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Complement System in the Elderly

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In rheumatology, levels and functional performance of Complement System proteins need to be interpreted in combination with other laboratory results to avoid baffling the interpretive skills of physicians. On its own, the complement system serves both innate and adaptive immunity and gets activated through more than one entry with immune complexes, involving at times rheumatoid factors, being the most prominent in rheumatic diseases. On Figure 1, we schematically present three levels of complements involvement; for reasons of clarity, the control proteins C1 Inhibitor, Factors H and I as well as the cell membrane protecting proteins CD 55 and CD59 are omitted.

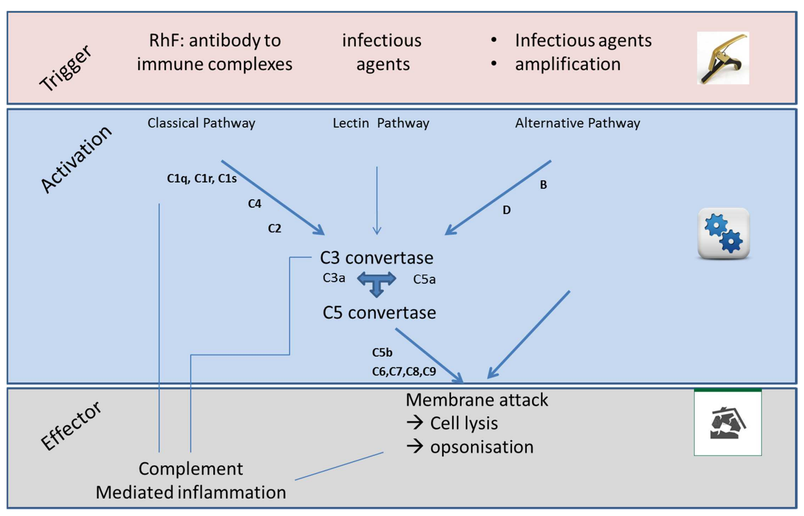

Fig 1. The three levels of complement activation

Limited knowledge is available on physiopathological particularities of the complement system in healthy elderly and even less in geriatrics despite recent strides in immunosenescence research. Here, we present published and unpublished data on the quantitation of complements C4 and C3 components performed in the SENIORLAB study (1) and discuss results in relationship to selected adjunct parameters, an intricate undertaking.

Subjects and Methods

Subjects. An observational, prospective cohort of subjectively healthy residents of Switzerland aged 60 years and older were included for baseline examination. Feeling healthy is a relative condition lacking a universal definition but was assumed here on the basis of an exhaustive demographic and anthropometric questionnaire for candidates. After the usual exclusion based on the questionnaire, a further 179 subjects were excluded because of their elevated serum concentrations of C-reactive protein (CRP). SENIORLAB is registered in the International Standard Randomized Controlled Trial Number registry (ISRCTN53778569) (1). Of the 1291 healthy volunteers lab results of whose are shown on **Figure 2**, 558 were between 60 and 69 years old, 498 between 70 and 79 and 235 >80 years (2).

Laboratory testing. All assays were done at our institution according to up-to-date national regulations. For immunoassays of C4 and C3 we used sodium azide preserved anti-C3c < 6.4 mg/ml and anti-C4 < 5.4 mg/ml antibodies. Siemens recommends for its Prospec Nephelometry System (Siemens, Zurich, Switzerland) reference intervals (RIs) for C3/C3c of 0.9 to 1.8 mg/ml and for C4/C4c of 0.1 – 0.4 mg/ml. 25(OH)vitamin D:liquid chromatography; CRP: turbidimetry.

Statistical procedures. Receiver operating curve (ROC), univariate and multivariate linear regression analyses and descriptive statistics were used in combination. Comparisons were performed by the student t test/ Mann-Whitey U test and Fisher exact tests using MedCalc Statistical software ver. 11.2.1 (Belgium) and SPSS software version 14.0 (IBM, Zurich Switzerland). P < 0.05 was considered significant.

Results and Discussion

The reference intervals calculated for C4 and C3 of the entire cohort of 1291 people studied did not significantly differ from the intervals put forward by the producer of the nephelometry platform, remaining in the physiological range known and practiced in clinics. However, half of surprise and half of awe, a correlation between the complement component levels and Vitamin D became apparent, as can be seen on the below left hand panel of **Figure 2**: with increasing 25(OH)D complement component C3 decreases (left hand panel, A and B) as well, whereas C4 increased with decreasing 25(OH)D (left hand panel, C and D). (2). Seasonal fluctuations are shown on the right hand panel.

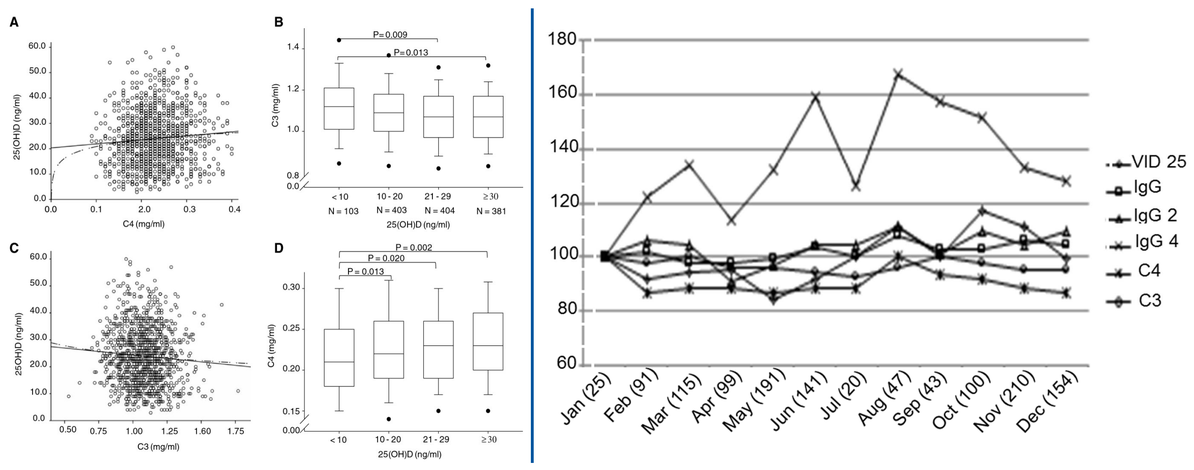

Fig 2. *left panel* relationship between the complements C4 and C3 with vitamin D; *right panel* seasonal fluctuation in levels of vit 25(OH)D and different factors of the immune system.

These findings once again keep reminding us on interpretive skills of physicians to extract data from different subspecialities of laboratory medicine, in this case from immunological and clinical chemistry-vitaminology (**Figure 3**) (3).

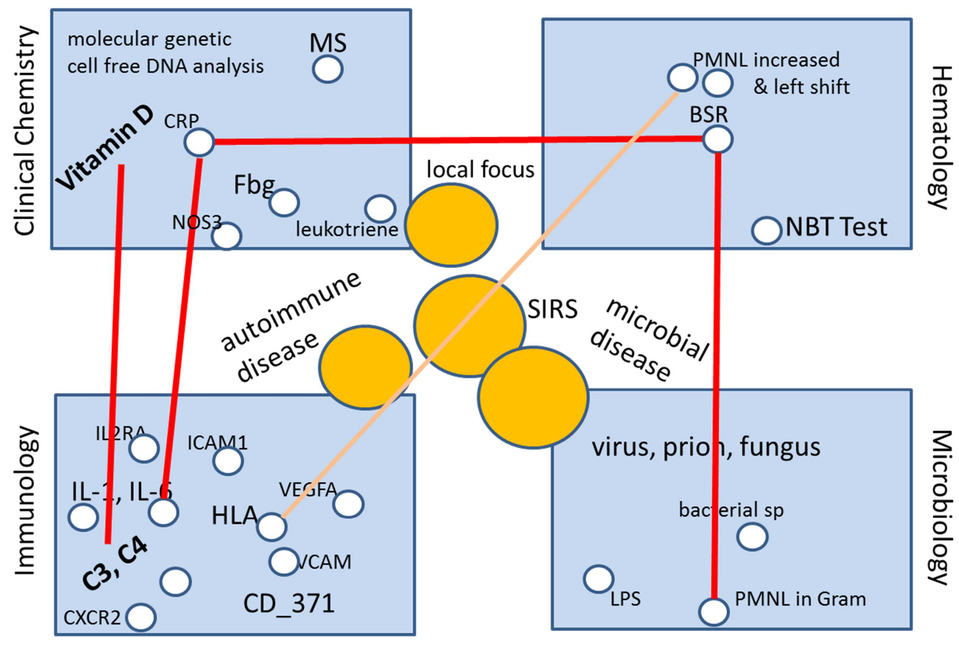

Fig 3. Interplay between the different laboratory disciplines

Conclusions

What is already known	Complement Components C4 and C3 play a role as inflammation-effectors in rheumatic disease
What the new findings are	Levels of C4 and C3 should be interpreted in the context of other lab assays

Bibliography
1. Risch M et al. SENIORLAB: a prospective observational study investigating laboratory parameters and their reference intervals in the elderly. Medicine (Baltimore) 2017 96(1):e5726
2. Sakem B et al. Serum concentrations of 25-hydroxyvitamin D and immunoglobulins in an older Swiss cohort: results of the Senior Labor Study. BMC Medicine 2013:11:176
3. Nydegger U et al. Inflammation thread runs across medical laboratory specialities. Mediators of Inflammation 2016;ID 4121837, 9 pages