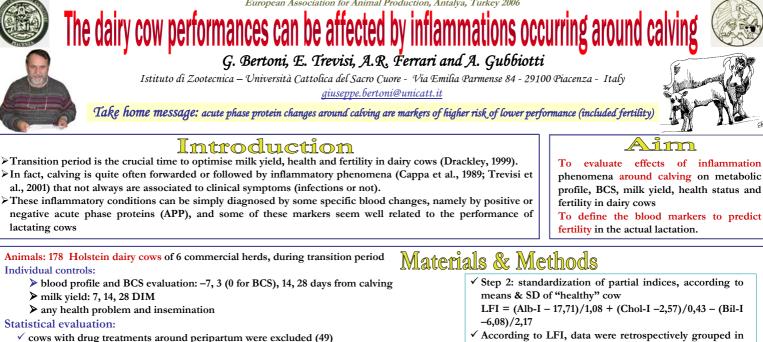
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- quartiles: LO-LFI=lower (6 PR; 26 PL), ✓ the remaining (129: 7 PR & 122 PL) were used to calculate a Liver Function Index (LFI) INLO-LFI=lower intermediate (1 PR; 32PL), that include either plasma albumin, lipoproteins (cholesterol) and bilirubin changes between INUP-LFI=upper intermediate (32 PL), 3th (V3) to 28th (V28) DIM, standardized according to the optimal pattern of changes of the 3
 - UP-LFI=upper (32 PL), ✓ Analysis of repeated measures (PROC MIXED of SAS) Model: cow, group, DIM, group x DIM

128 esu Health problems: during first 30 DIM, 26.3% of cows suffered of some Table 1 – Fertility indices in lower (LO), lower and upper intermediate (INLO, INUP) and upper (UP) quartile of LFI. Milk Yield (kg/d) problem (of whom about 1/4 more than one pathology). LO-LFI Indices Groups The more frequent problems were: lameness, metritis & retained placenta I O-I FI INUP-I FI UP-I FI INI O-I FI 41 INLO-LF (11, 7 & 6 cases respectively). 34.0 30.0 38.0 PFS 44.0 UP-LFI LO showed the highest frequency of clinical problems: 53.1% vs 39.4, 18.8 36 DO[#] 123.47+66. 124 91+59 3 113.01+57.8 100.72±57.02 & 28.1% of INLO, INUP & and UP respectively. 2.17±1.68 2.21±1.47 2.06±1.43 1.58±1.02 NSC 31 % culled 19.0 9.0 0.0 16.0 Milk yield & fertility: higher in UP vs LO groups (fig. 1 & tab.1) FSI 23.20 29.66 55 4/ 61 13 BCS: at calving was similar between groups (2.80 points), but body Legend: # Normalized data PFS (%) Prognant to First Service); IFS (Interval calving to 1st service); NSC (Number of Services per Conception); DO (Days Open); FSI (Fertility Status Index) = (PFS/NSC) – (DO - 125) – (% culled – 25) 28 DIM losses at 28th DIM were higher in LO vs UP group (-0.53 vs -0.38 Figure 1 – Milk Yield in the points; P<0.06) month of lactation BCS Cholesterol (mmol/l) Albumin (g/l) Bilirubin (µmol/l) Haptoglobin (g/l) 2.3 12 2.5 DIM DIM DIM IM 0.2 -14 -7 14 21 14 21 28 7 28 35 14 -14 -7 14 21 28 21 -14 3 -14 14 28 28 Figure 2 – BCS and some blood parameters in lower (LO-LFI, \bigcirc), lower intermediate (INLO-LFI, \bigcirc), upper intermediate (INUP-LFI \triangle) and upper 48 80 Globulin (g/l) Paraoxonase (U/ml) Vitamina A (µg/100ml Urea (mmol/l) 44 (UP-LFI,▲) quartile of LFI. * P<0.05; ** P<0.01; *** P<0.001: significant difference between LO and others groups, at the same DIM DIM DIM -7 21 -14 -7 14 21 28 35 -14 -7 21 -14 14 21 28 35 -14 14 28 35 28 35 According to the criteria used to estimate LFI index, cholesterol (=lipoprotein), albumin and bilirubin (only at 3rd & 14th DIM) significantly discriminate the 4 groups (figure 2).

- + APP showed the highest values in LO and INLO groups: in some cases only around calving (haptoglobin, figure 2) in others till 28th DIM (globulin figure 2 and ceruloplasmin; P<0.01). In addition, blood Ca and Zn (figure 2) - markedly reduced during inflammation - showed the more marked reduction around calving in LO and INLO groups. -APP (Vitamin A = Retinol Binding Protein and Paraoxonase) had showed similar patterns of the cholesterol in the 4 groups (figure 2). Interestingly, all these differences are begun before calving and are maintained or grown during first 28 DIM (P<0.05 between LO and UP groups).
- * UP vs LO showed higher values of glucose immediately before and after calving (P<0.001). On the contrary, NEFA & βHOB were lower in UP vs LO (P<0.001 at 3^{el} DIM). Often INLO and INUP showed intermediate values.
- UP (and also INUP from 14th DIM) exhibited significant higher value of urea since 3th DIM vs LO group (P<0.01);</p>

albumin (Alb-I) and cholesterol (Chol-I) index = 50% V3 + 50% (V28-V3)

Finally, LO vs UP group showed higher values of GGT (P<0.01) & GOT.</p>

parameters, obtained from healthy cows at the same DIM

bilirubin (Bil-I) index = 67% V3 + 33% (V3-V28)

✓ Step 1:

Discussion

> The LFI index have well discriminated the patterns of all the APP (+ and -) between the 4 groups. > Therefore, LFI is related to liver function:

- positively with -APP (RBP, PON, lipoproteins, ...), usual proteins synthesised to satisfy many metabolic function:
- ✓ negatively with +APP (haptoglobin, globulin, ...), proteins synthesised to answer to immune system challenge (by cytokines release), and other parameters (i.e. bilirubin, GGT) that increase when usual liver function are impaired.
- > Interestingly, LFI index appear also well related to performances of each group: clinical problems (negatively), milk yield and fertility (positively).
- > The reduction of performances with low LFI could be justified:
- ✓ <u>directly</u>: trough the systemic action of pro-inflammatory cytokines
- ~ indirectly: by the worsening of the negative energy balance around calving due to the inflammatory-like conditions. In fact, the LO group showed the lowest levels of glucose & urea and the highest of NEFA & BOHB, suggesting a lower DMI and a higher lipomobilization (as confirmed by the more marked decrease of BCS)

Conclusions

- These data confirm that:
 - ✓ high milk yield in "healthy" cows did not impair the reproductive function
 - ✓ clinical and sub-clinical health problems in transition period, eliciting the an inflammatory-like condition, are the responsible of reduced performances;
- A complex index of liver function as LFI a promising tool to diagnose seems inflammatory conditions around calving, to predict poor performances (milk yield & fertility) and to advance appropriate therapies.