Virchows Arch (2000) 436:52–58

ORIGINAL ARTICLE

Efthimios Sivridis · Alexandra Giatromanolaki
Michael Koukourakis · Niki Agnantis

Lectin-binding patterns in normal, hyperplastic and neoplastic endometrium: the prognostic value of concanavalin A

Received: 12 April 1999 / Accepted: 1 July 1999

Abstract Lectins are proteins and glycoproteins of non-immune origin which bind specifically to carbohydrate residues, agglutinate cells and/or precipitate complex carbohydrates. Lectin-binding patterns in normal, hyperplastic and neoplastic endometria were studied using four biotinylated lectins (Con A, LCA, e-PHA, l-PHA) and the avidin-biotin-peroxidase technique. *Canavalia ensiformis* agglutinin (ConA) and *Lens culinaris* agglutinin (LCA) reacted strongly with the luminal borders and the cytoplasm of epithelial cells but, whilst in normal and benign endometrial tissues the cytoplasmic staining was confined to the apical and the basal aspect of the cells, in endometrial carcinomas and in some atypical hyperplasias lectin binding also occurred in the lateral cytoplasm (Con-A-lat), although in differing proportions of cells. Interestingly, extensive Con-A-lat in the tumour cells was much more frequent in non-endometrioid carcinomas ($P<0.05$) and was significantly associated with poor histological differentiation ($P<0.0001$), low oestrogen and progesterone receptor content ($P<0.01$ and $P=0.0001$, respectively) and an unfavourable long-term survival ($P<0.05$). With *Phaseolus vulgaris* erythroagglutinin (e-PHA) and leucoagglutinin (l-PHA) a linear, rather inconsistent, staining at the level of the basement membranes was observed in the glands: this, also noted with LCA, appeared intact in normal and hyperplastic glands without cytological atypia, and fragmented or absent in malignant glandular structures and in most hyperplastic glands showing cytological atypia. It is concluded that changes in the distribution of lectin-binding molecules in the endometrial cells are associated with the malignant state, whilst the extent of Con-A-lat reflects the biological behaviour of the tumours.

Key words Endometrium · Endometrial carcinoma · Lectins · Con A · Prognosis

E. Sivridis (✉) · A. Giatromanolaki
Department of Pathology, Democritus University of Thrace, General Hospital Alexandroupolis, Alexandroupolis GR-68100, PO Box 128, Greece
e-mail: pathlab@users.duth.gr
Tel.: +30-551-22212, Fax: +30-551-37833

M. Koukourakis
Department of Radiotherapy and Oncology, University Hospital of Iraklion, Iraklion, Greece

N. Agnantis
Department of Pathology, University of Ioannina, Ioannina, Greece

Introduction

The cell membrane structures are rich in glycosylated proteins and lipids [9]. These molecules, particularly the glycoproteins, are important for regulating cell behaviour [9] and, in this connection, many of the aberrant properties expressed by malignant cells, e.g., loss of growth control, local invasiveness and the ability to metastasise, are related to modifications in the structure and/or distribution of carbohydrate groups from the normal [4, 29]. Evidence in support of this assumption is provided by several avenues of investigation, including biochemical analyses of cell surface glycoproteins and glycolipids, cell agglutination experiments with lectins and, more recently, histochemical studies of lectin reactivity directly onto tissue sections [15, 28]. The latter approach constitutes an improvement over the other methods for it allows examination of cells in their natural environment, in addition to providing the means of valid retrospective studies. Despite these advantages, little has been reported on the significance of lectin binding in the human endometrium [2, 22, 27]; however, it is hoped that information to be gained from such studies would be useful.

With this anticipation the present investigation was undertaken in order (a) to study the patterns of lectin binding in normal, hyperplastic and neoplastic endometrium and relate possible differences in the distribution of these molecules in malignant cells with histopathological features, and (b) to evaluate the biological significance of the observed differences by relating these to long-term survival data.

Materials and methods

Materials

Surgical specimens from 42 normal, 45 hyperplastic and 150 neoplastic endometria were retrieved from the files of the Department of Pathology, Democritus University of Thrace (Table 1) and studied for their patterns of reactivity with the biotinylated lectins: *Canavalia ensiformis* (ConA), *Lens culinaris* agglutinin (LCA), *Phaseolus vulgaris* erythroagglutinin (e-PHA), and *Phaseolus vulgaris* leucoagglutinin (l-PHA). The tissues were fixed routinely in 10% formalin. None of the patients concerned had received preoperative treatment.

Histochemical method for lectins

Reagents

All biotin-labelled lectins and their respective inhibitory sugars were obtained as lyophilised preparations from Sigma Chemical Co. From this source were also obtained: avidin, peroxidase-biotin labelled and trypsin type II crude from porcine pancreas. Normal swine serum was purchased from Dako Immunoglobulins and diaminobenzidine tetrahydrochloride, from Aldrich Chemical Co. The sugar specificities of the lectins used are shown in Table 2.

The avidin–biotin–peroxidase complex (ABC) method was used in the present study for the detection of saccharide residues in endometrial tissues [22]. In brief, 5-µm paraffin sections were dewaxed in xylene and hydrated through graded alcohols. Endogenous peroxidase activity was blocked by immersing the sections in acidified absolute methanol containing 0.3% hydrogen peroxide for 30 min. The sections were subsequently washed, first in running tap water and then in 0.05 M Tris-buffered saline (TBS) at pH 7.6. Non-specific background staining was reduced by covering the slides with 1:10 dilution of normal swine serum (NSS) for 15 min. Excess NSS was drained off and the sections then incubated with the appropriate biotin-labelled lectin at concentration 10 µg/ml in TBS with 1 mM calcium chloride ($CaCl_2$) for 30 min at room temperature. Following washes in TBS and $CaCl_2$, the sections were incubated for 60 min with a solution of 52 µl avidin in 5135 µl TBS, to which was added 13 µl biotin-peroxidase (ABC complex), prepared 30 min before required. After a wash in TBS, the sections were stained for peroxidase with the diaminobenzidine (DAB) reaction: the slides were immersed for 5 min in a filtered freshly prepared solution of 50 mg of DAB in 100 ml of TBS and 0.02 ml of 30 vol. hydrogen peroxide per 100 ml of substrate solution. Finally, the slides were counterstained with methyl green, dehydrated to xylene and coverslipped with permount.

Representative sections of normal, hyperplastic and neoplastic endometrium were treated with trypsin (0.1% for 15 min) prior to application of biotinylated lectins.

Controls

Specificity controls were performed by substitution of Tris-buffered saline pH 7.6 for the biotinylated lectins and by incubation of the conjugates with the appropriate inhibitory sugars at a concentration of 0.1 M. Normal kidney served as a positive tissue control, but most endometrial sections also had built-in positive controls in the form of mast cells [14].

Evaluation and quantitation of results

The reactivity of lectins with endometrial cells was evaluated in relation to the cytoplasm (basal, apical and lateral), the luminal border, the basement membranes and the intraluminal secretions. The extent of binding to carcinomas could be assessed efficiently only for Con A and LCA, and was scored in relation to the lateral cytoplasm. The following semiquantitative scale was used: limited, where <10% of malignant cells reacted; moderate, where 11–50% of tumour cells reacted; extensive, where >50% of tumour cells reacted; in general, the intensity of the reaction was graded as strong (++), moderate (+), weak (±) and absent (–).

Table 1 Tissues studied for patterns of *Canavalia ensiformis* agglutinin (ConA), *Lens culinaris agglutinin* (LCA), *Phaseolus vulgaris* erythroagglutinin (e-PHA) and *Phaseolus vulgaris* leucoagglutinin (l-PHA) reactivity in the human endometrium

	No. of cases
Normal endometria	
Proliferative	24
Secretory	18
Simple endometrial hyperplasia	15
Complex hyperplasia	15
Atypical hyperplasia	15
Endometrial carcinomas	
Endometrioid	123
Non-endometrioid[a]	27

[a] Adenosquamous 4, serous papillary 9, clear cell 6, mucinous 2, mixed 2, and undifferentiated 4

Table 2 The specificity of lectins used in this study

Lectin and source	Abbreviation	Sugar specificity
Canavalia ensiformis (Jack bean)	ConA	Mannose, glucose
Lens culinaris agglutinin (lentil)	LCA	Mannose, glucose
Phaseolus vulgaris erythroagglutinin (red kidney bean)	e-PHA	Bi-antennary *N*-linked sequences
Phaseolus vulgaris leucoagglutinin (red kidney bean)	l-PHA	Tri- and tetra-antennary *N*-linked sequences

Immunohistochemical method for oestrogen and progesterone receptors

Antibodies

Mouse anti-human oestrogen receptor (ER) and progesterone receptor (PR) antibodies (ER; clone 1D5, AMAC, Westbrook, Me.; PR, clone 1A6, NCL-PGR, Vector Laboratories, Burlingame, Calif.) were used and distinct nuclear staining were obtained.

Serial 5-µm paraffin-embedded sections were cut and assayed immunohistochemically for detection of ER and PR, using the ABC method. In brief, the sections were deparaffinized in xylene and rehydrated through graded alcohols. Endogenous peroxidase activity was blocked by exposure to 3% hydrogen peroxide for 5 min followed by a wash for 5 min with phosphate-buffered saline (PBS). The sections were then incubated with anti-ER (undiluted) and PR (diluted 1:10 in PBS with 1% bovine serum albumin). Sections were washed twice for 5 min in PBS, and incubated for 20 min with horse anti-mouse biotinylated secondary antibody (Vector) diluted at 1:200 in PBS. Slides were washed twice in PBS for 10 min and incubated for 20 min in preformed ABC (Vectastain Elite kit, Vector). Sections were washed and developed with diaminobenzidine tetrahydrochloride substrate (Sigma, Paisley, UK), lightly counterstained with Mayer's haematoxylin, dehydrated, cleared and mounted.

Endometrial carcinomas were regarded as being hormone receptor rich if more than 40% of the proliferating tumour cells were labelled by the primary antibody [24]. Estimations were made using an eyepiece graticule without knowledge of the clinical course.

Histological methods

Normal endometria were "dated" by using the criteria of Noyes et al. [19].

The endometrial hyperplasias were classified along the lines suggested by Norris et al. [18] and Buckley and Fox [5] as simple endometrial hyperplasia, complex hyperplasia and atypical hyperplasia.

The endometrial carcinomas were typed morphologically in accordance with the classification of Buckley and Fox [5], a classification that differs from that recommended by WHO [21] only in its recognition of the adenosquamous carcinoma as a discrete entity. The depth of invasion into the myometrium was assessed in terms of invasion of inner and outer halves. Grading and staging criteria were those defined by the International Federation of Gynaecology and Obstetrics (F.I.G.O.) in 1988 [8]. Also recorded were the presence or absence of lymphatic invasion and the extent of lymphocytic response in and around the primary tumour (trivial, moderate and prominent).

Statistical analysis

Statistical analysis and graphic presentation were performed using the GraphPad Prism 2.01 package (USA). Fisher's exact test was used to assess correlations between categorical variables. Survival curves were plotted using the method of Kaplan-Meier, and the log-rank test was used to determine statistical differences between life tables. A P-value <0.05 was considered significant.

Results

Histochemical staining

Controls

All the sections with built-in positive controls and the kidney tissues gave the expected positive result. The omission of the biotinylated lectins and their substitution by Tris-buffered saline resulted in totally negative results. With the exception of PHA (e-PHA, l-PHA), whose competitive inhibitor was not available, absorption or displacement of lectins by the appropriate sugars eliminated or completely abolished the staining reactions.

Sections with and without trypsin digestion showed similar staining patterns and comparable intensities.

Normal endometria

ConA reacted strongly with the luminal membrane surfaces and with cytoplasmic constituents, both apical and basal, of essentially all normal epithelial cells. The staining was diffuse and finely granular and involved the intraluminal secretions also, particularly during the secretory phase of the menstrual cycle. No other difference in ConA binding was noted between proliferative and secretory endometria.

Tissues treated with LCA showed a similar, though not identical, pattern of reactivity: it was somewhat less extensive and in some areas showed a weak but continuous, linear staining at the level of the basement membranes.

This linear pattern of staining, equally infrequent and weak, was the single most important feature in both proliferative and secretory endometria stained with e-PHA and l-PHA. There was no apparent cytoplasmic binding, and very little staining was seen in the form of intraluminal secretions.

Hyperplastic endometria

In endometrial hyperplasias without cytological atypia (simple and complex), the distribution and the extent of staining with ConA, LCA, e-PHA and l-PHA was, in general, similar to that seen in the normal endometria. With respect to atypical hyperplasias, variance from normal was observed only in the most severe forms of the disease, where some neoplastic glands showed disruptive basement membranes (e-PHA, l-PHA) and cells with a distinctive staining of the lateral cytoplasm (ConA, LCA).

Endometrial carcinomas

The binding of ConA to the cytoplasm of tumour cells appeared diffuse and finely granular; it was consistent, rather extensive and strong. It involved basal, apical and, to a variable extent, lateral aspects of the tumour cells (Figs. 1, 2). At this intracellular site, 36% of the endometrial carcinomas bound ConA extensively, 18% of the carcinomas bound ConA to a moderate extent, 43% of them bound Con A to a limited extent, and only 3% showed complete absence of lateral cytoplasmic binding (Table 3).

Tumour cells reacted equally strongly, but to a lesser extent, with LCA; however, staining of the lateral cytoplasm was again a feature. Thus, 17% of the endometrial carcinomas showed extensive lateral cytoplasmic binding, 18% moderate, 27% limited, and 38% no binding (Table 3). Staining of basement membranes could be seen in some cases, but only in a very small proportion of glands and these were mostly disrupted. It is noted

Table 3 Endometrial carcinomas according to the number of tumour cells reacted with ConA and LCA to the lateral cytoplasm

Extent of lateral cytoplasmic staining	ConA		LCA	
	Cases No.	%	Cases No.	%
Extensive	54	36.0	26	17.3
Moderate	27	18.0	27	18.0
Limited	64	42.7	40	26.7
None	5	3.3	57	38.0

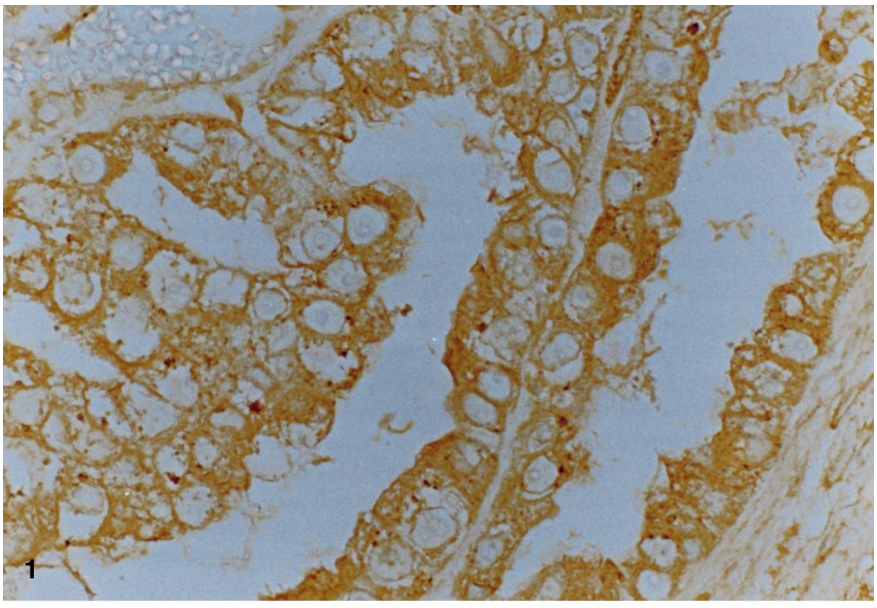

Fig. 1 Endometrial carcinoma: extensive binding of *Canavalia ensiformis* agglutinin (ConA) to the lateral cytoplasm (*Con-A-lat*) of tumour cells

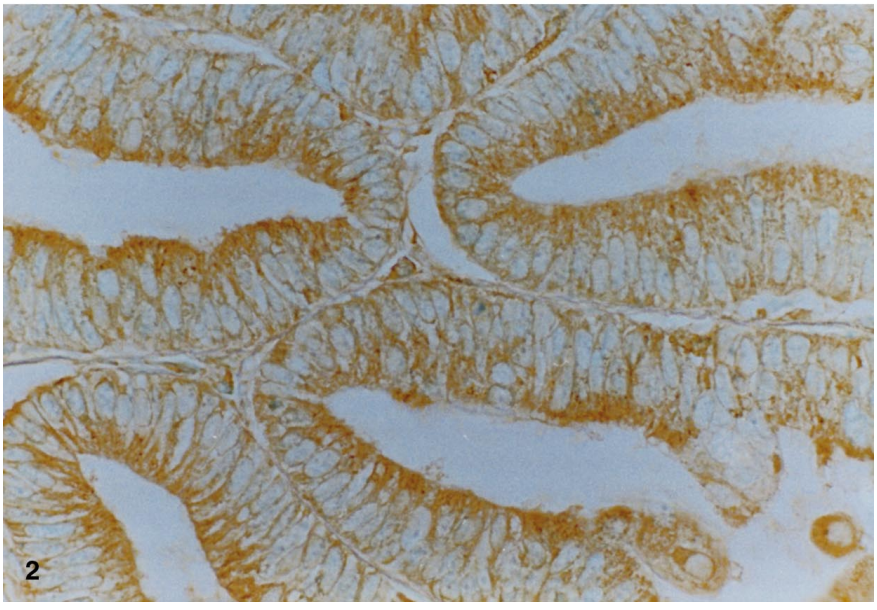

Fig. 2 Endometrial carcinoma: ConA binding to the apical and basal cytoplasm of tumour cells

that areas of squamous differentiation within endometrial tumours reacted strongly with these lectins, whilst clear cells usually reacted weakly, with an accentuation of staining at the cell periphery.

There were no differences from normal in the e-PHA and l-PHA staining properties of carcinoma cells, but the discrete linear staining of basement membranes was inconsistent, somewhat less frequent and only exceptionally intact.

Pathological correlates of "specific" ConA and LCA binding

There was a highly significant association between extensive binding of ConA to the lateral cytoplasm of tumour cells (Con-A-lat) and the histological grade ($P<0.0001$). Well-differentiated endometrial adenocarcinomas were less frequently reactive, whereas almost all poorly differentiated neoplasms bound ConA extensively to this intracellular site (Table 4). This tendency was also noted for LCA but was of no statistical significance. Similarly, when endometrial carcinomas were analysed according to the histological type, significantly more carcinomas of the non-endometrioid cell type than endometrioid carcinomas bound to Con-A-lat (17/27 vs 37/123; $P<0.05$).

Other histological and clinical characteristics of malignant endometrial disease (depth of myometrial invasion, lymphatic vascular space invasion, F.I.G.O. stage of disease and patients' age) were independent of the "specific" ConA and LCA binding (data not shown). Such relationships were not sought for e-PHA and l-PHA because of inconsistency of staining.

Table 4 Extensive binding of ConA to the lateral cytoplasm of tumour cells (*Con-A-lat*) in relation to histological type and tumour differentiation

Histological characteristic	Con-A-lat		
	No./total	%	*P*-value
Histological type			0.05
Endometrioid	37/123	30.1	
Adenosquamous	3/4	75.0	
Serous papillary	7/9	77.8	
Clear cell	2/6	33.3	
Mucinous	1/2	50.0	
Mixed	1/2	50.0	
Undifferentiated	3/4	75.0	
Tumour differentiation			0.0001
G1	15/99	15.1	
G2	15/26	57.7	
G3	24/25	96.0	

Table 5 Relationship of extensive binding of ConA to the lateral cytoplasm of the tumour cells (*Con-A-lat*) with ER and PR in endometrial carcinoma

Steroid hormone receptor status	Con-A-lat		
	No./total	%	*P*-value
ER rich	14/59	23.7	
ER poor	40/91	43.9	0.01
PR rich	12/70	17.1	
PR poor	49/80	52.5	0.0001

"Specific" lectin binding patterns versus survival. Relationships with ER and PR status

Patients with Con-A-lat had an overall poorer survival than those without (Figs. 3, 4). This association was of statistical significance for both extensive (P=0.02) and combined moderate / extensive (P=0.04) ConA binding, and was shown by corrected disease-specific survival rates. However, using different multivariate models, F.I.G.O. stage was the only independent prognostic factor (data not shown).

Interestingly, a highly significant association was established between Con-A-lat and endometrial carcinomas of PR-poor status (P=0.0001; Table 5), a marker of known unfavourable prognosis. The extent of LCA binding to the lateral cytoplasm of tumour cells was not related to patient survival, neither was the reactivity or otherwise of the basement membranes to LCA, e-PHA and l-PHA.

Discussion

Two points of interest emerged from this study. First, the distribution of saccharides in the endometrium has a relevance to the neoplastic state, though it is not useful in distinguishing frankly invasive from pre-invasive lesions. Secondly, the "specific" pattern of ConA in malignant cells is predictive of patient's survival, and this is independent of clinical and most histopathological factors of known prognostic significance.

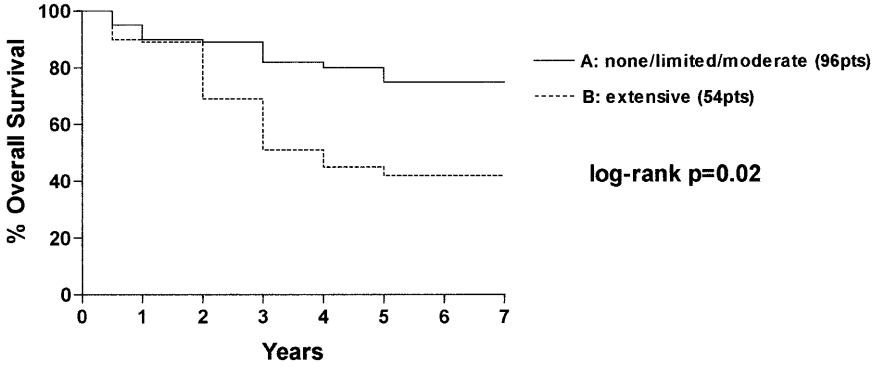

Fig. 3A, B Corrected disease-specific survival by extent of ConA binding to the lateral cytoplasm of tumour cells for all patients with endometrial carcinoma: **A** absent/limited/moderate binding, **B** extensive binding (log-rank P=0.02)

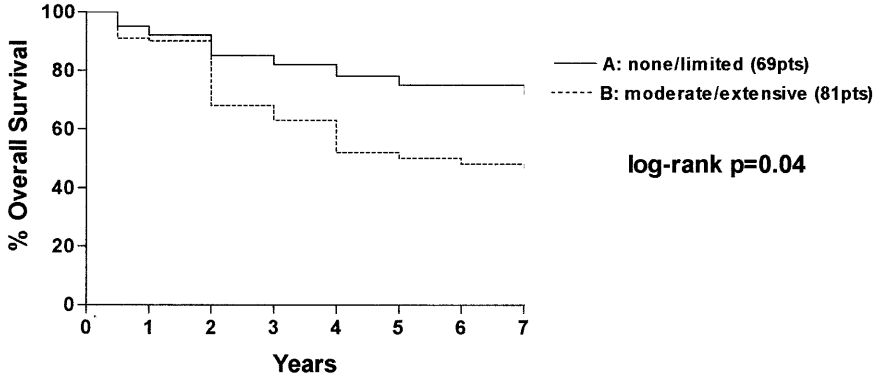

Fig. 4A, B Corrected disease specific survival by extent of ConA binding to the lateral cytoplasm of tumour cells for all patients with endometrial carcinoma: **A** absent/limited binding, **B** moderate/extensive binding (log-rank P=0.04)

Lectin binding to malignant endometrium differed from normal in the distribution of saccharide residues. Thus, in normal endometrial tissues specific ConA and LCA binding was exclusively on the basal and apical cytoplasm of the epithelial cells, showing a polarised expression. By contrast, in endometrial carcinomas a lateral cytoplasmic binding of ConA and LCA was also seen in tumour cells, resulting in a circumferential pattern of expression. With e-PHA and l-PHA, the predominant staining pattern observed was an inconsistent and rather inconspicuous linear deposit outlining the periphery of some glands; this, also noted with LCA, was intact in normal endometrium, whilst in carcinomas a mixture of intact and fragmented staining of the basement membranes was seen. Kluskens et al. [15], using fluorescent labelled lectins, reported comparable results with respect to ConA: a strong staining reaction at the luminal border of normal and hyperplastic endometrial cells; increased intensity of staining in adenocarcinomas with involvement of the entire cell periphery. A range of other lectins employed by Kluskens' group [15] was unreactive, while PHA and LCA were notable absentees from this study. Others found that *Ulex europaeus* agglutinin (UEA) bound extensively to most endometrial carcinomas, but failed to stain normal endometrial glands [2, 3, 28].

Although such observations demonstrate the usefulness of lectins in contrasting normal and malignant tissues, we found, as indeed have others [26], that the boundary between invasive and pre-invasive lesions is less clear. Apparently, simple and complex endometrial hyperplasias and the atypical hyperplasias of mild and moderate form had lectin-binding characteristics similar to those described for normal endometria, but there was an overlap in the more severe cases of atypical hyperplasia (closely packed glands with epithelial multilayering and nuclear atypia) [11] which showed disruption of basement membranes and epithelial cells exposing mannose/glucose residues in their lateral cytoplasm. The presence of such altered staining patterns in a borderline endometrial lesion, that is a lesion not readily recognised either as a severe case of atypical hyperplasia or as a well-differentiated endometrioid adenocarcinoma, far from being diagnostic of malignancy, may well be the first sign of an incipient malignant transformation.

It is of interest that, in our series, although almost all endometrial carcinomas showed some circumferential reactivity with ConA (Con-A-lat), those with the most extensive involvement were the carcinomas that displayed the most aggressive behaviour. This was borne out from our long-term survival data and the striking association of Con-A-lat with high histological grade and the non-endometrioid carcinomas [25]. This is consistent with previous suggestions that the appearance of excessive amounts of mannose and glucose residues in breast carcinomas is related with local invasiveness [17] and an increased risk of early recurrences [12]. Other features related to prognosis of endometrial cancer, such as the patient's age, the F.I.G.O. stage of disease, the depth of myometrial invasion and the presence or absence of lymphatic involvement [1, 7, 23, 25], were not significantly associated with depolarised ConA expression. Endometrial carcinomas with high affinity to *Ulex europaeus* agglutinin-I (UEA-I), however, did relate to the presence of myometrial invasion, lymphatic penetration and an unfavourable outcome [20]. Presumably, the difference in reactivity and therefore survival, within malignant endometrial tissues reflects a genuine alteration in the structure or rate of synthesis of the oligosaccharide chains to which ConA or UEA-I bind.

The predictive value of ConA on prognosis was demonstrated by neither the "isolectins" of *Phaseolus vulgaris* e-PHA, l-PHA, nor the agglutinin of *Lens culinaris* (LCA), though the latter is known to have a very similar affinity for simple sugars with that of ConA [10]. This of course illustrates the value of using two lectins with ostensibly the same monosaccharide specificity. For although differences in the staining properties of lectins expected to react with the same sugar have been well documented [10], the present report extends this observation to include a difference in the ability to expose the biological behaviour of the tumour in addition. Such differences are most probably due to the recognition of complex oligosaccharides on the cells by lectins, rather than simple sugar residues [13]. It is possible that other lectins with similar or different monosaccharide specificities may also be proved to form a useful basis for evaluating prognosis, as did biotin-labelled ConA in this investigation.

While these results would have to be verified by other independent studies, the absent or limited binding of ConA to the lateral cytoplasm of tumour cells was significantly correlated with a rich ER and PR status. This, as reported elsewhere [24], is a very favourable prognostic factor in the endometrium. Furthermore, it should be recalled that none of the patients in the series received any form of preoperative treatment, indicating that Con-A-lat identifies a different evolution of endometrial tumours independent of treatment intervention.

Finally, it should be noted that lectin binding to normal endometrium remained largely unaffected by the cycle-related changes reported earlier [6, 16], although ConA did express intraluminal reactivity more frequently during the secretory, rather than during the proliferative, phase of the menstrual cycle.

References

1. Abeler VM, Kjorstad KE (1991) Endometrial adenocarcinoma in Norway. Cancer 67:3093–3103
2. Ambros RA, Kurman RJ (1993) Association of *Ulex europaeus* agglutinin I binding with invasion in endometrial carcinoma. Int J Gynecol Pathol 12:301–306
3. Aoki D, Nozawa S, Iizuka R, Kawakami H, Hirano H (1990) Differences in lectin binding patterns of normal endometrium and endometrial adenocarcinoma, with special reference to staining with *Ulex europeus* agglutinin 1 and peanut agglutinin. Gynecol Oncol 37:338–345
4. Bhavanandan VP, Davidson EA (1982) Cell surface glycoprotein markers for neoplasia. Methods Cancer Res 19:53–105

5. Buckley CH, Fox H (1989) Biopsy pathology of the endometrium. (Biopsy pathology series) Raven Press, New York, pp 149–165
6. Bychkov V, Toto PD (1986) Lectin binding to normal human endometrium. Gynecol Obstet Invest 22:29–33
7. Connelly PJ, Alberhasky RC, Christopherson WM (1982) Carcinoma of the endometrium. III. Analysis of 865 cases of adenocarcinoma and adenoacanthoma. Obstet Gynecol 59:569–575
8. Creasman W. Announcement (1989) FIGO stages – 1988 revision. Gynecol Oncol 35:125–127
9. Crumpton MI, Owens RJ, Gallagher CJ, and Davies AA (1983) The cell surface and its metabolism. J Pathol 141:235–248
10. Debray H, Decout D, Strecker G, Spik G, Montreuil J (1981) Specificity of twelve lectins towards oligosaccharides and glycopeptides related to *N*-glycosylproteins. Eur J Biochem 117:41–55
11. Fox H, Buckley CH (1982) The endometrial hyperplasias and their relationship to endometrial neoplasia. Histopathology 6:493–510
12. Furmanski P, Kirkland WL, Gargala T, Rich MA, and the Breast Cancer Prognostic Study Clinical Associates (1981) Prognostic value of Concanavalin A reactivity of primary human breast cancer cells. Cancer Res 41:4087–4092
13. Holthofer, H, Virtanen I, Pettersson E, Tornroth T, Alfthan O, Linder E, Miettinen A (1981) Lectins as fluorescence microscopic markers for saccharides in the human kidney. Lab Invest 45:391–399
14. Kirkpatrick CJ, Jones CJP, Stoddart RW (1987) Lectin binding to mast cells granules: a new tool to study mast cell heterogeneity. J Pathol 151:69A
15. Kluskens LF, Kluskens JL, Bibbo M (1984) Lectin binding in endometrial adenocarcinoma Am J Clin Pathol 82:259–266
16. Kupryjanczyk J (1989) Cycle- and function-related changes in lectin binding to human endometrium: a histochemical study with pronase treatment. Arch Gynecol Obstet 246:211–221
17. Louis CJ, Sztynda T, Cheng Z-M, Wyllie RG (1983) Lectin binding affinities of human breast tumors. Cancer 52:1244–1250
18. Norris HJ, Connor MP, Kurman RJ (1986) Preinvasive lesions of the endometrium. Clin Obstet Gynaecol 13:725–738
19. Noyes RW, Hertig AT, Rock J (1950) Dating the endometrial biopsy. Fertil Steril 1:3–25
20. Ookuma Y, Hachisuga T, Iwasaka T, Sugimori H (1994) Assessment of lectin binding for prognosis in endometrial carcinoma. Pathology 26:225–229
21. Silverberg SG, Kurman RJ (1992) Tumors of the uterine corpus and gestational trophoblastic disease. (Atlas of tumor pathology, 3rd ser, fasc 3) Armed Forces Institute of Pathology, Washington
22. Sivridis E, Agnantis N (1996) The loss of lectin reactivity from human endometrium is a feature of malignant change. Pathol Res Pract 192:989–997
23. Sivridis E, Buckley CH, Fox H (1987) The prognostic significance of lymphatic vascular invasion in endometrial adenocarcinoma. Br J Obstet Gynaecol 94:991–994
24. Sivridis E, Buckley CH, Fox H (1993) Type I and type II estrogen and progesterone binding sites in endometrial carcinomas: their value in predicting survival. Int J Gynecol Cancer 3:80–88
25. Sivridis E, Fox H, Buckley CH (1998) Endometrial carcinoma: two or three entities? Int J Gynecol Cancer 8:183–188
26. Soderstrom KO (1987) Lectin binding to human endometrial hyperplasias and adenocarcinoma. Int J Gynecol Pathol 6:356–365
27. Toda T, Sadi AM, Egawa H, Atari E, Qureshi B, Nagai Y (1998) Affinity of four lectins for endocervical and endometrial non-neoplastic and neoplastic glandular epithelium. Histopathology 32:257–263
28. West KP, Cope JL (1989) The binding of peroxidase-labelled lectins to human endometrium in normal cyclical endometrium and endometrial adenocarcinoma. J Clin Pathol 42:140–147
29. Yogeeswaran G (1983) Cell surface glycolipids and glycoproteins in malignant transformation. Adv Cancer Res 38:289–350