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**Routine repeated echocardiographic monitoring of fetuses exposed to maternal anti-SSA antibodies: time to question this dogma.**

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**ABSTRACT:**

In around 1% of exposed pregnancies, anti-SSA/SSB antibodies lead to congenital heart block (CHB), the main feature of neonatal lupus syndrome (NLS). It is therefore widely recommended that echocardiographic screening to detect CHB be performed every other week from 16 to at least 24 weeks' gestation in anti-SSA-positive pregnant women. Such screening is now routinely performed in many centres around the world.

Here, we call this dogma into question for several reasons. Even if CHB is discovered (which is rare), the usefulness of treatment with fluorinated steroids has not been demonstrated, whereas their side effects are well known. This discovery so early in the pregnancy does not modify obstetric management. At least 500 ultrasounds are needed to find one CHB that would be found in any case and does not lead to any specific immediate management. And finally, this screening misses most CHB cases since most women with fetal CHB are not known to have anti-SSA antibodies.

Accordingly, except for research protocols, which are certainly needed and do not fall within the scope of this viewpoint, rejecting the dogma of routine repeated screening for CHB could save staff time and money and prevent maternal stress without any significant clinical consequences.

**Search Strategy.** This review was performed by searching within the Pubmed database using the keywords “Congenital heart block”, “neonatal lupus”, “cardiomyopathy AND anti-SSA OR anti-Ro”, “endocardial fibroelastosis AND anti-SSA or anti-Ro”. English-language full publications up to April 2019 were considered.

Passive transplacental passage of maternal anti-SSA and/or anti-SSB antibodies may cause neonatal lupus syndrome (NLS), manifested by cardiac neonatal lupus, skin rash and, more rarely, haematological, hepatic or neurological manifestations.<sup>1,2</sup> The main cardiac manifestation is advanced (second- or third-degree) congenital heart block (CHB) (Figure 1), associated with significant mortality (16 to 28%) and morbidity (70 to 75% require pacing at 10 years).<sup>1-8</sup> The case fatality rate approaches 50% when extranodal disease that includes endocardial fibroelastosis and dilated cardiomyopathy is present.<sup>5-7, 9, 10</sup> Histologically, CHB is manifested by fibrosis, calcification and infiltration of macrophages and giant cells in, and sometimes extending beyond, the atrioventricular (AV) node.<sup>11</sup>

The identification of CHB as early as possible to enable in-utero treatment with fluorinated steroids and thereby reduce its morbidity and mortality has long been a basic precept of antenatal care of pregnant women with known anti-SSA antibodies. Their routine close monitoring by serial echocardiography is thus widespread.<sup>12-14</sup> Here, we call this dogma into question for several reasons, most especially its ineffectiveness and lack of utility, since the only known treatment, administration of fluorinated steroids (dexamethasone or betamethasone), should not be routinely recommended, except in clinical trials (this discussion of routine screening in primary care does not include clinical research in expert centres).

**Incidence of autoimmune CHB.** We have reported that the incidence of CHB in offspring of mothers with connective tissue diseases (CTDs) and anti-SSA with no previous

fetuses or children with CHB ranges between 1 and 2%.<sup>15, 16</sup> A 2015 review of studies that included a total of 705 anti-SSA-positive women with no history of CHB and a total of 823 pregnancies found that 10 fetuses had advanced CHB, for a prevalence of 1.2% per pregnancy.<sup>1</sup> This incidence was even lower among the SLE patients included in the prospective PROMISSE study (0.65%, that is, one case of CHB among 154 anti-SSA-exposed fetuses).<sup>17</sup> It was however higher in a study restricted to anti-SSA 52 antibody-exposed pregnancies, with a risk of 2.9% (6/204).<sup>14</sup> Second-degree CHB accounts for less than 10% of all fetuses with CHB,<sup>5-7</sup> that is, around 1‰ of all anti-SSA pregnancies.

Most antibodies specific for the SSA antigen recognize one, or both, of the 52-kDa and 60-kDa proteins, and some studies suggest that anti-SSA52 antibodies play a predominant role in the development of autoimmune CHB.<sup>1</sup> Others, however, especially those using more sensitive methods, also report a very high frequency of anti-SSA60 antibodies.<sup>1</sup> These antibody levels may also be involved in the risk of CHB, as higher levels have been associated with a higher risk.<sup>18, 19</sup>

Note that this incidence is much higher when the mother has previously had a fetus of child with CHB: the risk of recurrence is around 12-18%.<sup>1, 14, 20, 21</sup> Since this situation is rare and should be handled by experts, we chose to exclude it from this review, even though some of our arguments may also apply to it.

**Term at CHB diagnosis.** Large retrospective series show that CHB is usually detected in utero at a median term of 23 weeks (range: 16-39 weeks)<sup>6</sup> or a mean term of  $24 \pm 4$  weeks<sup>7</sup> (data not available in the US registry). The review by Brito-Zeron et al.<sup>1</sup> reports that in more than half of the cases, AV block was diagnosed at 20–24 weeks and in 75% before 29 weeks. Only 2% of reported cases were diagnosed at birth or in the neonatal period (<27 days after birth). As these

authors note, it is unlikely that all cases had serial echocardiographic surveillance from week 16, given that most mothers are asymptomatic and not screened for CHB before the diagnosis during routine fetal ultrasound.<sup>1</sup> Four prospective studies have shown that in closely monitored pregnancies, CHB is usually diagnosed before 24 weeks.<sup>22-25</sup>

**Current recommendations for echocardiographic monitoring.** Echocardiography is aimed at finding advanced CHB (third- or less frequently second-degree CHB), whether or not it is associated with extranodal manifestations; in some cases, it also seeks to measure the atrioventricular conduction (AV) to detect first-degree CHB.

It is usually recommended that pregnant women with known anti-SSA antibodies be monitored with serial echocardiograms performed weekly or more commonly every other week starting at 16 weeks, with a reduction in frequency in the absence of CHB after 24 to 28 weeks.<sup>1, 12-14, 26</sup> Clowse et al.<sup>12</sup> analysed a survey of a group of 49 international clinicians with a special interest in pregnancy and rheumatic disease and found that most of them recommended these fetal echocardiograms for pregnant women with known anti-SSA antibodies but no history of neonatal lupus at a frequency of every other week (44%), followed by weekly (28%), with half of respondents starting at 16 weeks and 90% by 18 weeks. The clinicians also recommended stopping the screening between 23 and 34 weeks, on average; the most common response was to stop at 28 weeks.<sup>12</sup> Depending on whether ultrasounds were performed weekly or every other week, each woman would undergo 6 to 11 more ultrasounds than she would in a normal pregnancy. Therefore, more than 500 echocardiograms (6 per patient with an incidence of 1.2%) would be needed to find one case of CHB that would be found in any case by routine clinical and ultrasound monitoring. Although fetal echocardiography is safe and non-invasive, its cost is not trivial, especially at this rate of repetition. Another problem with frequent fetal ultrasounds is the

identification of first-degree heart block and other findings of unknown clinical significance that may lead to unnecessary treatment.

**Maternal status and CHB.** It is well known that mothers whose fetus is diagnosed with CHB for the first time are often asymptomatic or paucisymptomatic, so they are not usually receiving follow-up for an autoimmune disease until anti-SSA antibodies are found after the CHB.<sup>5-7, 27-29</sup> A systematic review of underlying maternal autoimmune diseases among 856 affected mothers found that more than half were classified as asymptomatic carriers of anti-SSA antibodies.<sup>1</sup> Interestingly, in our experience, even when mothers have symptoms that justify a CTD diagnosis, it is often made only after their child is found to have CHB. The study by Jaeggi et al. shows that among 40 cases of cardiac neonatal lupus, only 4 mothers had had fetal echocardiographic screening for known anti-SSA antibodies. The other 36 were referred after the fetal diagnosis.<sup>18</sup> Our experience is similar (unpublished data). This shows that most women will not be screened before the diagnosis of CHB, because they are not known to be positive to anti-SSA antibodies; at the same time, most of those who are monitored do not develop CHB.

**Management of advanced CHB.** When fetal CHB is discovered, physicians are naturally eager to do something to improve the situation.<sup>12</sup> The rationale for treatment of identified heart block (or cardiomyopathy) is to diminish the inflammatory insult and consequent fibrotic reaction and to reduce or eliminate maternal autoantibodies. Various therapeutic approaches have been reported, including corticosteroids, plasmapheresis, intravenous gamma globulin (IVIG), B cell depletion therapies, immunosuppressive agents (i.e., azathioprine), hydroxychloroquine and various combinations of these.<sup>30</sup> Except for steroids, these treatments have been described only in case reports or very small series, and no conclusions about their effectiveness can be drawn.



Fluorinated steroids are only partially inactivated by the placental 11 $\beta$ -hydroxysteroid dehydrogenase complex and have satisfactory bioavailability to the fetus.<sup>31</sup> Their use to prevent and treat CHB by reducing inflammation therefore seems quite logical, and they have been widely used since the 1980s.<sup>32</sup> Most respondents to the survey by Clowse et al. recommended starting dexamethasone for second- (88%) and third- (55%) degree CHB.<sup>12</sup> However, the effectiveness of this treatment in improving CHB has been seriously challenged over the past decade.<sup>6, 33-38</sup> Resolution of associated pleuropericardial effusions and ascites has been reported in some cases,<sup>39</sup> but without proof of its translation into improvement of the overall prognosis.

One would expect that an effective treatment would reduce at least one of the following outcomes: mortality, morbidity, especially the need for pacemaker implantation, the degree of CHB, or the occurrence of late-onset cardiomyopathy. As we see below, fluorinated steroids reduce none of these (although the limitations of the current literature, mainly retrospective and observational, must be kept in mind).

Globally, the mortality of fetuses with CHB ranges between 16% and 28% including in-utero and postnatal deaths.<sup>1-8</sup> The only study describing a positive effect by fluorinated steroids on mortality reported a one-year survival rate of 90% (95% CI, 78% to 100%) among the 21 fetuses receiving them in utero, compared with 46% (95% CI, 19% to 75%) of the 13 untreated fetuses ( $p = 0.015$ ).<sup>4</sup> These authors, however, compared 2 historical cohorts, from 1990 to 1996 and from 1997 to 2003, including a total of 37 fetuses; most of the treated fetuses were in the later cohort.<sup>4</sup> Larger series have not confirmed these results.<sup>5-7, 33, 37, 40</sup> In the treated and untreated fetuses of the French cohort at a median follow-up of 7 years (birth to 36 years), the survival rates were 81.8% and 85.9%,<sup>6</sup> respectively; in the American RRNL (Research Registry for Neonatal Lupus; with no length of follow-up available), they were 80.9% and 83.1%.<sup>5</sup>

Although it might be argued that more severe cases are more likely to be treated, data from the RRNL show that fluorinated steroids did not improve mortality in a homogenous cohort of 156 anti-SSA fetuses with isolated advanced CHB.<sup>38</sup> 90.1% of the treated fetuses survived, compared with 91.2% of those not treated (although median follow-up was not available, some children were followed up for 5 years). The adjusted HR for mortality associated with fluorinated steroid treatment at diagnosis of isolated advanced CHB was 1.63 (95% CI 0.43 to 6.14;  $p = 0.47$ ). Interestingly, if we go back to the only study that found a mortality benefit,<sup>4</sup> the control group had an unusually low rate of survival (54%) at 1 year, much lower than that of untreated cases in the other series (at least 90%), whereas survival of their treated fetuses was not higher than that of untreated fetuses in other studies.<sup>5-7, 33</sup> This point suggests that the only evidence that fluorinated steroids have a positive effect on mortality was due to a bias in the control group.

The rate of pacemaker implantation ranges between 70 and 75% at 10 years in the French and American series,<sup>5, 6</sup> and data from the RRNL found it had no benefit in their homogeneous cases: 66% of 64 live births exposed to fluorinated steroids were paced compared with 75% of the 78 unexposed, for an adjusted HR of 0.87 (95% CI 0.57 to 1.33;  $p = 0.53$ ).<sup>38</sup>

Once CHB has reached complete third degree at any point, regression has never been observed, regardless of the treatment, except for one untreated case described by our team in 2015.<sup>6</sup> The irreversibility of third-degree CHB makes the concept of early detection of CHB appealing to treat earlier and prevent complete CHB. Nonetheless, early detection of subtle signs of CHB development by measuring the PR interval proved unsuccessful in the prospective PRIDE study:<sup>22</sup> the data did not support a clear progression from first to second and then third-degree CHB, since none of the 3 fetuses with third-degree CHB had previously gone through a stage with an abnormal PR interval. As expected, the three third-degree blocks were irreversible,

whether treated or untreated.<sup>22</sup> Similarly, Sonesson et al. observed that second- and third-degree CHB developed within 7 days after a normal or near-normal AV conduction measurement in 4/7 cases. Conversely, they observed that a significant number of fetuses had delayed AV conduction without progressing to advanced CHB.<sup>14</sup>

It is difficult to draw any conclusions about the utility of treating second-degree CHB, given the scarcity of data, mainly retrospective and observational, and the rarity of permanent reversal of fetal second-degree CHB in anti-SSA-positive mothers. Eliasson et al.<sup>7</sup> reported reversion of incomplete CHB in five steroid-treated fetuses, but only two of these children (with known outcomes) remained in sinus rhythm at a follow-up of 1 and 2.7 years (and their antibody status was unknown). Combining the French and American registries, we see that CHB switched to first-degree CHB or normal sinus rhythm in 5 of 26 (19.2%) treated fetuses, compared with 4 of 19 (21.1%) untreated.<sup>5,6</sup> Finally, Fredi et al. recently published data from the Italian registry concerning 24 fetuses with initially incomplete CHB, all treated.<sup>37</sup> One “reverted” to variable CHB and four reverted to first-degree CHB or no CHB during treatment with a combined protocol of fluorinated steroids plus plasmapheresis plus IVIG; one received fluorinated steroids plus plasmapheresis and one only fluorinated steroids.<sup>30,37</sup> Even after adding these cases, fluorinated steroids do not appear to be clearly effective in this setting since 10 of the 50 (20%) treated fetuses with second-degree CHB reverted to first-degree CHB or normal sinus rhythm, compared with 4 of 19 (21.1%) untreated fetuses.

Cardiomyopathy was the leading cause of death in both the American and French series.<sup>5</sup>  
<sup>6</sup> In the RRNL homogenous cohort of 156 anti-SSA cases with isolated advanced CHB, early institution of fluorinated steroids did not prevent the extension of injury to the extranodal system, in particular, the development of endocardial fibroelastosis, dilated cardiomyopathy, and

hydrops.<sup>38</sup> In our French series of 187 neonates with a median follow-up of 7 years (birth to 36 years), 18.8% (n = 35, 1 with missing data) had or developed a cardiomyopathy at a median age of 5.5 months (birth to 22.8 years).<sup>41</sup> The risk factors associated with postnatal dilated cardiomyopathy on multivariate analysis were in-utero dilated cardiomyopathy, non-European origin and pacemaker implantation. After adjustment for risk factors, in-utero fluorinated steroids did not protect against postnatal dilated cardiomyopathy (p = 0.0872; HR 2.09, 95% CI, 0.85 to 5.13).<sup>41</sup> Focusing on late-onset cardiomyopathy in children who did not have myocarditis in the first month of life, as described by Moak et al. in 2001,<sup>9</sup> we found that non-European origin, in-utero mitral valve insufficiency and pacemaker implantation were associated with late-onset dilated cardiomyopathy. In-utero fluorinated steroids showed no protective effects against this severe complication.<sup>41</sup>

This absence of any demonstrated efficacy of fluorinated steroids must also be considered in light of their side effects in both mothers and neonates. Effects on mothers mimic the natural history of Cushing's disease with diabetes, hypertension and excessive weight gain, while for fetuses and neonates they may include early and late spontaneous miscarriage, as well as oligoamnios, in-utero growth restriction and adrenal insufficiency.<sup>4, 7, 22, 31, 33, 39, 40</sup> Delayed neuromotor development in infants has also been described<sup>40, 42</sup> but not confirmed by other studies.<sup>43, 44</sup> Although it may feel difficult to do nothing when confronted with this in-utero complication, we must bear in mind Hippocrates' instruction: *primum non nocere*. Thus, given the absence of any demonstrated benefit of fluorinated steroids and their well-demonstrated side effects, we, like others, have proposed that they should not be used routinely and indeed that they be considered only in research protocols.<sup>6, 33-36</sup>

**Management of first-degree CHB.** The definition and management of first-degree CHB are both even more controversial. In-utero prolongation of the AV conduction has been defined by different techniques including fetal kinetocardiography and measurement of mechanical AV conduction as an in-utero substitute for the PR interval, and with different cut-offs, from 2 to 3 standard deviations.

Most respondents to the Clowse survey reported that they would recommend starting dexamethasone (53%) or HCQ (43%) for first-degree CHB.<sup>12</sup> Normalisation has been observed both with and without treatment.<sup>22, 25, 45</sup> The plasticity of the AV prolongation is further supported by the return of all abnormal values obtained on newborn ECG to normal values several weeks later in the study by Sonesson et al.<sup>45</sup> Indeed, reports of improvement by treatment of first-degree CHB should be interpreted with extreme caution, given that the clinical significance of isolated first-degree block remains unknown; progression to more advanced block in the absence of treatment has not been established, and spontaneous reversion is known to occur frequently. A prospective study of the outcome of untreated fetal AV among 165 fetuses of 142 anti-Ro/La antibody-positive women assessed fetal AV conduction weekly between 19 (range: 17 to 23) and 24 (range: 23 to 35) weeks of gestation.<sup>46</sup> Fifteen fetuses had either AV prolonged between 2 and 6 z-scores or type 1 second-degree block. None were treated, and none developed progressive heart block. Only three of these 15 fetuses (20%) had a neonatal diagnosis of first-degree block; on follow-up, it spontaneously resolved for two and did not progress for the third. This study thus confirms that fetal AV prolongation does not predict progressive heart block until birth and does not support the rationale of a management strategy that relies on the early identification and treatment of fetal AV prolongation to prevent complete CHB.<sup>46</sup>

**Screening cost effectiveness and maternal consequences.** Evers et al. recently analysed the cost-utility for three models of CHB screening.<sup>47</sup> They reported an average cost of “prenatal standard screening” in which mothers are screened weekly between 16 and 28 weeks of gestation, as recommended by the American Heart Association,<sup>26</sup> of \$18 880 per pregnancy. They concluded that the current commonly used screening strategy is not cost-effective except in situations in which the prevalence of disease is elevated, as would be the case for a woman with a prior affected fetus.<sup>47</sup>

An alternative screening strategy may be to identify a better predictor of cardiac neonatal lupus than the simple presence of maternal auto-antibodies. Some studies have suggested that it would be sufficient to screen women with high anti-SSA antibody levels<sup>18, 19</sup> or those with more specific profiles.<sup>1</sup> Two studies report no cases in mothers with low anti-SSA antibody levels.<sup>18, 19</sup>

Finally, the effects of standard screening on the mothers may include inconvenience, anxiety, costs and the indirect costs of work days missed because of the frequent visits. These consequences make this strategy even less appealing and less practical as a universal approach. Tingström et al. found that one-third of the women who had undergone such screening reported stress in relation to the examinations, although 61% reported that the increased number of ultrasound examinations influenced their pregnancy in a positive way, with information from experts and additional support from healthcare personnel in conjunction with the examinations.<sup>48</sup>

**Proposal for screening in primary care.** The primary question presented by this viewpoint is how these patients might be managed, especially in primary care. Echocardiographic screening to detect CHB performed every other week from 16 to at least 24 weeks' gestation in anti-SSA-positive pregnant women is clearly a non-satisfactory and not effective monitoring. Unfortunately at present there is no evidence to support any alternative

protocol. Taking all these limitations into account, a minimal proposal in primary care might be the following. First, the screening and treatment plan should be discussed and planned with women and their partners at the beginning of the pregnancy or even better, at a preconceptional clinic, trying to explain the available literature and its limitations. Whenever possible, woman should be offered the possibility of participating in research protocols. In primary care, auscultation of the fetal heart can easily be performed at each routine antenatal visit (usually performed monthly in most countries) to screen for dysrhythmia. Routine fetal ultrasound is performed at 22 weeks in most countries. A single echocardiogram at 26-28 weeks seems universally accepted (Figure2). The rationale is that most cases of CHB are seen during the 22-week ultrasound; if it was missed, it will be found at 26-28 weeks in any case, at a term at which the diagnosis may begin to have obstetrical consequences in terms of follow-up and management. The additional cost or burden for the patient and physician is limited to the 26-28 week echocardiogram only.

**Future research.** Finally, it might be hypothesised that although the currently recommended screening may not fail to detect CHB, it does fail to find it at a time when it can be reversed. Accordingly, handheld Doppler appears to have substantial potential. This device costs around 30-50 euros. Cuneo et al. recently monitored fetal heart rate both classically and with home monitoring in 273 anti-SSA-positive women. Four fetuses had first-degree CHB diagnosed by echocardiography, one only was treated with fluorinated steroids and all had normal sinus rhythm at birth. Abnormalities were subsequently found by 21 mothers (6.7%) who sought medical attention after more than 12 h of detection ( $n = 7$ ), between 3 and 12 h ( $n = 9$ ), or before 3 h ( $n = 5$ ). Finally, 18 fetuses had benign rhythms, while one had first-degree CHB alternating with rare episodes of second-degree CHB, and two had third-degree CHB. Treatment with

fluorinated steroids and IVIG of the fetus with first- and second-degree CHB less than 12 h after the abnormal home Doppler monitoring was associated with the restoration of a normal sinus rhythm. Early treatment with fluorinated steroids and IVIG of the two fetuses with third-degree CHB was ineffective. Home monitoring missed no cases of CHB.<sup>25</sup> Given the potential for spontaneous reversion of incomplete CHB, no conclusion can be drawn from a single case, but the use of such devices, which could both empower mothers and make ultrasound scans more cost-effective, definitely warrants more prospective studies. However, it appears that two of the CHB cases in the report by Cuneo et al. could be attributed to 'maternal error' (one woman missed one Doppler and found CHB on the next Doppler, while another heard some irregularity in the heartbeat but decided not to get checked until she confirmed it herself 12 hours later, when the fetus was in CHB).<sup>25</sup> Centralised real-time review of each Doppler might achieve the same goal of early heart block identification without inflicting mothers with life-long distress for having misinterpreted a medical test.

**Conclusion.** The 6 to 11 additional echocardiograms per pregnancy performed in anti-SSA women show no abnormality in more than 98% of cases. They very rarely identify cases of high-degree CHB, for which, in any case, no treatment has proven its efficacy, even if the limitations of the current literature should be acknowledged (retrospective and/or observational data on a rare condition). They may lead to findings of first-degree CHB, which might better be left untreated. Moreover, this screening cannot detect the vast majority of CHB cases, which occur in mothers with no known CTD. Rejecting the dogma of routinely screening for CHB could save money and maternal stress without any significant harmful consequences. Accordingly, the EULAR recommendations for the management of SLE and antiphospholipid syndrome pregnancies state only that fetal echocardiography is recommended in cases of



suspected fetal dysrhythmia or myocarditis, especially in women with positive anti-SSA and/or anti-SSB antibodies, without recommending more intensive screening.<sup>49</sup> At the most, routine screening should be reserved for women with high anti-SSA antibody levels and those with a history of a fetus or child affected by cardiac or cutaneous neonatal lupus.

Finally, these conclusions address routine monitoring and do not apply to research, which should aim at predicting and/or diagnosing cardiac manifestations of CHB before irreversible block occurs and at finding an effective treatment. In this setting, maternal use of a portable fetal monitoring device may be interesting. When, as we hope, a curative treatment of CHB has proven beneficial, we will be happy to recommend returning to the current or even more intensive routine monitoring.

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Conflicts of Interest

None.

Contributors section

NCC and NM wrote the viewpoint. RFB, MK, AB, AM and KL made modifications.

All the authors approved the manuscript.

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**Reshaping state / local communities relations in Tunisia:  
The socio-cultural and institutional challenges of the decentralization project**

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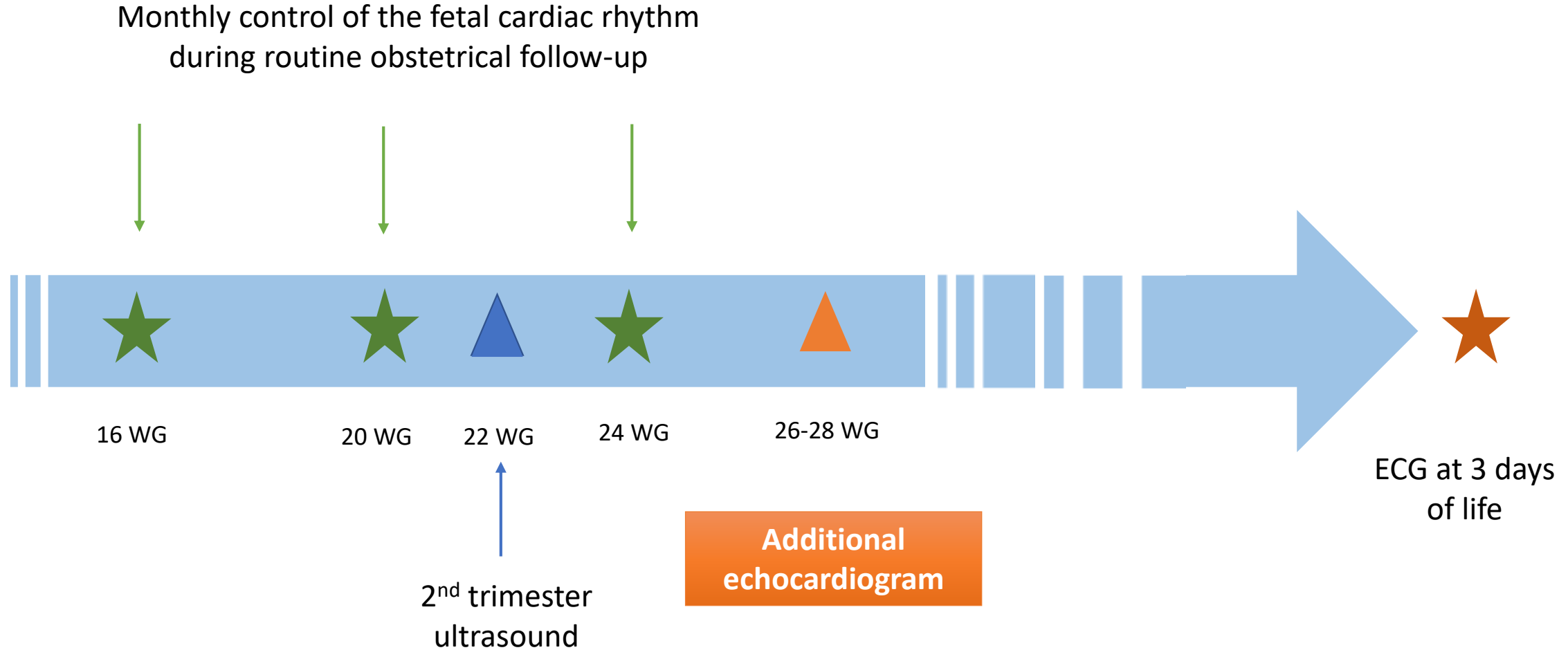
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**Abstract**

International development agencies believe that by adopting institutional reforms based on the best practices that have proved effective elsewhere, so-called « developing countries » could take their places in the globalised economy. Based on a case study carried out on the implementation challenges of a decentralization project in Tunisia, I will argue by using an interpretive approach that this thesis is not sustained. This article shows that institutions cannot be reduced to their technical functions but that they are based on particular collective imaginaries that ground what is legitimate or not and structure the relationship of individuals to power and the meaning given to their actions. It encourages the consideration of cultural framework of meaning; these local cultural references structure the governance modalities of a society, understood in terms of the modalities of exercise of power in a given group (state, company, local authority, etc.). It advocates the necessity to move from a technic- prone approach in the implementation of institutional changes towards a socio-cultural approach that integrates the local expectations of what "good governance" should be and on which depends the legitimacy of institutions and their appropriation by local populations.

Key words: decentralization, governance, public management, institutional change, national cultures, Tunisia



**A possible proposal for the minimal screening in primary care (outside clinical research) of pregnancies exposed to anti-SSA antibodies**

**Legend :** In addition to the routine monthly control of fetal cardiac rhythm and to the routine second trimester echography, an echocardiogram should be added at 26-28 WG. WG: weeks gestation; ECG: electrocardiogram.