

## ARIAS-STELLA REACTION—AN EVOLUTIONARY PHENOMENA

by

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Pregnancy in the human female is accompanied by numerous rather momentous changes in the genital tract and the uterus in particular. Many of these changes have been clearly defined, others, undoubtedly await discovery. It was not until 1954, when Arias-stella emphasized the atypical nature of endometrial epithelium when there is trophoblastic tissue within the body that attention began to be paid to these changes. He studied 182 cases of abortion, 26 cases of hydatidiform mole, 14 cases of chorion-epithelioma, 4 cases of syncytial endometritis and 1 case of ectopic pregnancy. He pointed out that finding atypical endometrial changes may be of value in making a presumptive diagnosis of pregnancy. The changes consist of focal enlargement of the glands, nuclear hypertrophy, hyperchromatism, with folding of nuclear membrane. The cytoplasm is vacuolated, abundant, slightly acidophilic. There is loss of polarity. Mitosis are frequent. Since Arias-stella's original paper, literature has repeatedly stressed the importance of Arias-stella reaction, in the diagnosis of extrauterine pregnancy (Tremner, 1956; Pildes and Wheeler 1957; Frederiksen 1959). Moller (1959) reported the Arias-stella reaction

in the opposite horn, with pregnancy in one horn of a bicornuate uterus. Arias-stella (1958) reported 3 instances of minimum atypia in apparently normal early intrauterine pregnancy. Roach *et al* (1960) have reported a higher incidence in term pregnancy than with choriocarcinoma, syncytial endometritis or hydatid mole. The purpose of this paper is to see the changes in endometrial glands in cases of intrauterine pregnancy and the value of atypical endometrial reaction.

### *Material and Method*

This report is based on the histological study of endometrial curettings on the files of the department of Pathology, S. V. Medical College, Tirupati during 1973 and 1974. There were a total of 1957 endometrial curettings out of which 243 were studied in detail for they showed either chorionic villi, or decidua with heavy infection or decidua with thick blood vessels, fibrinoid necrosis and inflammation suggestive of intrauterine pregnancy. Out of these, 152 were selected for this study for they showed adequate representation of anatomically normal endometrial glands, unaffected directly by the insertion of the placenta. In the rest endometrial glands were not present and hence the reaction of the endometrial glands could not be assessed and were eliminated. The clinical diagnosis in 152 cases is set out in Table I and the type of reaction

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of endometrium in Table II. The tissues were fixed in 10% formal saline processed in usual way, sections of 5 to 7 microns were made and stained with haematoxyline and eosin. Sections with Arias-stella reaction were stained with PAS and mucicarmine.

decidua with heavy infection. There were 5 cases with Arias-stella reaction, and 25 without Arias-stella reaction. Sixty-eight cases were in group II. These cases showed chorionic villi. Arias-stella reaction was seen in 8 cases. Fifty-four cases were in group III

TABLE I

*Clinical Diagnosis in 152 Cases Showing Endometrial Glands in Intrauterine Pregnancy*

Clinical diagnosis	With Arias-Stella reaction	Without Arias-Stella reaction	Total
Post abortional bleeding	6	79	85
Incomplete abortion	1	21	22
Septic abortion	—	2	2
Missed abortion	3	—	3
Vesicular mple	—	11	11
D.U.B.	8	11	19
Sterility	—	2	2
Secondary amenorrhea	2	—	2
Polymenorrhoea	3	3	6
Total	23	129	152

TABLE II  
*Reaction of Endometrium*

Secretory phase	5
Resting or proliferative phase	119
Mixed	5
Arias-stella reaction	23

showing thick blood vessels, fibrinoid necrosis, haemorrhage signifying that the pregnancy was intrauterine. Ten of them showed Arias-stella reaction.

### Results

Typical Arias-stella reaction was seen in 23 cases. The cases were grouped into 3, as shown in Table III. In group I, there were 30 cases. Curetting showed

The endometrial glands were greatly enlarged, the cells showed hypertrophy and hyperplasia, the cytoplasm was vacuolated and gave a negative reaction to PAS and mucicarmine. In areas the cells were so much proliferated that they were thrown into folds with very little stroma in between the glands. The

TABLE III

*Incidence of Arias-stella Reaction and the Changes Suggestive of Intrauterine Pregnancy*

	With Arias-stella reaction	Without Arias-stella reaction	Total
Group I Decidua with infection	5	25	30
Group II Chorionic villi.	8	60	68
Group III Fibrinoid necrosis of the blood vessels	10	44	54
Total	23	129	152

nucleus was also enlarged and hyperchromatic. Sometimes pyknosis was present. Mitosis was frequent.

#### Comment

It is well known that under chorionic gonadotrophins, the endometrial glands are stimulated. The nucleus is enlarged and the cytoplasm is foamy. This may be focal or involve several glands (Lloyd & Fienburg 1965). Ferguson (1949) mentioned that the enlarged irregular and hyperchromatic cells may be mistaken for cancer of the endometrium in cytospreads. Hilrich & Hipke (1955), Pildes & Wheeler 1957 and Mekles *et al* (1961) have made similar observations.

The incidence of Arias-stella reaction in intrauterine pregnancy has been quite variable. The reported incidence is as high as 70% and as low as 0 percent. This variation is explained on the basis whether minor degrees are included in the study. Those who have excluded minor degrees of atypism, like we, find that the incidence is low.

Group I cases were clinically diagnosed as intrauterine abortion. Examination of the uterine contents showed decidua and endometrium but no chorionic villi. Failure to find may be due to (1) chorionic villi and membranes were shed as a cast before curettage was performed. (2) chorionic villi were never present in the uterus i.e. pregnancy was extrauterine, provided adequate sample of material is submitted. In our cases we have excluded extrauterine pregnancy. In this group, the incidence of Arias-stella reaction was 16.7% compared to group II and III where the incidence was 11.8% and 18.9% respectively. It could be seen from this study that when the chorionic tissue is present in the sampling, the in-

cidence is lowest compared to Group I and III. It is probable that when chorionic villi are present there is likelihood of prolonged bleeding and shedding of atypical epithelial cells.

There are many theories to explain the etiology of the Arias-stella reaction. According to Deelman (1933) the atypical changes can be attributed to inflammatory and degenerative process in the endometrium so frequently seen in abortions. Aguerro (1950) explained its histogenesis as a result of pregnancy and inflammation. In the series of Kulj *et al* (1963), there is no evidence of infection associated with Arias-stella reaction. Arias-stella (1955) came to the conclusion that the endometrial changes are the result of hormonal activity of chorionic tissue and confirmed this in experimental rats. Pildes & Wheeler (1957) agreed with this view. The greatly enlarged vacuolated clear cells are due to hydropic degeneration as the cells were negative for PAS and mucicarmine stains. This change, together with folding of the nuclear membrane and pyknosis indicate that the Arias-stella reaction is due to involutionary change consequent to the death of foetus (Overbeck 1962). The appearance of mitosis is due to resumption of cyclic ovarian function.

When Pathologists suggest the diagnosis of Arias-stella reaction from the study of curettings, the clinician expects the presence of chorionic villi. In the absence of chorionic villi decidua in the curettings, the reaction suggests ectopic gestation (Birch and Collins 1961).

Since Abortion Law is liberalised in India, in future it will be possible to study greater number of medically terminated early pregnancies and more light may be thrown on Arias-stella reaction.

*Summary*

One hundred and fifty two cases of curettings from intra-uterine abortions were studied for Arias-Stella reaction. Twenty-three showed Arias-stella reaction.

The clear cells characteristic of Arias-stella reaction are due to involutory change consequent to the death of the foetus. They do not contain glycogen. The atypical change in the endometrial glands helps in diagnosis of intrauterine pregnancy, when products have been aborted before admission into the hospital or when products are not accessible to the curette as in extrauterine pregnancy.

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See Figs. on Art Paper I