

The new International Federation of Gynecology and Obstetrics (FIGO) classification of ovulatory disorders: getting from here to there

In New England circles, there is a well-known story of the visitor to Maine who is lost on the backroads and pulls up to ask a wizened roadside denizen how to get to the desired destination and is told laconically, "You can't get there from here." Far be it from me to suggest that the investigators of this set of fertile battle articles are wizened, despite the fact that they are some of the most storied and trusted voices in our field. Rather, they represent the traveler seeking a new and far, far better place for the classification of ovulatory disorders than the current standards. On that, both groups of investigators are agreed. The disagreement is on which road ahead.

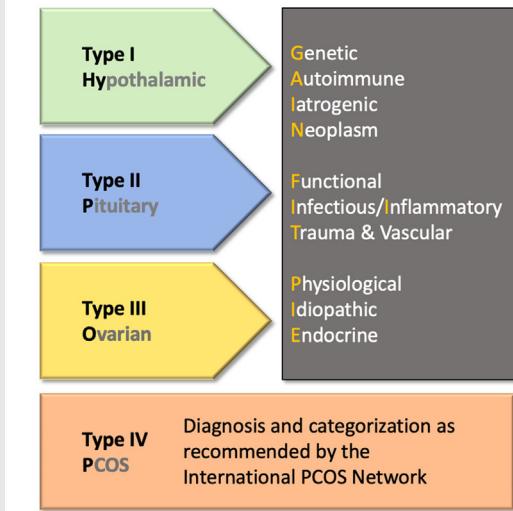
Profs. Balen and Munro summarize the history of the *World Health Organization* (WHO) adoption of the classification of ovulatory disorders, noting that they were established more out of habit and chance than by any predetermined expert consensus conference (1). They were often indiscriminately modified by the presenting investigator in a form of common law rather than a firmly written constitution by a constitutional convention with a process for amendments. This haphazard development of the classification system is confirmed by their opponents Profs. Fauser and Lunenfeld and Dr. O'Neill, with the added carrot that Prof. Lunenfeld was one of the key thought leaders in establishing this classification nearly 50 years ago and saw it as a first step, not the final classification (2). This is as straight from the horse's mouth that we can get on this issue. Both groups are ready to move on from the WHO classification.

Profs. Balen and Munro as key leaders in the process of developing the modification to ovulatory disorders for the *International Federation of Gynecology and Obstetrics* (FIGO) adopted current best practice models by using a Delphi process. Moreover, a Delphi process involves multiple layers of expert and stakeholder opinions and multiple rounds with the goal of achieving consensus. It is a frequently used method for determining the diagnostic and therapeutic pathways that are not unknown to either myself or the journal (3). In this case, the Delphi process had stakeholders from specialty journals, experts at large, national, specialty obstetrical and gynecological societies, and informed lay representatives. They conducted a total of 2 face-to-face meetings and 5 Delphi rounds to develop this consensus diagnostic schema which is anatomy based and carves polycystic ovary syndrome out into its own anatomically free or anatomically inclusive category (Fig. 1) (4). This was a significant improvement on the methodology (or lack thereof) in the WHO classification schema, a classic version of which is included here (Table 1).



FIGURE 1

FIGO Ovulatory Disorders Classification (HyPO-P)



Graphical depiction of the proposed FIGO Ovulatory Disorders Classification System. Note: After the individual is diagnosed with an ovulatory disorder, the core or first level of the system is the allocation to type I, II, or III disorders according to their presumed primary source: hypothalamus, pituitary gland, or ovary, respectively. Polycystic ovary syndrome (PCOS) comprises the type IV category and the criteria proposed by the *World Health Organization* are to be used to determine this categorization. The second level stratifies each anatomic category (types I-III) into the known or presumed mechanism according to the "GAIN-FIT-PIE" mnemonic as appropriate and applicable. FIGO, the International Federation of Gynecology and Obstetrics; PCOS, polycystic ovary syndrome. (From Munro et al. [2]. Reprinted by permission of the publisher.)

Legro. *Fertile Battle. Fertil Steril* 2023.

The FIGO proponents note in the true spirit of the debate, that this in-person consensus process underlay the development of the Rotterdam Criteria for the diagnosis of polycystic ovary syndrome led by Prof. Fauser (and including both Prof. Balen and myself as stakeholders) (5). The FIGO opponents hint the Delphi process may be superior to none at all, but such an expert-based process remains flawed compared with other data-derived methods for classifying human disease. They note the proliferation of human data through electronic medical records to better identify presenting complaints and life stage dependent changes in disorders as well as the opportunity to use newer hormones, such as anti-müllerian hormone with better defined cutoffs for diagnosing disorders. Finally, they advocate incorporating the use of genomic markers in defining these disorders, as has become common for many cancers.

There is the rub, of course. Although the step from no clear consensus to an accepted form of consensus, such as the Delphi process, is small, it is nevertheless a way to begin to get from here to there. Less certain is how to harness the endless reams of electronic medical records and -omics data

TABLE 1**World Health Organization classification of anovulation**

- **Group I ovulation disorders due to hypothalamic pituitary failure (hypogonadotropic hypogonadism)**
 - This category includes conditions such as hypothalamic amenorrhea. Typically, women present with amenorrhea, primary such as due to Kallman's syndrome or secondary due to anorexia nervosa. Approximately 10% of women with ovulation disorders have a group I ovulation disorder.
- **Group II ovulation disorders due to hypothalamic-pituitary-ovarian axis dysfunction.**
 - This category includes conditions such as polycystic ovary syndrome and hyperprolactinemic amenorrhea. Approximately 85% of women with ovulation disorders have a group II ovulation disorder.
 - Although follicle stimulating hormone and estrogen levels tend to be normal, luteinizing hormone levels can be elevated above the normal range as can androgen levels, most commonly noted in polycystic ovary syndrome.
- **Group III ovulation disorders are caused by ovarian failure (hypergonadotropic hypogonadism).**
 - These are also commonly referred to in women of reproductive age as primary ovarian insufficiency and may be autoimmune as well as iatrogenic after radiation or chemotherapy. Around 5% of women with ovulation disorders have a group III ovulation disorder.

Legro. *Fertile Battle*. *Fertil Steril* 2023.

to create a truly data-driven diagnosis of the ovulatory disorders. That journey will not take place in cars on winding country roads but require a giant data-driven leap to get from here to there the means of which elude many backwoods denizens including myself.

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