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Blood group A/B-defined glycosyltransferase and A/B blood group antigens in human normal and malignant endometrium in relation to morphology, age and oestrogen levels

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We have used monoclonal antibodies to study the expression and regulation of A/B antigens and A/B transferase in normal and malignant human endometrium by immunohistochemistry. Staining was evaluated against blood group status, morphology, age and serum oestrogen levels. The expression of the antigens, in contrast to the expression of the transferase, was related to the A subtype (A_1/A_2) and the ABH secretor status. Normal, non-secretory endometria and most well-differentiated endometrial carcinomas from ABH secretors expressed the antigens and the transferase, but showed a morphology-dependent variation in the expression and degree of coexpression. In contrast, most grade 2 and 3 carcinomas were found to lack both structures, whereas secretory endometrium had a high expression of the transferase but expressed the antigens on only a few cells. The transferase expression was correlated inversely with age and positively with the level of free oestradiol in serum. Our findings suggest that A/B antigenic expression in the endometrium may be regulated at different levels – at the A/B transferase level and at a precursor substrate level – and that both genetic and hormonal factors are probably involved in the regulatory process.

Keywords: A/B gene-defined transferase, blood group ABO carbohydrate antigens, endometrial carcinoma, human endometrium

Introduction

Malignant transformation of epithelial cells is associated with changes in the carbohydrates of the blood group ABO system [1–4]. Deletion of ABH antigens, the major allogenic antigens present on erythrocytes and on most normal epithelial cells, is of prognostic significance in many carcinomas [2, 6, 7]. However, only a few studies have investigated the expression of A/B antigens in normal and malignant endometrial tissues [8–10].

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The histology of normal endometrial tissue varies in relation to ovarian function, which is further related to age and menstrual cycle [11]. Studies of murine and human endometrium have suggested that glycosylation of endometrial epithelial cells is influenced by hormonal and genetic factors [3, 4, 12–17]. Studies evaluating the expression of the A/B carbohydrate antigens in normal endometrium in relation to morphology, hormonal stimulation and genetic background are therefore needed in order to characterize possible tumour-associated changes in A/B antigen expression in endometrial carcinomas.

Cell-surface carbohydrates are secondary gene products formed by the sequential action of many different enzymes, the glycosyltransferases, which are coded for by distinct genes (Figure 1). The A/B gene-defined transferase catalyses the final step in synthesis of A/B antigens from the H-antigen. The availability of substrate (H-antigen) as well as competition between enzymes for the same substrate may influence carbohydrate synthesis and expression [18, 19]. Loss of A/B expression may be due to lack of any of the enzymes catalysing the build-up of the carbohydrate chain or to competition between enzymes at branch points (Figure 1).

The recent development of an anti-A/B transferase monoclonal antibody (mAb) [20–22] has made it possible to study immunohistochemically the presence of A/B transferase in tissue. We have used this mAb together with mAbs to A/B antigens to analyse the cellular expression of these components in human normal, premalignant and malignant endometrial tissues, in order to investigate whether the absence of A/B antigens was due to the absence of A/B transferase.

Materials and methods

Biopsies of normal and malignant endometrial tissues were obtained from hysterectomies [performed for leiomyoma ($n = 22$), irregular bleeding or dysmenorrhoea ($n = 25$), uterine prolapse ($n = 5$), ovarian tumour ($n = 2$), cervical carcinoma ($n = 15$), adenomatous hyperplasia ($n = 6$) or endometrial cancer ($n = 28$)]. The biopsies were divided into two parts. One part was mounted in Tissue-Tek and quickly frozen in precooled isopentane and the rest was fixed in formalin and embedded in paraffin. Only specimens with a defined (Table 1) histology in haematoxylin and eosin-stained sections were included [11, 23–25]. The main clinical data are summarized in Table 1.

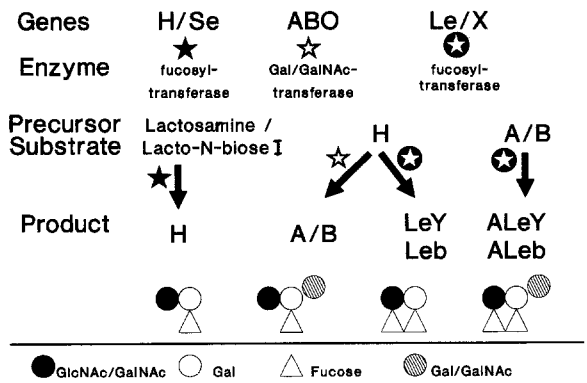

Figure 1. Biosynthesis of ABH carbohydrate structures.

ABO status (including A_1/A_2 subtyping) and Lewis blood group typings were performed by routine procedures on erythrocytes. The ABH secretor status was tested on saliva from 72 women [12]. If saliva was not available, the erythrocyte Lewis phenotype was used to predict the ABH secretor status in Le^{a-b+} and Le^{a+b-} individuals; four Le^{a-b-} individuals were of unknown secretor status (Table 1) [12, 26, 27]. Only endometrium from women with blood group A, AB or B was included in the study. Endometrium from blood group O individuals served as a negative tissue control.

Hormone analysis was carried out on blood drawn the morning before hysterectomy in 51 women. The analyses included oestrone (E_1), 17β-oestradiol (E_2), oestrone sulphate (E_1SO_4), sex hormone-binding globulin (SHBG), non-protein-bound E_2 (free E_2) and non-SHBG-bound E_2. The methods used have been described previously [4].

Immunohistochemistry

Antibodies. Details of the mAbs used are given in Table 2. The mAb HH5 was used as it has recently been shown that staining with this mAb varies during the menstrual cycle [12]. All mAbs were hybridoma culture supernatants and were used at approximately 10–40 μg/ml, except for the anti-B mAb, which was diluted 1:35 with phosphate-buffered saline (PBS) containing 15% bovine serum albumin (BSA). In addition, peroxidase-conjugated rabbit anti-mouse Ig (P260, Dako, Copenhagen, Denmark) and the ingredients supplied with the StrAviGen kit (Biogenex, Denmark) were used.

Immunohistochemical staining. The WKH1 antibody showed no reactivity in formalin-fixed tissue [28] and was therefore used on frozen sections that were post-fixed for 10 min with acetone. All other mAbs were used on sections of formalin-fixed paraffin-embedded tissue. A decrease in AH16 reactivity in formalin-fixed tissue was overcome by using the 'supersensitive' StrAviGen staining method.

Immunohistochemical staining was performed either as an indirect two-layer immunoperoxidase staining (Table 2), as previously described in detail [12], or as an indirect three-layer immunoperoxidase staining performed according to the manufacturer's instructions [13]. In all cases, the first-layer

Table 1. Morphology, ABO blood group and ABH secretor status and clinical data for specimens investigated

Morphology	Total	ABO blood type				Secretor status[a]			Hormone[b]		Median age years (range)
		A_1	A_2	B	AB	Secretor	Non-secretor	Unknown	Analysis	Treatment	
Atrophic/inactive	9	4	3	2	0	8 (1)	1	0	6	0 (1)	75 (54–81)
Weakly proliferative	8	4	3	1	0	6	2	0	6	0 (4)	49 (31–52)
Normal proliferative[c]	6	5	0	1	0	6	0	0	2	1 (1)	48 (40–50)
Normal cycling[d]	34	24	3	7	0	27 (2)	7 (1)	0	17	0 (17)	41 (24–45)
Irregular proliferative[e]	5	2	2	0	1	4	1	0	3	2 (2)	53 (42–63)
Adenomatous hyperplasia[f]	9	6	0	2	1	6 (1)	3	0	4	1 (3)	63 (51–67)
Adenocarcinoma grade 1[g]	17	11	4	2	0	12 (1)	3	2	7	5 (4)	65 (53–84)
Adenocarcinoma grade 2	9	3	4	1	1	7 (1)	2 (2)	0	3	1 (4)	69 (58–88)
Adenocarcinoma grade 3	6	2	2	2	0	2	2	2	3	1 (2)	60 (54–70)

[a]Blood group secretor status was determined as described in the text; values in brackets were predicted from the Lewis phenotype.
[b]Women who had received hormone treatment within the previous month or (in brackets) more than 1 month before.
[c]Normal proliferation based on morphology.
[d]Normal cycling indicates age below 46 years, no recent hormonal treatment and day of cycle based on clinical information (or corresponding to the subphase) [12, 33].
[e]Irregular proliferating endometria included irregular proliferative and irregular hyperplastic endometria.
[f]Adenometous hyperplasia included five patients with severe and four with mild to moderate hyperplasia.
[g]Endometrial adenocarcinomas were typed, graded and staged according to WHO and FIGO [21, 22].

Table 2. Monoclonal antibodies used in this study

Name/source	Specificity	Ig isotype	Method used[a]	Reference
WHK1	A/B transferase	IgG1	Frozen two-layer	22, 28
AH16	A determinant	IgG3	Para three-layer	29
A582/Dako	B determinant	IgM	Para two-layer	Unpublished
HH5	Chain 3/4 A	IgM	Para two-layer	30
HH2[b]	ALe^y	IgG3	Para two-layer	31
HH3[b]	ALe^b	IgG2a	Para two-layer	31

[a]Frozen, frozen acetone-fixed tissue; Para, formalin-fixed paraffin-embedded tissue; two-layer, simple indirect two-layer peroxidase staining [12]; three-layer, three-layer staining.
[b]Since the mAb to A-determinants (AH16) may not recognize difucosylated A-determinants such as ALe^b and ALe^y, all carcinomas were also investigated using mAbs to these structures.

mAb was incubated for approximately 18 h and 0.04% 3-amino-9-ethylcarbazole was used as the chromogen.

Control of specificity. The primary antibody was replaced with an irrelevant antibody of the same isotype, diluent buffer or supernatant from the myeloma cell line used for producing the hybridoma. Tissues of stratified squamous epithelium from the uteri of A_1/B ABH secretors and O individuals served as positive and negative tissue controls, respectively, in every run [32, 33].

Immunohistochemical evaluation. Staining was scored semiquantitatively (score 0, no stain; score 1, $< 10\%$ of the cells stained; score 2, between 10% and 25% of the cells stained; score 3, between 25% and 75% of the cells stained; and score 4, more than 75% of the cells stained). The reproducibility of this scoring system has been documented in a previous study [12]. The staining intensity was evaluated, but is not included.

Statistics
The Spearman rank correlation test was used to evaluate correlation between arbitrary staining scores and serum hormone levels, age, and time since last menstruation by using the computer program Medstat (Astra). $P < 0.05$ was chosen as the level of significance.

Results

A and B carbohydrates antigens were exclusively demonstrated in endometrium from women with the A and B blood groups respectively. Blood group A_1 individuals showed the highest expression of A antigen in both epithelial and endothelial cells. In epithelial cells, 40 out of 45 normal endometria from ABH secretors stained for A/B antigens, whereas only six out of 21 ABH-non-secretors expressed A/B antigens (data not shown). Vascular endothelium and erythrocytes expressed A/B antigens irrespective of the ABH secretor status. Stromal cells were unstained.

A/B transferase was expressed in a similar way in endometria from A_1, A_2 and B individuals. No staining was observed in endometrium from blood group O individuals ($n = 5$). Tissue staining patterns showed no difference between endometria from ABH secretors and ABH non-secretors. Endothelial cells, stromal cells and erythrocytes were unstained.

Both A/B antigens and A/B transferase were demonstrated in most cells in the basalis gland (Figure 2). Carbohydrate antigens were predominantly demonstrated at apical cell membranes (Figure 3) except for the type 3 chain A variant, which, like the transferase, was exclusively expressed in supranuclear cytoplasmic Golgi-like granules. The findings for the epithelial cells of the functionalis layer are now described in more detail.

Non-secretory normal endometrium
In ABH secretors, all but two out of 34 endometria stained for A/B determinants. Staining varied with morphology (Table 3, Figures 2 & 3). Only one out of five endometria from ABH non-secretors expressed A antigen and exclusively as the type 3 chain variant. Staining for A/B transferase also varied with morphology (Table 3, Figures 2 & 3). Agreement between A/B transferase and A/B antigen staining was observed in all but three of 34 non-secretory endometria from ABH secretors (Table 4). The degree of coexpression varied with morphology.

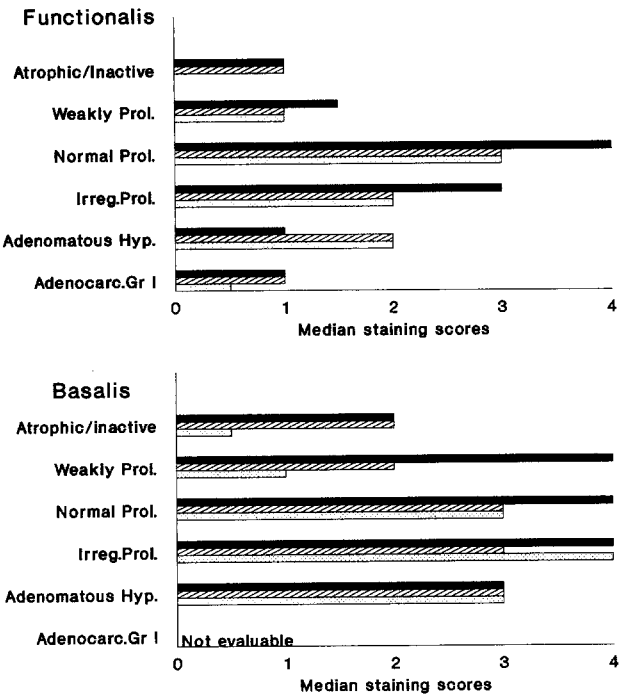

Figure 2. Median staining scores for A antigen and A/B transferase in functionalis (top) and basalis layers (bottom) of the endometrium in relation to morphology. Scores for A/B transferase include all A/B blood types and both secretors and non-secretors, whereas staining results for A antigen (AH16) are given for blood type A secretors only. The normal proliferative group includes only mid to late normal cycling endometria. ■, A/B transferase; ▨, A; □, A-3.

Secretory normal endometrium

In ABH secretors, 14 out of 17 endometria were stained for A/B antigens. Lower staining scores were found in early to mid-secretory endometria compared with the late proliferative endometria (Table 3). Secretory endometria from ABH non-secretors expressed the A determinant in one out of four cases, but expressed the type 3 A variant in three out of four cases. A/B transferase was demonstrated in most cells of all luteal and menstrual endometria. Concurrent staining for A/B antigens and A/B transferase was found in 14 out of 17 endometria from ABH secretors. However, fewer cells expressed A/B antigens than the A/B transferase (Tables 3 & 4 and Figure 3).

Adenomatous hyperplasia

In ABH secretors, A/B antigens were expressed in four of the six cases, and the type 3 chain variant of A antigen in four of five endometria (Table 3). One of three ABH non-secretors expressed A antigen in the apical cytoplasm of a few cells. A/B transferase was expressed in six out of nine cases (Table 3). The expression varied: A/B transferase was demonstrated in a few scattered cells in most cases and in most cells in two cases. Concurrent staining for A/B antigens and A/B transferase was found in all ABH secretors (Table 4).

Endometrial carcinomas

In ABH secretors, 13 out of 21 carcinomas stained for A/B antigens. Three of these stained carcinomas exclusively expressed A antigen as ALe^b or ALe^y. The type 3 chain A variant was infrequently expressed. Staining was related to grade (Table 3). In general, only a few cells were stained (Table 3 and Figures 2 & 4). A/B antigens were demonstrated in one out of seven carcinomas from the ABH non-secretors. A/B transferase was expressed in 13 out of 32 carcinomas. Expression was related to grade (Table 3), and in all but one case only single cells were weakly stained. Agreement between A/B antigen and A/B transferase staining was found in 66% of carcinomas from the ABH secretors (Table 4); nine carcinomas from ABH secretors coexpressed A/B antigens and A/B transferase, while five expressed neither of them (Table 4).

A/B transferase expression in relation to age, days since last menstruation and hormone levels

Staining scores for A/B transferase were inversely correlated with age ($R = 0.53$, $P < 0.0005$) and time since last menstruation ($R = 0.64$, $P < 0.005$) and positively correlated with serum levels of E_2, free E_2, non-SHBG-bound E_2, E_1SO_4 and E_1 (Table 5). Figure 4 shows the relationship between free E_2 levels and A/B transferase staining scores in functional endometrium.

Discussion

The presence of A/B transferase is a prerequisite for the correct termination of the synthesis of A/B antigens. The expression of A/B antigens varies in the endometrium. The present study demonstrates for the first time that the expression of A/B transferase also varies on human endometrial epithelial cells.

Whether any lack of A/B antigen expression is directly caused by a lack of A/B transferase is unknown. A/B transferase was localized in the Golgi region of endometrial cells, and its expression was very similar to the type 3 A determinant.

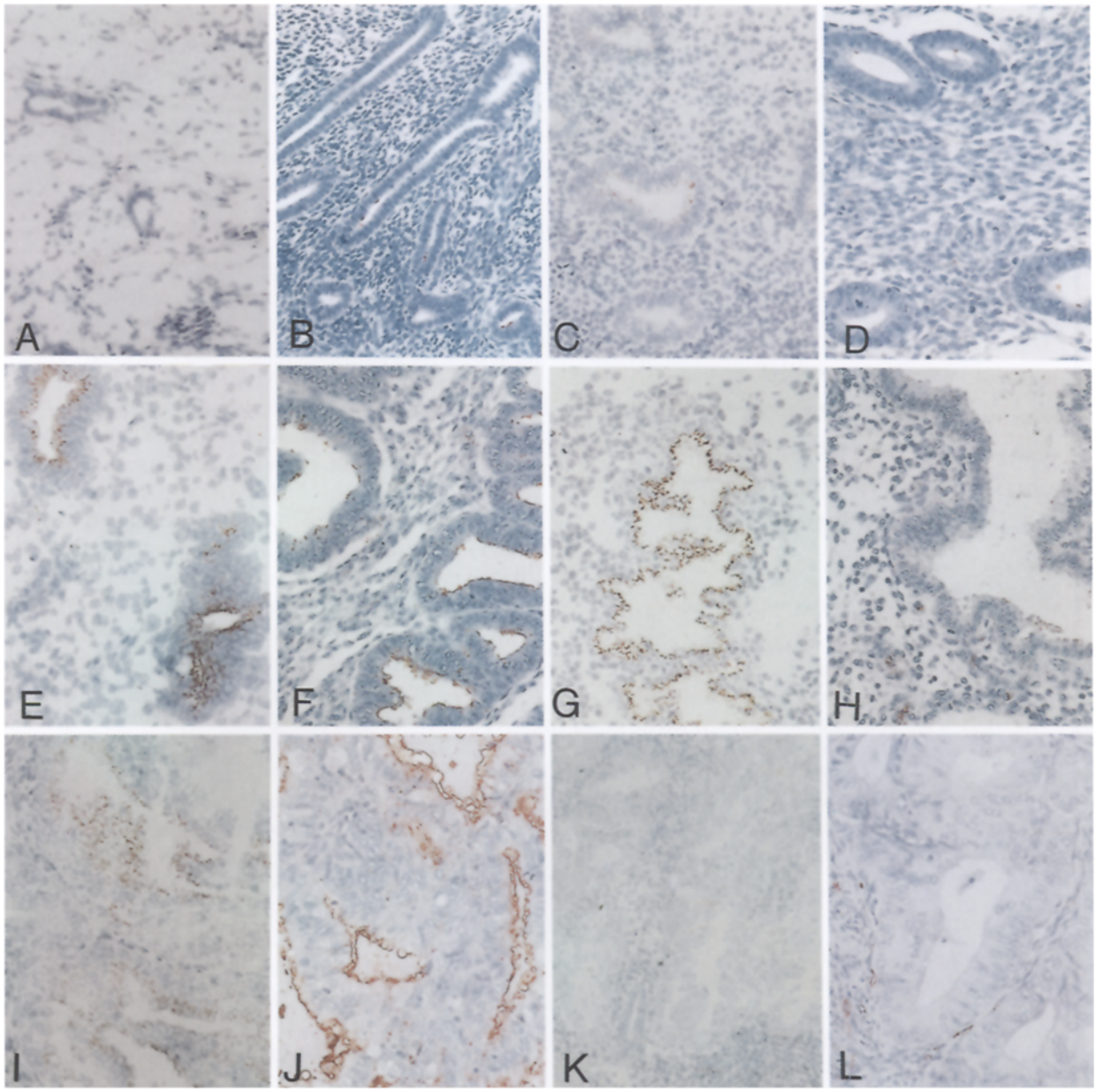

Figure 3. Immunohistochemical staining for A/B-transferase (A, C, E, G, I & K) and A-determinants (mAb AH16) (B, D, F, H, J & I). (**A & B**) Atrophic endometrium from an A_2 Le^{a-b+} secretor, (free $E_2 = 1.0$). (**C & D**) Weakly proliferative endometrium from an A_1 Le^{a-b+} secretor (free $E_2 = 4.3$). (**E & F**) Late proliferative phase endometrium from an A_1 Le^{a-b+} secretor (free $E_2 = 20.0$). (**G & H**) Mid-secretory phase endometrium from an A_1 Le^{a-b+} secretor (free $E_2 = 12.0$). (**I–L**) Grade 1 endometrial carcinomas from an A_1 Le^{a-b-} secretor (no hormone analysis available) (I & J) and from an A_1 Le^{a-b+} secretor (free $E_2 = 1.6$) (K & L). Note staining of endothelial cells in H & L. ×180.

This is in accord with recent immunohistological studies from other tissues and previous cell fractionation studies [28, 34, 35]. However, immunohistochemistry provides no information regarding enzymatic activity. Our conclusions would have been further strengthened if such an analysis had been carried out.

Although the semiquantitative method used in this study was subject to some uncertainty, it was reproducible [12]. Both A/B antigens and A/B transferase were expressed variably by endometrial glands when compared with staining of endothelial cells and of stratified squamous epithelium in positive control sections. These variations in expression seem to be related to both genetic and hormonal factors.

Table 3. Staining results in endometrium functionalis in relation to morphology

Morphology	A/B transferase[a]		A-determinant[b]		A-3 variant[b]	
	Positive/total	Score[c]	Positive/total	Score[c]	Positive/total	Score[c]
Atrophic/inactive	7/9	1 (0–4)	6/7	1 (1)	2/7	0 (0–1)
Weakly proliferative	8/8	1–2 (1–3)	5/6	1 (0–2)	3/6	$\frac{1}{2}$ (0–1)
Proliferative[d]	6/6	3 (1–3)	6/6	2–3 (1–3)	5/6	1 (0–2)
Mid to late proliferative[e]	9/9	4 (2–4)	7/7	3 (2–4)	6/6	3 (2–3)
Irregular proliferative	5/5	3 (3–4)	3/3	2 (1–3)	4/4	2 (1–3)
Early secretory[e]	8/8	4 (3–4)	5/5	1 (1–2)	4/4	1 (1–3)
Mid to late secretory[e]	8/8	4 (3–4)	4/5	1 (0–2)	4/5	1 (0–1)
Adenomatous hyperplasia	6/9	1 (0–3)	4/5	2 (0–4)	4/5	2 (0–4)
Adenocarcinoma grade 1	10/17	1 (0–4)	7/12	1 (0–4)	6/12	$\frac{1}{2}$ (0–2)
Adenocarcinoma grade 2	3/9	0 (0–4)	2/6	0 (0–1)	0/6	0
Adenocarcinoma grade 3	0/6	0	0/1	0	0/1	0

[a]Results are given for both ABH secretors and non-secretors.
[b]Results are given for ABH secretors only.
[c]Median and ranges.
[d]Excluding normal cycling proliferative.
[e]Normal cycling.

Table 4. Comparison of staining for A/B transferase and A/B antigens in endometrium functionalis from ABH secretors in relation to morphology

Group	A/B antigens[a]	A/B transferase		Agreement between antigen and transferase staining	
		−	+	Number/total	%
Normal non-secretory endometrium	−	0	2[b]		
	+	1	31	31/34	91
Normal secretory endometrium	−	0	3		
	+	0	14	14/17	82
Adenomatous hyperplasia	−	2	0		
	+	0	4	6/6	100
Adenocarcinoma grade 1	−	0	3		
	+	3	6	6/12	50
Adenocarcinoma grade 2	−	3	0		
	+	1	3	6/7	86
Adenocarcinoma grade 3	−	2	0		
	+	0	0	2/2	100

[a]Includes staining with mAbs HH2, HH3, AH16 and A582.
[b]Both endometria were from blood group A_2 individuals.

Table 5. Correlation between the staining score for A/B transferase and serum hormone levels.

Hormone	Group (correlation coefficient)[a]		
	All morphologies (51)	Normal non-secretory endometrium (24)	Neoplastic endometrium[b] (17)
SHBG	0.13 (NS)	–	–
E_2 (oestradiol)	0.67***	0.50**	0.61*
E_1 (oestrone)	0.37*	0.22 (NS)	0.33 (NS)
Non-SHBG-bound E_2	0.66***	0.55*	0.48*
Free E_2	0.71***	0.62**	0.58*
E_1SO_4 (oestrone sulphate)	0.52***	0.52*	0.41 (NS)

[a]Spearman's test: $***P < 0.0005$; $**P < 0.005$; $*P < 0.05$; NS, non-significant.
[b]Adenomatous hyperplasia and endometrial carcinomas. The number of specimens investigated is given in parentheses.

Expression of the transferase was uninfluenced by the A, B, A subtype and ABH secretor status. In contrast, the A/B antigens were expressed differently according to A subtype (A_1/A_2) and ABH secretor status. This is in agreement with previous findings [12–14]. A lower expression of A determinants in A_2 individuals is related to a lower efficiency of the A_2 enzyme compared with the A_1 enzyme [18, 30, 36]. As might be expected, this qualitative difference was not recognized by the antitransferase antibody.

Expression of A/B transferase and A/B antigens was stronger, more constant and more often concurrent in glands of the basalis than found in the functionalis. The cell morphology, expression of other blood group antigens and of oestrogen (ER) and progesterone receptors (PgR) differ between the layers on the endometrium [11–14, 37]. The so-called progenitor cells in the basalis are thought to be responsible for regenerative growth during menstruation. Thus, the observed differences in carbohydrate antigen expression may play a part in the regulation of receptor involved in cell function.

In normal endometrium from ABH secretors the functional glands were found to coexpress A/B transferase and A/B antigens but with a morphology-dependent variation in both expression and degree of coexpression. Expression of A/B transferase was related to age and E_2 levels. A/B antigen expression can be regulated at the level of

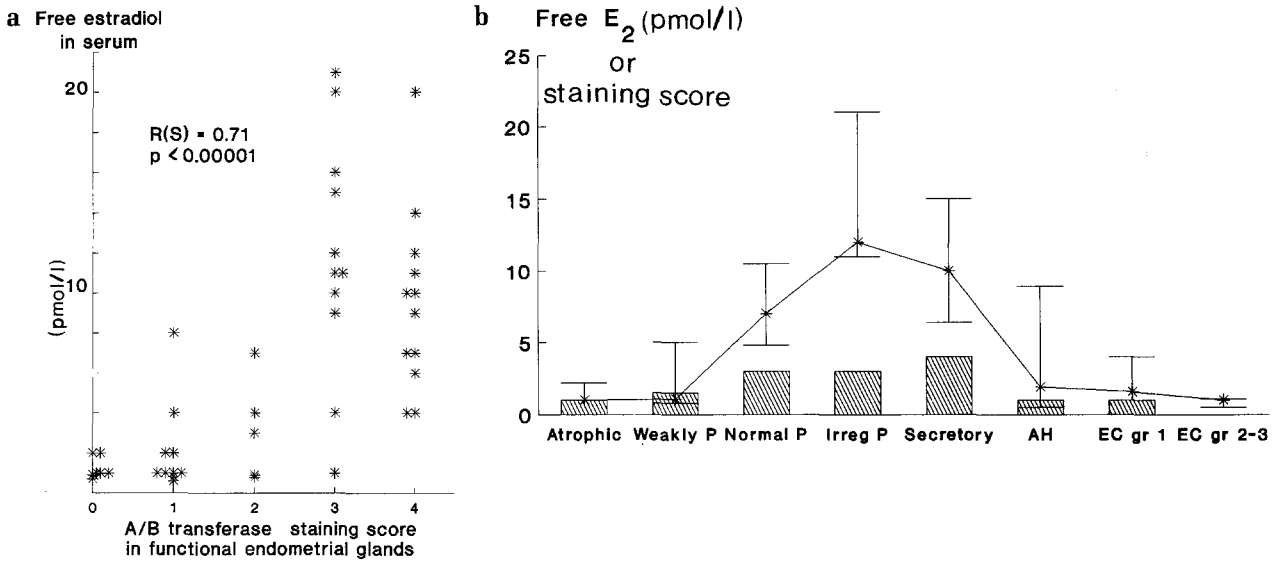

Figure 4. Serum levels of free estradiol (E2) in relationship to median staining scores for A/B transferases in the functionalis layer. In Figure 3A hormone levels are plotted against transferase scores for all morphologies (n = 51); in Figure 3B, hormone and enzyme levels are given for the different groups, the former being shown as a horizontal line and 25% and 75% percentile levels and the latter as a histogram. I, 75% percentile E2; I, 25% percentile E2; —✳—, median E2 value; ▧, A/B transferase.

the A/B transferase, as shown for stratified oral epithelia and urothelium [28, 34, 38, 39], or at a precursor substrate level, as shown in the case of distal colon [40, 41]. However, the level at which antigenic expression is regulated in normal endometrium cannot be accurately predicted from our results. The concurrent expression of A/B transferase and A/B antigens found in most cases (Table 4) indicates the presence of active enzyme and makes regulation at the A/B transferase level possible. On the other hand, the variations in degree of coexpression and the lack of concurrency found in some cases suggest other mechanisms, such as variations in enzymatic activity, presence of truncated enzyme or a regulation at a precursor substrate level.

Variations in the activity of the A/B transferase cannot be excluded since our mAb is reactive not with the catalytic site on the enzyme but with another part of the transferase molecule. In other studies measuring enzyme activity, the B-transferase activity in serum was found to vary during the menstrual cycle, with the lowest values in the first half of the luteal phase [42]. Such a decrease in A/B transferase activity could explain our present findings in secretory endometrium, which expressed high levels of A/B transferase but showed a low A/B antigenic expression when compared with late proliferative phase endometrium.

Regulation of A/B antigenic expression at a precursor substrate level in both normal non-secretory and secretory endometrium is likely; H-determinants show an insignificant expression in all normal endometria. However, Le^y, the fucosylated derivative of H-antigen, has a very high expression in atrophic endometrium compared with expression in proliferating endometrium [3, 4, 12–14]. In the secretory endometrium, short sialylated precursor-chain carbohydrates such as sialosyl-Tn and monosialosyl-Le^a accumulate coincident with the decrease in A/B carbohydrate expression [12, 13]. Thus, the availability of H-antigen could vary with morphology, but in an opposite manner to the content of A/B transferase. It has recently been shown that oestrogen stimulates and progesterone inhibits α-1–2-fucosyltransferase activity in murine endometrial epithelial cells [43]. A complex and possibly hormonally influenced regulation of A/B antigenic expression at different levels in the normal endometrium is therefore likely.

Most endometrial carcinomas from ABH secretors showed a concurrent low expression or a concurrent lack of A/B transferase and A/B antigens. In previous studies, these tumours have been shown to accumulate H-determinants [3, 4]. This suggests regulation of A/B antigen expression at the transferase level. Previous studies have also suggested an increased fucosylation in endometrial carcinoma cells [3, 4, 9, 13]. In accordance with this, A-antigen was demonstrable exclusively as

the difucosylated variants of A-antigen (ALe^b or ALe^y) in some carcinomas. Adenomatous hyperplasias and grade 1 carcinomas with high levels of free E_2 showed a high A/B transferase and, in ABH secretors, a high A/B antigenic expression. The significant correlation found between E_2 levels and A/B transferase staining scores was preserved in the malignant endometrium. Receptors essential for the mediation of oestrogen (ER) and progesterone (PgR) actions are preserved in most adenomatous hyperplasias and grade 1 endometrial carcinomas [44]. Thus, the expression of A/B antigens in endometrial carcinomas is possibly related to serum oestrogen levels. However, no studies have evaluated the impact of ageing on glycosylation in adult cells or tissues.

Total lack of A/B transferase and A/B antigen expression was related to tumour grade and was found mainly in grade 2 and grade 3 carcinomas [10]. This indicates that deletion of the transferase and consequently the A/B antigens may be a rather late event in neoplastic transformation. The diagnostic use of A/B transferase or A/B antigens seems to be limited owing to the varied and possible hormonal influence on the transferase activity and the additional genetic influence on antigenic expression. Any prognostic significance remains to be elucidated.

In conclusion, the present study shows that both A/B carbohydrate antigens and A/B transferase are variably expressed in the human endometrium. Apart from genetic factors, hormonal factors also seem to influence antigen expression. Our findings suggest that antigen expression may be regulated at different levels in the stepwise synthesis of A/B determinants, and that the loss of antigen expression in endometrial carcinomas is likely to be related to a loss of A/B transferase.

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