EQALM Meeting 2022

WG Haemostasis:
HIL survey in coagulation

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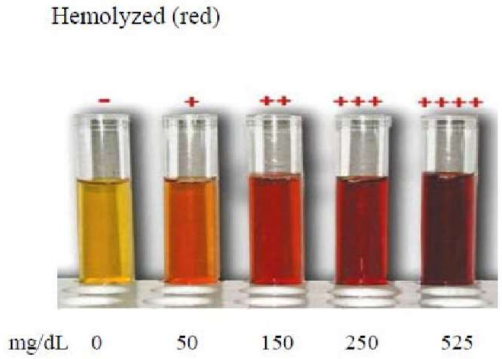
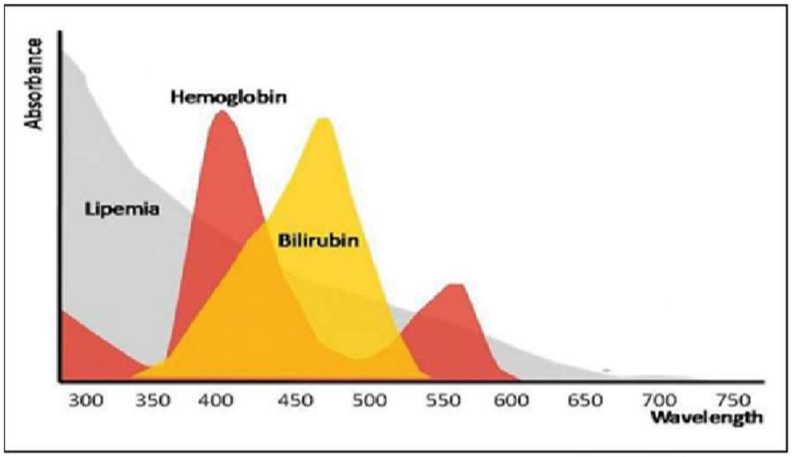
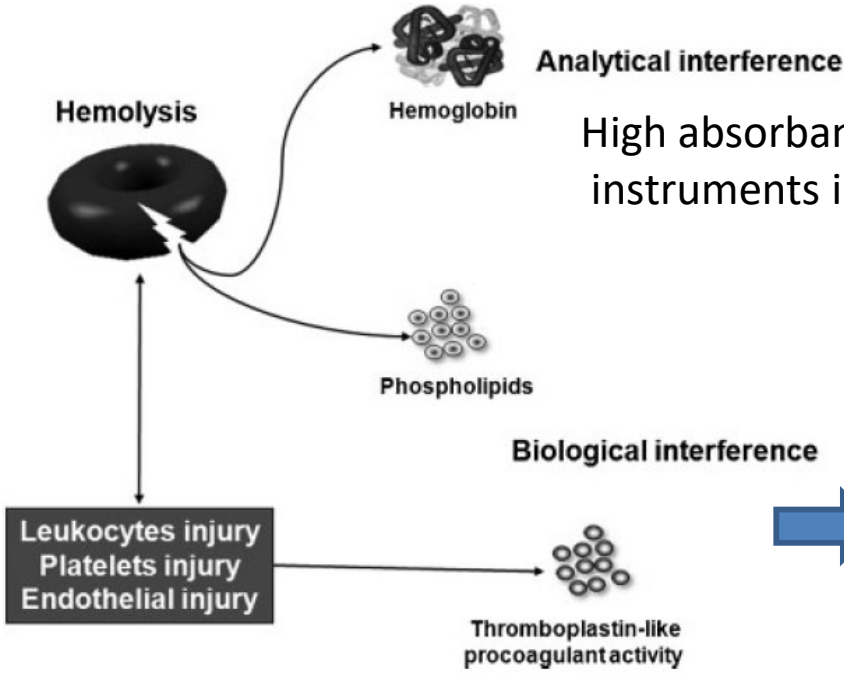
HIL interference in coagulation



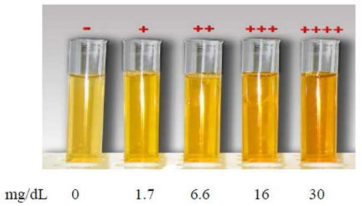




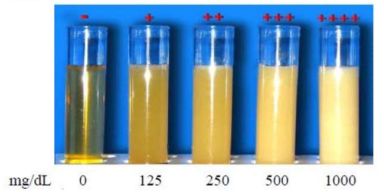
High absorbance at wavelenghts used by instruments in coagulation testing

Activation of coagulation

Icteric (yellow)



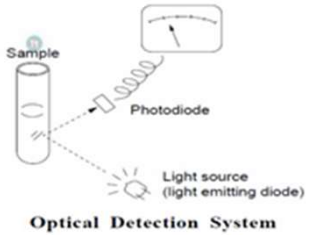
Lipemic (turbid)



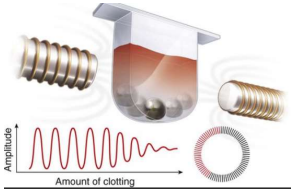
Lippi G et l. Sem Thromb Haemost 2013
https://pdfs.semanticscholar.org/c32c/f5aa792307bcd7be142fa8d5dce1e30d7bbc.pdf

Coagulation tests

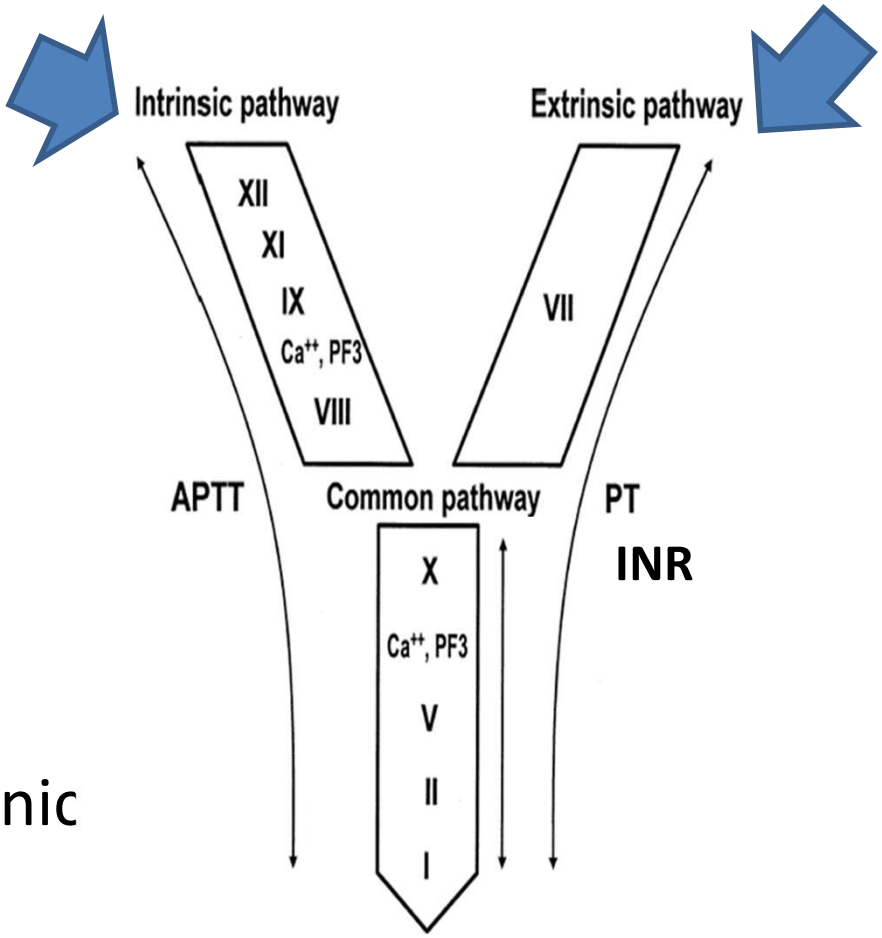
- Clot detection e.g.
  - **APTT, PT/INR, fibrinogen**
  - **Coagulation factors**



- Optical clot detection
  - Siemens and IL instruments
- Mechanical clot detection
  - Stago



- Immunoturbidimetric and Chromogenic
  - E.g. D-dimer and antithrombin
  - Always «optical»



Gezer S. Dis Month 2003

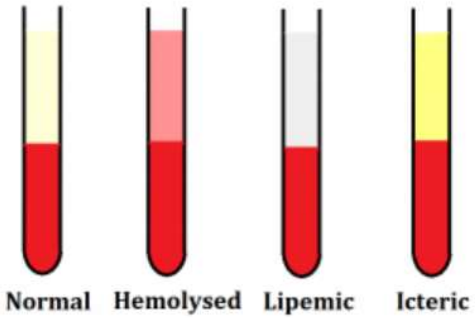
HIL detection in coagulation

- Automatic HIL detection - more recent
- Few guidelines for HIL in coagulation
- Studies on HIL interference conflicting↓↑↔
  - May depend upon
    - Method of «artificially» hemolysis vs «natural» hemolysis
    - Instruments
      - Optical vs Mechanical clot detection
    - Reagents
    - Sample: Level of analyte (normal or pathological)
    - Acceptance criteria for bias
  - Also important for interpretation of HIL EQA programs

Why is knowledge of HIL interference important?

- Accepting inappropriate results
  - Clinical decisions based upon unreliable data
- Rejection of (almost) appropriate results
  - Delayed results and thereby clinical actions
  - Diagnosis may be missed if sample is not repeated
- HIL => increased use of resources both in laboratory and in the clinic

Pre-analytical questionnaire for laboratories regarding HIL in coagulation testing.



Tests Affected by Hemolyzed, Lipemic and Icteric Samples And Their Mechanism - LaboratoryInfo.com

Aims of the HIL questionnaire

- Study the practical handling of HIL in samples for coagulation testing
  - Are HIL checks performed?
  - How are they performed?
  - Do HIL checks have consequences for further management of the result?
  - Are internal and external quality assessment implemented?
- Highlighting particular problematic areas in need for harmonization/recommendations

Methods

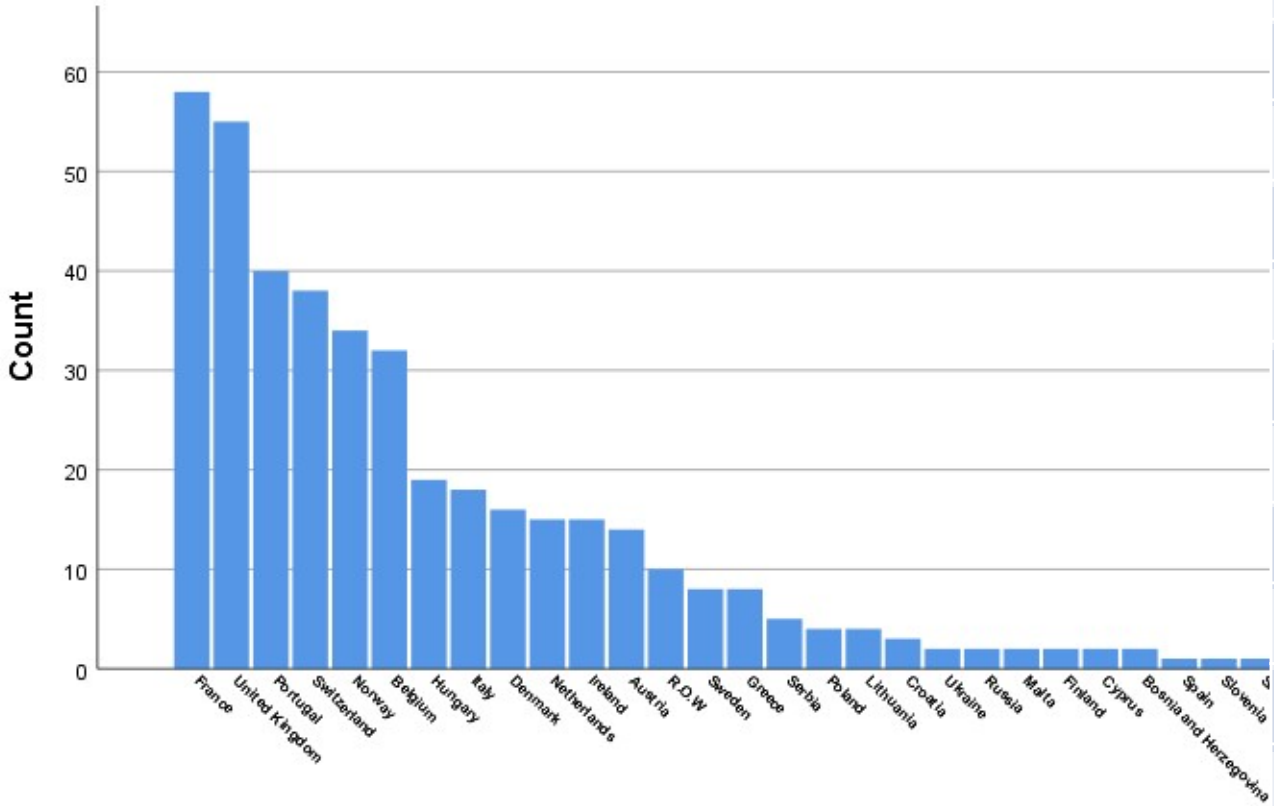
- EQALM members (EQA organizers) invited to distribute a questionnaire to their laboratories
  - Survey Monkey link
    - Distributed June-Sept 2022
    - APTT, PT, INR, Fibrinogen, D-dimer, Antithrombin
    - Hemolysis, Icterus/bilirubinemia and Lipemia
    - Only laboratories analysing patient samples

Preliminary results from the HIL questionnaire

Examples for APTT and Hemolysis

Cadamuro J.

Countries, n=417

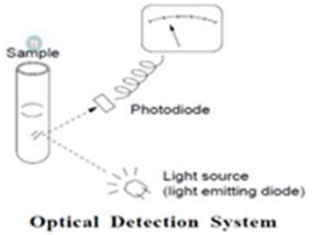


Country	Number
France	58
United Kingdom	55
Portugal	40
Switzerland	38
Norway	34
Belgium	32
Hungary	19
Italy	18
Denmark	16
The Netherlands	15
Ireland	15
Austria	14
Sweden	8
Greece	8
19 countries ≤ 5 labs	37
Non-European	10
Total	**417**

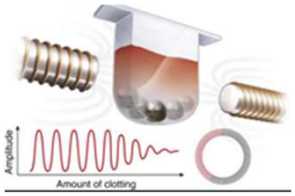
Several different countries,
but similar groups of instrument methodology are in use

Instruments

- Instruments:
  - Optical clot detection
    - Siemens instruments: 41% (n=171)
    - Instrumentation Laboratories (IL): 27% (n=111)
  - Mechanical clot detection
    - Stago: 27% (n=114)



Optical Detection System



- Automatic HIL detection: 57%

Do laboratories check for HIL?

- Hemolysis 79% (+12% in specific situations)
- Icterus 60% (+9%)
- Lipemia 65% (+8%)

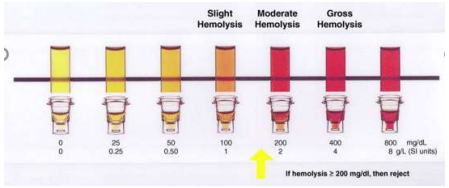
- Only visual: 36%
- Only coag H-index: 31%
- Combinations: 33%

If initial visual; how establish for Hemolysis

By experience 46%

By visual scale 24%

Only positive or negative 29%



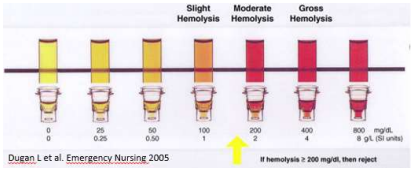
Dugan L et al. Emergency Nursing 2005

In clinical chemistry for hemolysis (Lippi G, CCLM 2018):

- *Visual inspection should be replaced by automatic detection*
- *Chart/picture if automatic detection unavailable*

Consequences of HIL checks?

Comment- and rejection-levels. Part 1



Example Hemolysis	APTT Comment	APTT Reject	APTT Comment	APTT Reject	APTT Comment	APTT Reject
	Siemens, n=171		IL, n=111		Stago, n=114	
Slight	8%	0.6%	3%	0	4%	2%
Level 1 - 2	12%	5%	0	2%	3.5%	5%
0.01 - 0.4- 0.5- 0.6 g/L	0.6%	0	0	2%	0	1%
1- 1.2 - 1.3 - 1 .5 g/L	0	3.5%	8%	4%	0	0
2 - 2.6 g/L	0	0.6%	0.5%	0.5%	1%	2%
Moderate	3.5%	2%	0.5%	2%	1%	3.5%
Level 3 - 4	2.3%	3%	0	5%	8%	6%
4 - 4.5 g/L	0.6%	2%	1%	0	0	3%
Gross	2%	9%	0.5%	7%	1%	3.5%
Level 5 - 6	0.6%	5%	2%	4%	1%	4%
5 - 6 g/L	0.6%	6%	3%	3%	0	3.5%
8 - 10 - 500 g/L	0.6%	0.6%	0.5%	5%	0	0

Consequences of HIL checks?
Comment- and rejection-levels. Part 2

Example Hemolysis	APTT Comment	APTT Reject	APTT Comment	APTT Reject	APTT Comment	APTT Reject
	Siemens, n=171		**IL, n=111**		**Stago, n=114**	
Reject if hemolysed	-	**8%**	-	2%	-	2%
Comment if hemolysed	3.5%	-	6%	-	3%	-
Manufacturer advice	2%	5%	6%	2%	2%	5%
Individual assessment	4%	9%	7%	5%	9%	5%
No comment-level*	**16%**	**-**	**25%**	**-**	**28%**	**-**
No rejection-level	**-**	**9%**	**-**	**22%**	**-**	**20%**
No answer	30%	28%	28%	28%	32%	25%

36% would report results even if higher than the rejection level if:
*in vivo hemolysis, *difficult to draw or *emergency.

In your comment, Do you indicate the potential direction for change of the result?

- APTT and hemolysis:
  - APTT↑ 2.6%
  - APTT↓ 6%
  - No comment on direction: 92%

Lippi G et al. CCLM 2018

"..results of hemolysis-sensitive tests can be released in association ***with a comment describing the direction*** in which data are potentially altered, suggesting to recollect another sample…"

Last questions in the survey:

- **Are HIL results reported in the lab.system?**
  - 8% report HIL results visible for clinicians
  - 33% report in lab.system only visible for lab

- **Internal quality control:** 20% of those who perform HIL
- **External quality control:**
  - About 15% for the coagulation instrument
  - About 15% for clinical chemistry instrument
  - About 70% would be interested in participating in EQAs

HIL results should be provided in laboratory report
Both Internal and external QC should be used for continuously monitoring the analytical performance of the H-index.
Lippi G et al. CCLM 2018.

Summary

- Large heterogeneity in several aspects of HIL evaluation for coagulation
  - From rejecting no samples to rejecting all samples
  - Huge number of different ways of presenting HIL
  - Few do internal and external QC

- Needed:
  - More knowledge regarding the effect of HIL on the coagulation results for the different methods
  - Harmonization regarding reporting and evaluation

Further plans

- Data evaluation
- Review of the literature
  - Studies
  - Guidelines
- Feedback report for the laboratories (and EQAs)
- Publication of paper(s)
- Potential follow-up studies

- **Project group:**
- Ann Helen Kristoffersen (Noklus)
- Piet Meijer (ECAT)
- Martine van Essen-Hollestelle (ECAT)
- Eva Ajzner (Hungary)
- Janne Cadamuro (EFLM WG-PRE)
- Andreas Hillarp (EQUALIS)
- Gunn BB Kristensen (Noklus)
- Gro Gidske (Noklus)
- Sverre Sandberg (Noklus)
- Dagmar Kesseler (CSCQ)
- Steve Kitchen (UKNEQAS)
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