; Gown and Vogel 1985; McNutt et al. 1985; Dabbs et al. 1986; Puts et al. 1987), other reports have denied vimentin coexpression in these normal and neoplastic tissues (Ramaekers et al. 1983, 1983a, b; Czernobilsky et al. 1984).

The reasons for the discrepancies include the use of frozen or fixed and embedded material, the effects of different fixatives on the immunoreactivity of IFs, the use of different mono- and polyclonal antisera, and the choice of the immunocytochemical method. Moreover, at least with regard to ovarian tumours, many reports include a small number of cases (Bonazzi del Poggetto et al. 1983; Miettinen et al. 1983; Ramaekers et al. 1983a, b; Czernobilsky et al. 1984; Gown and Vogel 1985; Puts et al. 1987), without defining their histotype or the degree of differentiation (Ramaekers et al. 1983b; Gown and Vogel 1985; McNutt et al. 1985; Puts et al. 1987).

The present study was aimed to ascertain, on a large series of cases, the capability of common epithelial tumours of the ovary to coexpress cytokeratins and vimentin, with regard both to the different oncotypes and to the degree of differentiation of the malignant cases. For comparison, normal epithelia of the female genital tract have also been examined, to provide immunocytochemical support to the alleged divergent differentiation of the neoplasms arising from the multipotential coelomic epithelium of the ovary.

Moreover, we have immunostained adjacent serial sections of each case for the two distinct IF proteins and carried out double immunocytochemical staining procedures in order to verify whether the possible coexpression of IFs reflects heterogeneity of the neoplastic cell population or a real capability of these cells to co-synthesize cytokeratins and vimentin.

Materials and methods

Eighty-three cases of surgically removed common epithelial tumours of the ovary were studied in the current investigation. The histopathological diagnoses of the tumours were made according to the W.H.O. classification of ovarian tumours (Serov et al. 1973), and are summarized in Table 1. Undifferentiated and unclassified carcinomas were excluded from the study. For comparison, 10 cases of ovarian endometriosis were also investigated, together with normal ovaries, or portions thereof (10 cases), normal fallopian tubes (10 cases), normal proliferative (5 cases) and secretory (5 cases) endometria, and normal endocervical mucosa (10 cases).

Table 1. Histopathological diagnoses of the 83 ovarian tumours included in this study and summary of the immunocytochemical findings

Diagnosis	Number of cases	Number of positive cases	
		CK	Vim
Serous tumours			
benign[a]	16	16	15
of borderline malignancy[b]	3	3	3
malignant[c]	15	15	9
Total	34	34	27
Mucinous tumours			
cystadenomas	16	16	0
of borderline malignancy[d]	3	3	0
cystadenocarcinomas	10	10	1
Endometrioid adenocarcinomas	12	12	4
Clear cell carcinomas	4	4	4
Brenner tumours, benign	4	4	0

CK: cytokeratins; Vim: vimentin

[a] 4 cystadenomas, 4 papillary cystadenomas, 8 cystadenofibromas

[b] 2 cystadenomas, 1 papillary cystadenoma

[c] 2 adenocarcinomas, 5 papillary adenocarcinomas, 8 papillary cystadenocarcinomas

[d] 2 cystadenomas, 1 cystadenofibroma

The tissue samples were fixed in 10% formalin and embedded in paraffin, according to routine histopathological procedures.

From the paraffin blocks, 5 μm thick serial sections were cut, collected on albumin-coated slides, and left to dry overnight at 37° C. The immunocytochemical reactions for the localisation of cytokeratins (using the lu-5, the PKK1 and the CAM 5.2 monoclonal antibodies) and vimentin (using the V9 monoclonal antibody and a rabbit polyclonal antiserum) were performed according to the ABC staining method (Hsu et al. 1981), in a humidity chamber, at room temperature.

Briefly, the tissue sections were dewaxed, rehydrated, treated with 3% hydrogen peroxide in distilled water for endogenous peroxidase inhibition, washed in 0.05M Tris-buffered saline (TBS), pH 7.6, and then sequentially incubated with: 1) 1/30 dilution of normal goat or horse serum, for 30 min; 2) specific rabbit or mouse antiserum, for 1 h; 3) 1/200 dilution of biotinylated goat anti-rabbit or horse anti-mouse immunoglobulin sera, for 30 min; and 4) avidin-biotinylated peroxidase complex (ABC), for 30 min. The ABC solution was made 30 min before its use, by adding 10 μl of avidin DH and 10 μl of biotinylated peroxidase to 1 ml of TBS.

Washing in TBS, three changes of 5 min each, was performed after steps 2, 3, and 4. Peroxidase activity was developed in the DAB medium (Graham and Karnowsky 1966), in the dark, under gentle stirring. Finally, the sections were lightly counterstained with haematoxylin, dehydrated and mounted in permanent medium.

Double immunocytochemical experiments for the simultaneous localisation of cytokeratins and vimentin in the same tissue sections were performed in selected cases (2 cases each

Table 2. Source and working dilutions of specific antisera

Reagent	Dilution	Source	References
Anti-CK, broad range (lu-5 mAb)	1/100	Dr. C. Stähli[a]	von Overbeck et al. (1985); Franke et al. (1987)
Anti-CK, broad range (PKK1 mAb)	1/200	Lab System Inc.	Holthofer et al. (1983)
Anti-CK, 39–50 Kd (CAM 5.2 mAB)	1/15	Becton-Dickinson	Makin et al. (1984)
Anti-vimentin (V9 mAb)	1/5	Boehringer	Osborn et al. (1984)
Anti-vimentin (rabbit antiserum)	1/50	Eurodiagnostic	Herman et al. (1985)

CK: cytokeratins; mAb: monoclonal antibody

[a] Central Research Division, Hoffmann-La Roche & CO, Basel, Switzerland

of normal ovaries, fallopian tubes, proliferative and secretory endometria; 3 cases of benign serous tumours and 2 cases of endometrioid adenocarcinomas of the ovary), according to the double immunolabelling technique with primary antibodies from different species of Mason et al. (1983).

Pre-digestion of the tissue sections with 0.4% pepsin (BDH) in 0.01N HCl for 7 min at 37° C was performed prior to incubation with antibodies against cytokeratins.

A breast carcinoma sample was immunostained as known positive control for cytokeratins, while normal endothelial and stromal cells of the cases under study provided "built-in" positive controls for vimentin. All these positive controls displayed strong and specific immunoreactivity for the corresponding antigens. Negative controls were obtained replacing the specific antisera with TBS and with nonimmune rabbit or mouse sera, and constantly resulted unstained.

Normal goat and horse sera, biotinylated antisera and the ABC components in kit form were purchased from Vector (Burlingame, CA, USA). The specificities, working dilutions and sources of primary antisera are detailed in Table 2.

The results of the immunoreactions were evaluated semiquantitatively with regard to the mean percentages of stained cells over the total number of normal or neoplastic epithelial cells of at least 10 high power fields (250×), and graded in a scale ranging from − (no immunostained cells) to 4+ (over 50% of the cells immunostained).

Non-cohesive tumour cells lying free in the lumina of glandular or cystic spaces were disregarded, because it has been demonstrated that epithelial cells lying free in biological fluids often acquire the capability to synthesize vimentin in addition to cytokeratins (Ramaekers et al. 1983c).

Results

The results of the current study were not affected by the use of different antibodies to the same antigen.

In all the cases under study, the normal epithelial cells consistently displayed strong and diffuse cytoplasmic immunoreactivity for cytokeratins. Moreover, a considerable number of epithelial cells of the ovary, of the fallopian tubes (Fig. 1) and of the endometrium expressed vimentin in addition to cytokeratins, whereas the epithelial cells of the endocervical mucosa were consistently unreactive to the anti-vimentin antisera (Fig. 2). The percentage of vimentin-expressing cells in the coelomic epithelium of the ovary varied from 10 to almost 100%, whereas it was less variable and always higher than 50% in the epithelia of the fallopian tubes and of the endometrium.

Vimentin was constantly coexpressed with cytokeratins in the same epithelial cells -as shown by the comparative evaluation of serial sections stained for either IF protein, and by the results of double immunolabelling experiments- but its subcellular localisation was different from that of cytokeratins. Indeed, while cytokeratins were evenly distributed throughout the cytoplasm, vimentin was more concentrated at, or mostly confined to the basal portion of the cell cytoplasm. This was a consistent finding in the ovarian coelomic epithelium and in the fallopian tubes (Fig. 1), while the pattern of vimentin immunoreactivity in the endometrial glandular cells was different in pre- and post-ovulatory conditions. Indeed, in proliferative glands, immunoreaction for vimentin resulted in a fasciculated pattern of staining, parallel to the long axis of the cells (Fig. 3), whereas in secretory glands vimentin was strictly confined to the basal pole of the cytoplasm (Fig. 4).

All the tumours examined (Table 1) revealed strong immunoreactivity for cytokeratins in almost all the neoplastic cells, with a homogeneous staining pattern of the cell cytoplasm. Altogether, 36 (43.3%) of the 83 tumours exhibited vimentin-immunoreactive cells. However, the distribution of vimentin-expressing tumours and the relative number of immunoreactive cells were variable, according to the different oncotypes and to the degree of differentiation of the malignant cases. Irrespectively of their histological subtyping, 15 of the 16 benign serous tumours and the 3 serous tumours of borderline malignancy displayed a variable number of neoplastic cells expressing both cytokeratins and vimentin.

The results of vimentin immunostaining in malignant tumours were more heterogeneous. Indeed, vimentin-immunoreactive cells were identified in 4 of the 5 well differentiated carcinomas,

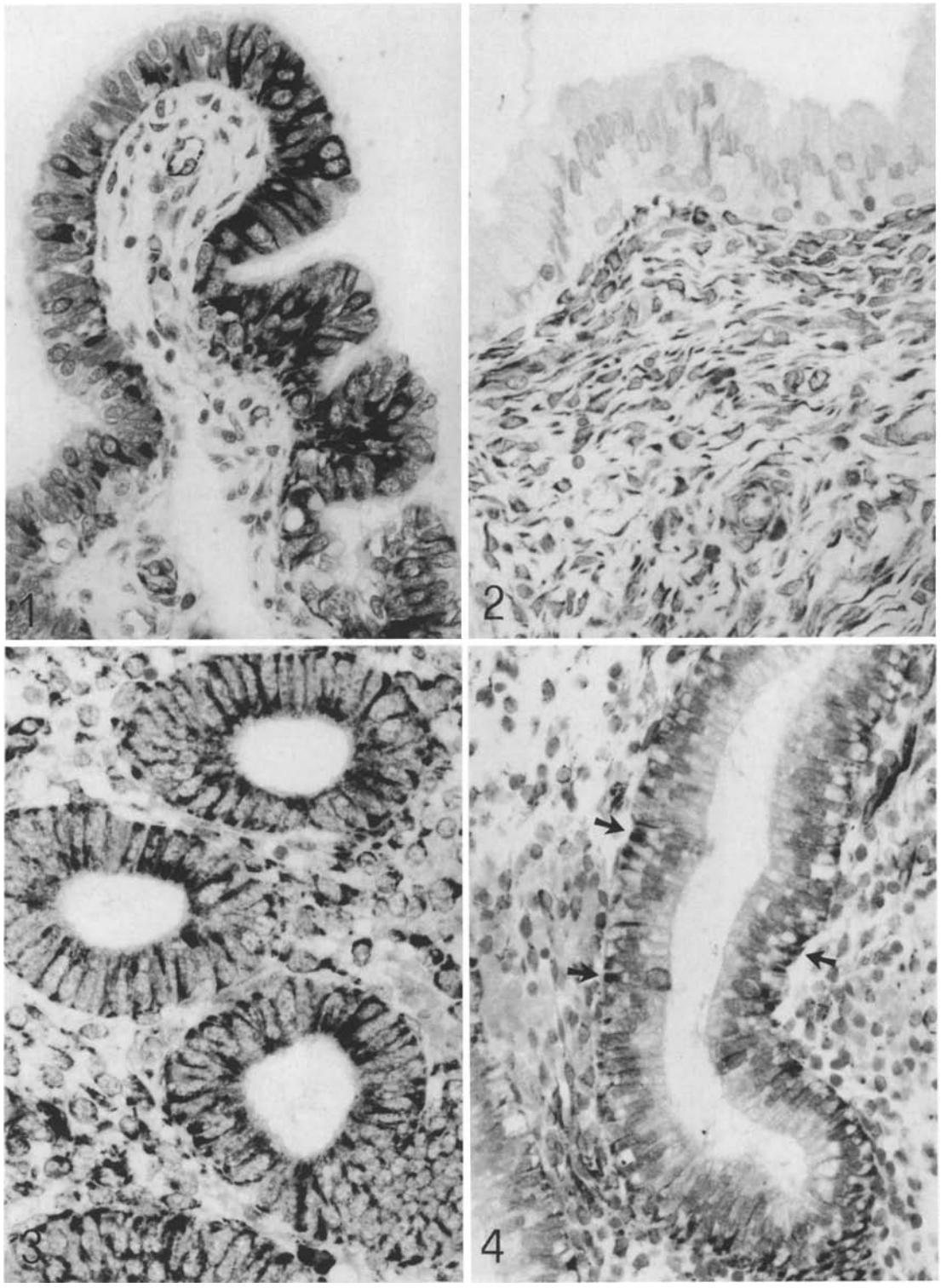


Fig. 1. The epithelial cells of the fallopian tubes show strong immunoreactivity for vimentin (V9 monoclonal antibody), which is concentrated at the lower portion of the cell cytoplasm. ×400

Fig. 2. The endocervical epithelium lacks vimentin-immunoreactive cells (V9 monoclonal antibody). ×400

Figs. 3 and 4. Immunocytochemical localisation of vimentin (V9 monoclonal antibody) in glandular cells of proliferative (**3**) and secretory (**4, arrows**) endometria, showing the different subcellular compartmentalization of this protein. ×400

Table 3. Distribution of immunoreactivity for vimentin in ovarian epithelial tumours

Diagnosis	Number of cases	Immunoreactivity[a]					
		−	(+)	1+	2+	3+	4+
Benign serous tumours	16	1	2	5	4	1	3
Serous tumours of borderline malignancy	3	0	0	1	0	2	0
Malignant serous tumours							
well differentiated	5	1	0	0	2	2	0
moderately differentiated	3	0	1	2	0	0	0
poorly differentiated	7	5	1	1	0	0	0
Mucinous cystadenomas	16	16	0	0	0	0	0
Mucinous tumours of borderline malignancy	3	3	0	0	0	0	0
Mucinous cystadenocarcinomas							
well differentiated	3	2	1	0	0	0	0
moderately differentiated	4	4	0	0	0	0	0
poorly differentiated	3	3	0	0	0	0	0
Endometrioid adenocarcinomas							
well differentiated	3	1	0	1	0	1	0
moderately differentiated	1	0	0	0	1	0	0
poorly differentiated	8	7	0	0	1	0	0
Clear cell carcinomas	4	0	0	0	2	1	1
Benign Brenner tumours	4	4	0	0	0	0	0

[a] − = tumour cells negative; (+) = less than 1% of tumour cells positive; 1+ = 1–10% positive cells; 2+ = 11–25% positive cells; 3+ = 26–50% positive cells; 4+ = more than 50% positive cells

in all the 3 moderately differentiated, and in only 2 of the 7 poorly differentiated tumours. Moreover, in this latter group, the number of vimentin-expressing cells never exceeded the 10% of the neoplastic cell population (Table 3).

Though vimentin and cytokeratins were coexpressed by the same neoplastic cells, they were not co-localised in the cell cytoplasm, since cytokeratins were evenly distributed, whereas vimentin was consistently concentrated at the basal portion of the cytoplasm (Figs. 5 and 6). This peculiar subcellular compartmentalization of vimentin was recognizable in all the cases, being more apparent in the fields with a papillary pattern of growth.

The neoplastic cells of benign, borderline and malignant mucinous tumours failed to express vimentin in addition to cytokeratins (Figs. 7 and 8), with the single exception of 1 mucinous adenocarcinoma, showing only occasional cells (less than 1% of the neoplastic population) immunoreactive for both IF proteins.

In ovarian endometriosis, more than 50% of the epithelial cells coexpressed cytokeratins and vimentin.

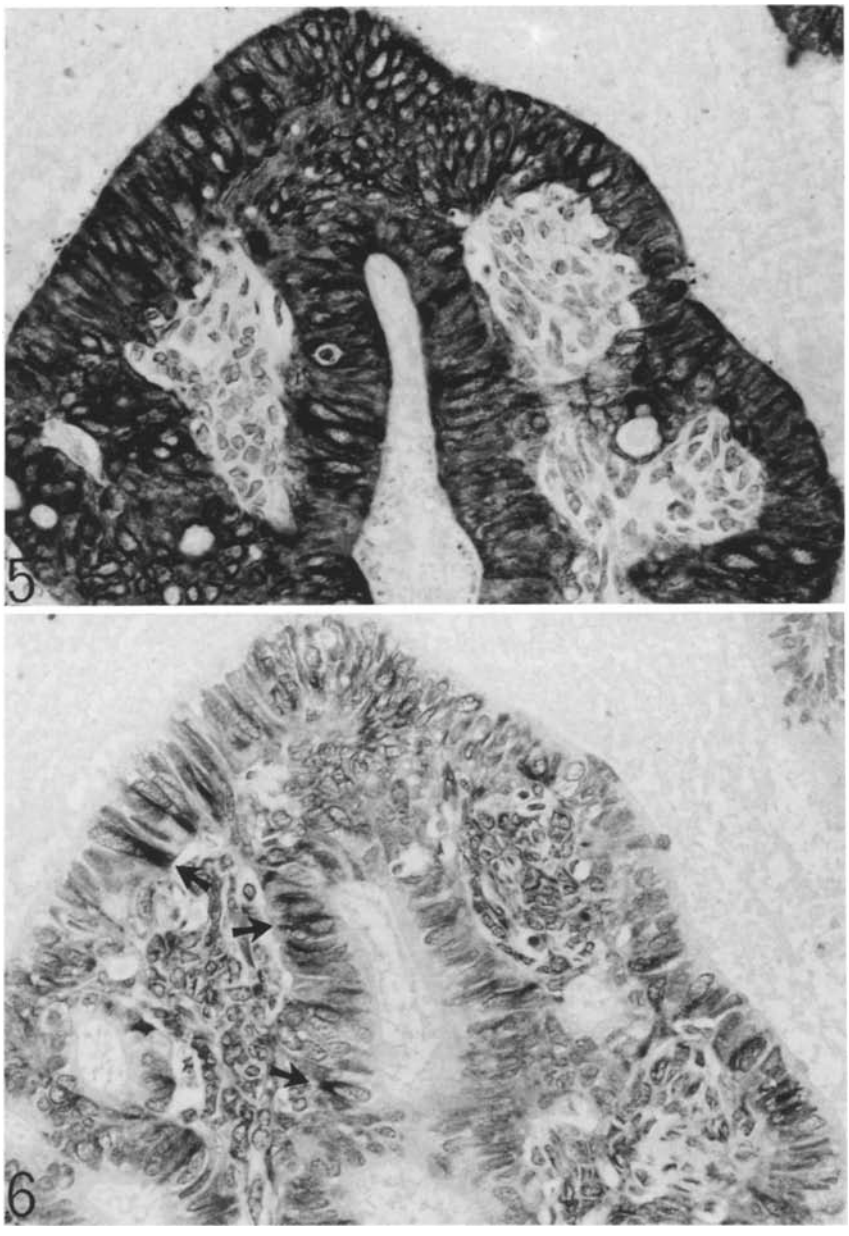
The neoplastic cells of endometrioid carcinomas showed a heterogeneous staining pattern for vimentin (Table 3). Eight of the 12 cases did not display any vimentin-immunoreactive cell, whereas in the remaining 4 cases a variable number of neoplastic cells coexpressing cytokeratins and vimentin were observed (Figs. 9 and 10). The percentage of vimentin-immunoreactive cells, however, never exceeded the 50% of the tumour cells.

The subcellular compartmentalization of vimentin in endometriosis and in gland-forming areas of endometrioid carcinomas was parallel to that of normal proliferative glands of the endometrium, whereas in the less differentiated neoplastic fields vimentin was irregularly distributed throughout the cell cytoplasm. In the 4 clear cell carcinomas under study, vimentin was always coexpressed with cytokeratins in a variable percentage of the neoplastic cells (Table 3), and was most often confined to the periphery of the cytoplasm. In none of the 4 Brenner tumours, by contrast, were neoplastic cells expressing vimentin and cytokeratins seen (Figs. 11 and 12).

Discussion

The present immunocytochemical investigation demonstrates that common epithelial tumours of the ovary show a heterogeneous pattern of IF expression. Such heterogeneity could account, at least in part, for the reported discrepancies of the IF content of these tumours (Ramaekers et al. 1982, 1983a, b; Bonazzi del Poggetto et al. 1983; Miettinen et al. 1983; Czernobilsky et al. 1984; Gown and Vogel 1985; McNutt et al. 1985; Puts et al. 1987). Indeed, while cytokeratins were invariably expressed in all the ovarian tumours of this series, the simultaneous expression of vimentin, in addition to cytokeratins, appeared to be closely related to the histological type of the neoplasms, and -to a lesser extent- to the degree of differentiation of malignant cases.

The different oncotypes of ovarian epithelial tumours share a common origin from the coelomic (surface) epithelium, which has the potential to differentiate into epithelia resembling those of müllerian derivation; the epithelium of the fallopian tubes, of the endometrium and of the endocervix (Scully 1977). Accordingly, the three major groups of ovarian epithelial tumours bear close morphological resemblances to these müllerian epithelia and their neoplasms (Cummins et al. 1974; Blaunstein 1981; Czernobilsky 1982). Our data provide

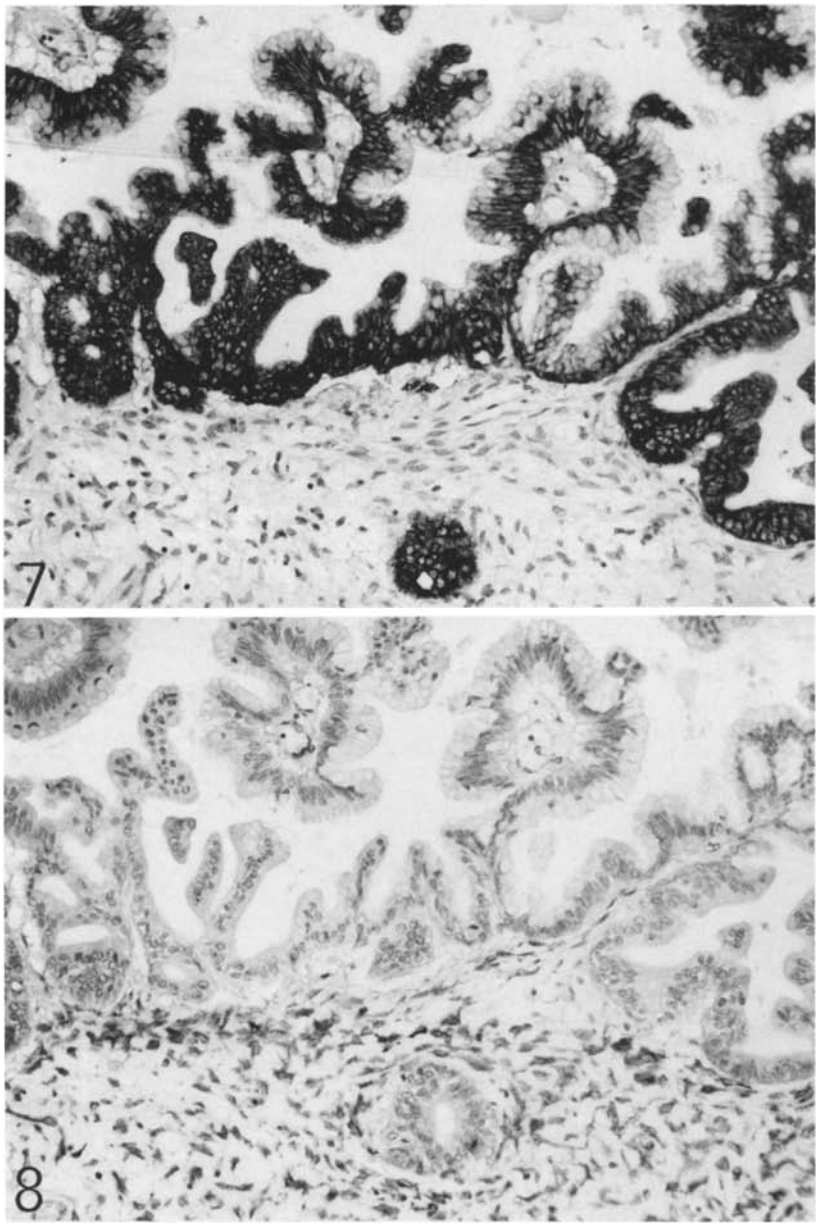


Figs. 5 and 6. In adjacent serial sections of a well differentiated serous papillary cystadenocarcinoma, several neoplastic cells coexpressing cytokeratins (lu-5 monoclonal antibody, **5**) and vimentin (polyclonal antiserum, **6, arrows**) are identifiable. ×400

further support to the suggested similarities between normal epithelia of the female genital tract and ovarian tumours of the serous, endometrioid and mucinous type, by showing that they also share a parallel pattern of IF expression.

At variance with previous findings (Moll et al. 1983), we have demonstrated that the fallopian tube epithelium consistently coexpresses vimentin in addition to cytokeratins, as does the ovarian coelomic epithelium. Adenocarcinomas of the fallopian tubes retain the capability of expressing the same two IF proteins as the parent cells (Gown and Vogel 1985), as we have also confirmed in unpublished observations. Ovarian serous tumours exhibit the same dual expression of cytokeratins and vimentin in the vast majority of cases (24/34, or 80%).

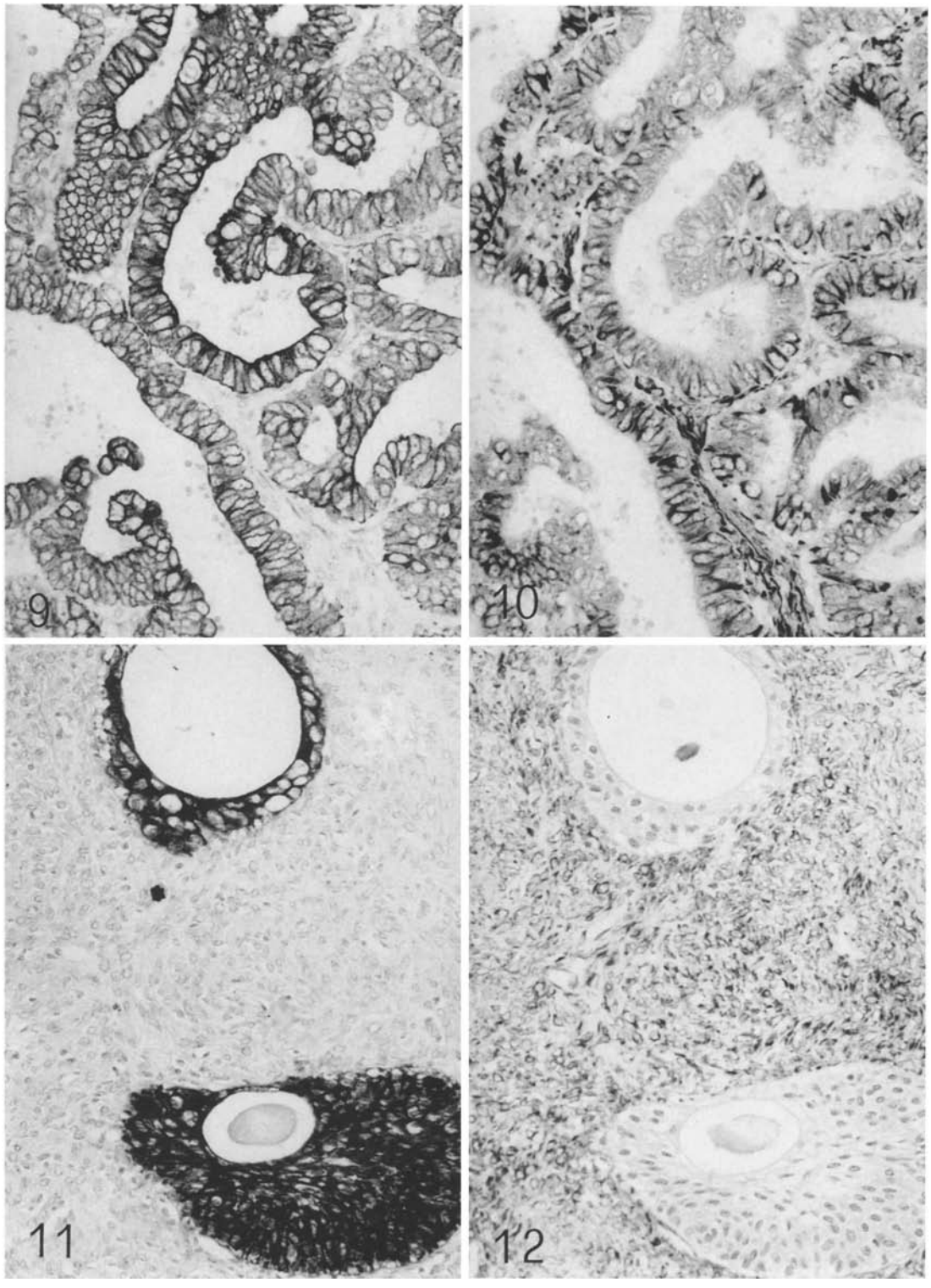
Though cytokeratins and vimentin are coexpressed by the same cells in the coelomic epithelium, in normal fallopian tubes and in ovarian serous tumours, they do not share the same subcellular localisation, since cytokeratins are evenly distributed throughout the cell cytoplasm, whereas vimentin is mostly concentrated at the basal portion of the cell. This conspicuous subcellular compartmentalization of vimentin is a common feature of normal and neoplastic cells coexpressing this IF protein with cytokeratins (Czernobilsky et al.



Figs. 7 and 8. Adjacent serial sections of a well differentiated mucinous cystadenocarcinoma immunostained for cytokeratins (lu-5 monoclonal antibody, **7**) and for vimentin (polyclonal antiserum, **8**). The neoplastic cells do not exhibit any vimentin coexpression. ×100

1985; Dabbs et al. 1986; Schröder et al. 1986; Buley et al. 1987; Doglioni et al. 1987; Henzen-Logmans et al. 1987) and probably reflects some still unknown different functional properties of the two IF proteins, when simultaneously expressed.

Vimentin immunoreactivity in serous tumours of the ovary has been previously reported as focal and restricted to a "small subset of serous carcinomas" by Gown and Vogel (1985), in 2 of 9 serous papillary carcinomas by Puts et al. (1987), and in 2 of 3 serous carcinomas (but in none of 4 serous cystadenomas) by Miettinen et al. (1983). Other investigators, in contrast, failed to detect any vimentin-expressing cells in ovarian serous tumours (Ramaekers et al. 1982, 1983a, b; Bonazzi del Poggetto et al. 1983; Czernobilsky et al. 1984). However, these previous investigations, unlike ours, have been performed on small series of cases, using mono- and polyclonal antibodies different from ours, and without taking into account the degree of differentiation of malignant tumours. In our series, vimentin was consistently coexpressed in benign, borderline and in well or moderately differentiated malignant tumours, irrespective of their histological subtypes, whereas 5 of 7 poorly differentiated serous carcinomas failed to express any vimentin immunoreactivity. This could be due to an actual reduction or suppression of vimentin syn-



Figs. 9 and 10. Most of the neoplastic cells of a well differentiated endometrioid adenocarcinoma coexpress cytokeratins (PKK1 monoclonal antibody, **9**) and vimentin (V9 monoclonal antibody, **10**) ×250

Figs. 11 and 12. The neoplastic cells of the Brenner tumours are immunoreactive for cytokeratins (CAM 5.2 monoclonal antibody, **11**) but they fail to immunostain for vimentin (polyclonal antiserum, **12**). ×250

thesis by the neoplastic cells, or to physico-chemical modifications of this protein, eventually leading to the loss of its immunoreactivity. Formalin fixation and paraffin embedding are unlike to play a major role in our failure to localise vimentin, since control structures -such as capillaries and mesenchymal cells- consistently displayed strong and specific immunoreactivity.

All the cases of ovarian endometriosis in the current investigation also showed a considerable number of cells expressing both cytokeratins and vimentin. Similar findings have been observed in normal endometrial glands, both in this study and in previous reports (McNutt et al. 1985; Dabbs et al. 1986), though we did not confirm the alleged decrease in the number of vimentin-immunoreactive cells in secretory glands in comparison with proliferative glands (Dabbs et al. 1986). Indeed, vimentin expression was always detectable in more than 50% of the glandular cells, irrespective of their functional conditions. In secretory epithelia, however, vimentin showed a different subcellular compartmentalization, since it was strictly confined to the basal pole of the cells.

Only 4 of the 12 endometrioid carcinomas of the ovary exhibited a variable number (from 1–10% to 26–50%) of neoplastic cells coexpressing cytokeratins and vimentin, with a staining pattern similar to that of normal proliferative glands of the endometrium. The better differentiated tumours showed a greater tendency to coexpress both IF proteins.

Vimentin immunoreactivity has not been reported in previous investigations on ovarian endometrioid tumours (Miettinen et al. 1983; Czernobilsky et al. 1984; Puts et al. 1987), though several reports have documented vimentin coexpression in endometrial carcinomas of the uterine corpus (Bonazzi del Poggetto et al. 1983; Gown and Vogel 1985; McNutt et al. 1985; Dabbs et al. 1986; Puts et al. 1987). Dabbs et al. (1986) reported vimentin immunostaining in a variable percentage (from 10 to 80%) of the neoplastic cells in almost 60% of endometrial adenocarcinomas. Though these authors did not ascertain any correlation between vimentin immunoreactivity and the degree of tumour differentiation, we cannot exclude the possibility that the lower percentage of vimentin coexpressing ovarian endometrioid carcinomas in our series might be related to the relative prevalence of poorly differentiated tumours (8 of 12 cases).

In contrast with serous and endometrioid neoplasms, ovarian mucinous tumours did not show any vimentin coexpression, with the single exception of a well differentiated adenocarcinoma, exhibiting occasional cells (less than 1% of the neoplastic population) immunoreactive for both cytokeratins and vimentin. The lack of vimentin in these ovarian tumours -which morphologically recapitulate the endocervical epithelium (Scully 1977) or, in almost 20% of the cases, the gastrointestinal epithelium (Fox et al. 1964; Langley et al. 1972; Fenoglio et al. 1975)- is in agreement with previous reports (Ramaekers et al. 1983a, Gown and Vogel 1985; Dabbs et al. 1986; Puts et al. 1987), and could be in keeping with the absence of vimentin-expressing cells in the endocervical and intestinal epithelium (Ramaekers et al. 1983b), as well as in cervical adenocarcinomas (Ramaekers et al. 1983a; Czernobilsky et al. 1984; Gown and Vogel 1985; Dabbs et al. 1986).

Clear cell tumours of the ovary are considered to be of müllerian nature, and closely related to endometrioid carcinomas (Scully and Barlow 1967). Our immunocytochemical findings further re-emphasize the close relationships between clear cell carcinomas of the ovary and the endometrial epithelium, showing that a considerable number of neoplastic cells coexpress cytokeratins and vimentin, as do normal endometrial glands.

Finally, Brenner tumours are composed of neoplastic cells resembling transitional cells (Cummins et al. 1973) and may originate from metaplastic coelomic epithelium (Roth 1974). These ovarian tumours lack vimentin immunoreactivity, in agreement with previous findings (Miettinen et al. 1983; Ramaekers et al. 1983a, b). This agrees with the failure of normal and neoplastic transitional cells to synthesize vimentin in addition to cytokeratins (Ramaekers et al. 1982, 1983b; Gown and Vogel 1985).

In conclusion, this investigation demonstrates that the diverse histotypes of common epithelial tumours of the ovary exhibit a different capability to coexpress cytokeratins and vimentin, according to their morphological differentiation towards müllerian-derived epithelia of the female genital tract or other (i.e., intestinal and transitional) epithelia. The divergent differentiation of these tumours includes (with the possible exception of some poorly differentiated carcinomas) the expression of the IF pattern peculiar of the normal epithelium which they recapitulate morphologically. Thus serous, endometrioid and clear cell tumours of the ovary coexpress cytokeratins and vimentin, in a similar manner as the epithelia of the fallopian tubes and of the endometrium.

This feature may be useful for distinguishing these tumours from other primary or metastatic neoplasms of the ovary, most of which express a

single class of IF proteins. Conversely, the dual expression of cytokeratins and vimentin in intra-abdominal metastatic deposits from unknown primary sites might suggest their possible ovarian origin.

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