NUTRITION OF PRETERM INFANTS AND RAW BREAST MILK-ACQUIRED CYTOMEGALOVIRUS INFECTION: FRENCH NATIONAL AUDIT OF CLINICAL PRACTICES AND DIAGNOSTIC APPROACH.

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Introduction: Raw breast milk is the optimal nutrition for infants, but it is also the primary cause of acquired cytomegalovirus (CMV) infection [1]. In the 1990s to 2000s, studies demonstrated that, in children born before a corrected age of 32 weeks or below a weight of 1500 g, the CMV transmission rate was over 50% in the first three months of life [2]. Moreover, 50% of preterm infants had symptomatic infections, and 15% of these infections were severe with a low C-reactive protein level and were called "sepsis-like" [1]. Thus, many countries have chosen to contraindicate to feed raw breast milk preterm infants from CMV-positive mothers before a corrected age of 32 weeks or under a weight of 1500 g [3-4]. However, since the 2010s this contraindication was more and more discussed [5]. In France, national recommendations have not been updated since 2005 [6] whereas several cases of postnatal breast milk-acquired before a corrected age of 32 weeks have been published by French neonatal units [7-10].

French neonatology units:	140
NICU:	66
Non-ICU:	74

Answers:	105 (75 %)
NICU:	58 (88 %)
Non-ICU:	47 (64 %)

CMV infections reported:	35
NICU:	26
Non-ICU:	9

Methods: An national audit of the French current clinical practices regarding breast milk nutrition in preterm infants was carried out using a questionnaire sent to all neonatal care units. Concurrently, a first national census of diagnosed postnatal milk-acquired CMV infections was carried out, and the validity of the diagnosis was analysed using hospitalisation reports. The reported cases have been classified as "proven", "highly probable", "probable" or "unlikely" breast milk-acquired infections.

Results: Seventy-five per cent of the neonatal units responded. The main results about breast milk nutrition are displayed graphically. Regarding mothers' raw breast milk nutrition in preterm infants, 24% f the units complied with the French recommendations, 20% contraindicated raw breast milk to all infants before 32 weeks regardless of the mothers' CMV-status whereas 25% fed all preterm infants unconditionally with raw breast milk. Thirty-five cases of infants with milk-acquired CMV infections have been reported. On the 17 hospitalisation reports obtained, the diagnosis was undeniable for five patients. Based on their history, two patients probably had congenital infections. The characteristics of the 15 other cases and the missing information in the diagnosis approach are described below.

Breastfeeding promotion

Access to a Human Bank Milk

NICU with
NICU without
Non-ICU without
Non-ICU with

Routinely used pasteurised women's milk before 32 weeks

Main barrier to the use of raw breast milk

CMV
HTLV-1
Recommendations
Bacteria

Summary of the current use of raw breast milk in France

Characteristics of CMV Breast milk-acquired infections

"Proven" infections	Term at birth	Weight at birth	Age (day)	Symptoms	Missing information	Source of reference
1	27 weeks 4 days	550 g	50	"Sepsis-like", NEC, death	/	[7]
2	27 weeks 4 days	1000 g	50	Asymptomatic	/	[7]
3	26 weeks	810 g	70	"Sepsis-like", NEC	/	This study
4	27 weeks	900 g	60	"Sepsis-like", NEC	/	This study
5	29 weeks	1200 g	53	Asymptomatic	/	[8]
"Highly probable" infections						
6	25 weeks 5 days	900 g	36	Thrombocytopenia, hyperleukocytosis	CMV PCR on residual blood from transfusions	This study
7	27 weeks	/	30	"Sepsis-like"	Elimination of congenital origin	This study
8	27 weeks 5 days	950 g	41	"Sepsis-like", thrombocytopenia, NEC, death	Elimination of congenital origin	This study
9	28 weeks	1125 g	60	Thrombocytopenia	CMV reactivation in breast milk	[9]
10	30 weeks	1500 g	15 and 40	Cholestasis "Sepsis-like"	CMV reactivation in breast milk	[10]
11	33 weeks	> 2000 g	20	"Sepsis-like", NEC	Elimination of congenital origin	This study
12	33 weeks	> 2000 g	20	Adenopathies	Elimination of congenital origin	This study
"Probable" infections						
13	25 weeks	570 g	90	Unconfirmed hearing loss	CMV reactivation in breast milk & Elimination of congenital origin	This study
14	32 weeks	> 2000 g	35	"Sepsis-like"		This study
15	32 weeks	1950 g	60	Severe leukopenia		This study

Conclusion: Due to a high rate of participation, this work offers a global vision of clinical practices in France. Thus, a high heterogeneity marks medical practices concerning the use of raw breast milk and the diagnostic approach for breast milk-acquired CMV infection is often incomplete with an important reporting bias. In this context, new recommendations seem challenging to formulate. The establishment of a structured diagnostic approach should be an effective way to assess the real infectious risk, identify a population at risk and, then, write new recommendations.

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