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Editorial

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# Why Aerobic Vaginitis (AV) should not be called Desquamative Inflammatory Vaginitis (DIV)

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## Editorial

Since several decades it has become increasingly clear that the presence of vulvovaginal complaints and vaginal discharge can be caused by more than Candidasp or bacterial vaginosis. The same gynecologist, Herman Gardner, who fist described bacterial vaginosis and saw his name been given to its main causative microorganism Gardnerella vaginalis, also was aware of another vaginal condition that caused distress and increased vaginal discharge, and described the condition 'desquamative inflammatory vaginitis' as early as 1968 [1]. He described 8 cases with an ulcerative disease of the vagina, demonstrating a combination of increased numbers of parabasal epithelial cells, loss of lactobacilli, and increased inflammation. As it was not recognized as an infection, some thought of it as a chemical vaginitis after vaginal douching with toxic ingredients [2], an emphysema-like disease like in the skin [3], vitamin D deficiency [4], an atrophy of the vagina despite normal circulation estrogens [1] or a condition linked to the presence of a cervical ectropion [5]. As treatment, originally, corticosteroids were thought to be most efficient [1], but later, also antibiotics like clindamycin [6] and vitamin D were tried [7], with some success in selected cases.

Some 50 years later, driven by the inconsistency of treatment results with metronidazole in many women with dysbiosis (i.e. loss of lactobacilli, vaginal dysbiosis, or 'Abnormal Vaginal Flora (AVF)'), we described another new entity in the vagina: Aerobic Vaginitis (AV). In this condition, like in bacterial vaginosis, there is an increased vaginal discharge, sometimes foul smelling, decrease or absence of vaginal lactobacilli and an increased pH above 4.5. But unlike in bacterial vaginosis, there are low numbers of clearly aerobic bacteria, instead of the highly abundant anaerobes, combined with increased

inflammatory cells in some women, and signs of vaginal atrophy indicated by the presence of increased numbers of parabasal vaginal epithelial cells in others **[8]**. Clearly, failure to recognize this condition amongst all women with AVF has led to many therapeutic failures with non-response to metronidazole or even clindamycin, and failure to prevent complications in pregnancy in women with dysbiosis **[9-11]**.

It is clear that some resemblances exist between the three conditions, bacterial vaginosis, aerobic vaginitis and desquamative inflammatory vaginitis. Soon it became clear that the non-inflammatory condition bacterial vaginosis, was very different in pathogenesis, diagnostic techniques and treatment options as compared to the other two. This has lead some authors to equalize the other two conditions as one and the same, as if AV is a small form of DIV, and should not be considered as a separate entity **[12]**? We disagree with this and since the beginning, we argued that DIV is an end stage of AV, representing the most severe form of AV, where all pathologic components of AV are present to a maximal extent. The diagnosis of AV has the strength that it studies both the bacterial abnormalities in the vaginal canal, as well as the host response. Five criteria are considered and receive 3 possible scores: 0 (absent), 1 (low grade present), and 2 (significantly present). Besides scoring the lactobacillary grades **[13]**, and recognizable aerobic pathogens (small rods, or cocci), also the level of inflammation is scored (proportional number of leukocytes in relation to epitheliocytes), the type of leukocytes (normal or toxic appearance) and, finally the level of atrophy, measured according to the proportional number of parabasal cells compared to superficial epithelial cells **(Table 1) [8]**. This allows to divide the vaginal disease in a quantitative (light, moderate or severe) pathology on the one **(Figure 1)**, and in a functional one (infectious, atrophic or inflammatory subtype) on the other hand **(Figure 2).** This severity level and functional characteristic is of crucial importance as it helps the physician to compose an adjusted treatment according to the needs of the patient, and tailor it during the course of healing. Indeed a purely infectious condition with overwhelming presence of aerobic bacteria may benefit most from a short antibiotic course, followed by supportive local treatment such as probiotics, while a predominantly inflammatory condition may require some additional local cortico steroid therapy in form of a cream or vaginal ovula **(Figure 2)**. The basic cornerstone of treatment, especially when the atrophic component is evident, is the local application of a stronger type of natural estrogen, such as estradiol valerate **[14]**. Indeed, sophisticated research using DNA based vaginal microbiome patterns in patients with AV, have demonstrated that immunologic and hormonal factors, such as vaginal estrogen receptor sensitivity, play a crucial role in its pathogenesis and, as a consequence, treatment options **[15]**.

| AV Score | LBG | No. of leukocytes | Proportion of toxic leukocytes | Background flora | Proportion of PBC |
|---|---|---|---|---|---|
| 0 | I and IIa | ≤10/ hpf | None or sporadic | Unremarkable or cytolysis | None or <1% |
| 1 | IIb | >10/hpf and ≤10/epithelial cell | ≤50% of leukocytes | Small coliform bacilli | ≤10% |
| 2 | III | >10/epithelial cell | >50% of leukocytes | Cocci or chains | >10% |

**Table 1:** Composition aerobic vaginitis score (AV score) using 400x magnification on phase contrast microscopy. AV score 1 to 2 represents normality. A score of 3 to 4 corresponds to light AV, a score of 5 to 6 to moderate AV, and a score above 6 (to maximum 10) to severe AV. The highest scores (AV score 8-10) corresponds to Desquamative Inflammatory Vaginitis (DIV) [8].

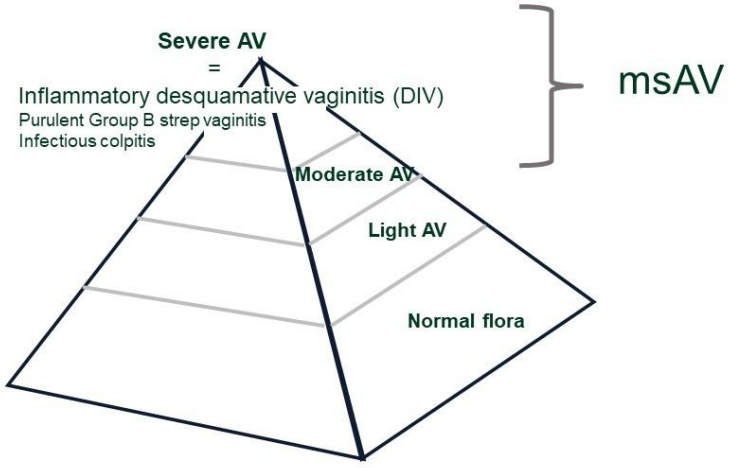


**Figure 1:** Diagram depicting the severity scores of AV. A score of >8 corresponds to the diagnosis of Desquamative Inflammatory Vaginitis (DIV). AV score > 4 corresponds to moderate-severe AV (msAV) and is linked to numerous pathologies [8].

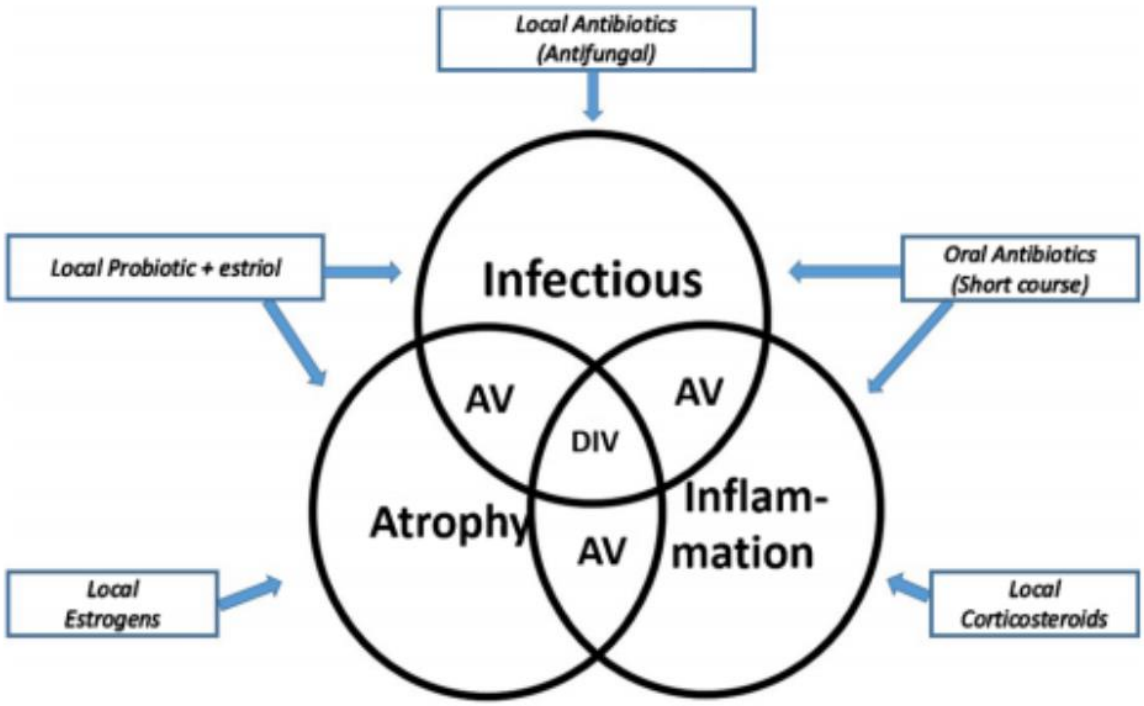


**Figure 2:** Subtypes of AV, as diagnosed in fresh wet mount microscopy. In circles, the different subtypes of AV are demonstrated. The 3 subtype components can present in a lesser or stronger way, and can co-exist in different combinations. This enables to compose the most appropriate therapy (in squares), combined in a local cream, applied vaginally, and allows a proper follow up and adjustment of therapy. In the middle, we severe forms of all components collide, a condition known as 'Desquamative Inflammatory Vaginitis' is found. AV is not the same as less severe DIV as the composition and consequent treatment of AV entirely depend on the differential microscopic findings. Courtesy to Elsevier France for the kind permission to reproduce this figure **[16]**.

The most extreme form of AV, when all three subtypes are maximally disturbed, is called DIV, and requires treatment with a combination of all above, in our hands leading to the best results. Follow up exams, with obligatory microscopy analysis of the vaginal fluid, often allow to downsize the complexity and dosage of the treatment, guided by the clinical and microscopy findings. Microscopy use in gynecology may be outmoded but is crucial to provide proper diagnosis and follow up in these conditions, as in general lab generated Gram stains and culture results will not be of much help to steer the therapy. While some women require some sort of maintenance treatment on the long term range, others can wane the therapy and eventually stop all interventions and stay well.

So while DIV is the 'tip of the iceberg', combining the most severe abnormalities of atrophy, infectious disruption and inflammation (AV Score of 8-10), AV describes in more detail the underlying arms of either inflammatory, atrophic or infectious disturbance, and its severity (light, moderate, severe), allowing tailored, individualized therapy. In the follow-up, detailed microscopic analysis of these arms allows individualized adjustment of the treatment, by changing the composition of the cream according to

the microscopic findings. Like the diagnosis and treatment of diabetes mellitus is not the same as diagnosis and treatment of 'a little version of diabetic coma', AV is also not a 'little bit of DIV'. Therefore, we propose to reserve the term DIV for this severe, disrupted condition with vaginal ulceration in which all three components of AV are maximally present (AV score >7), while the more common condition AV comes in different shapes and severity grades and hence cannot be looked upon as 'minor DIV'. Understanding the vaginal microflora abnormalities in this profound way, increases by and large the chances for patients to get optimal individualized treatment.

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