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Original Contribution

Jolt accentuation of headache and other clinical signs: poor predictors of meningitis in adults☆,☆☆

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103.07.15

Incidence in 1986 and 1995 of Bacterial Meningitis and Total Invasive Disease.

TABLE 3. INCIDENCE IN 1986 AND 1995 OF BACTERIAL MENINGITIS AND TOTAL INVASIVE DISEASE.

PATHOGEN	BACTERIAL MENINGITIS			TOTAL INVASIVE DISEASE		
	1986*	1995	PERCENT CHANGE	1986*	1995	PERCENT CHANGE
	cases per 100,000 population			cases per 100,000 population		
Haemophilus influenzae	2.9	0.2	−94	5.6	1.8	−68
Streptococcus pneumoniae	1.1	1.1	+4	15.0	26.1	+74
Neisseria meningitidis	0.9	0.6	−33	1.3	1.3	0
Group B streptococcus	0.4	0.3	−25	3.7	8.1	+119
Listeria monocytogenes	0.2	0.2	−5	0.7	0.5	−24

*Data are from Wenger et al.[3] During 1986, laboratory audits for invasive disease due to *S. pneumoniae* and group B streptococcus were limited to certain areas.[3]

The NEW ENGLAND JOURNAL of MEDICINE

Schuchat A et al. N Engl J Med 1997;337:970-976.

In-Hospital Mortality Rates According to Pathogen.

ORGANISM	No. of EPISODES	CASE FATALITY RATE: MENINGITIS-RELATED	CASE FATALITY RATE: TOTAL
		percent	
Strep. pneumoniae	120	25	28
Gram-negative bacilli	86	23	36
N. meningitidis	40	10	10
Streptococci	36	17	25
Enterococcus	4	25	50
Staph. aureus	36	28	39
L. monocytogenes	34	21	32
H. influenzae	19	11	11
Mixed bacterial species	18	39	44
Coagulase-negative staphylococci	16	0	0
Other*	12	0	8
Culture negative	72	7	10
All causes	493	19	25
1962–1970	172	21	24
1971–1979	186	18	26
1980–1988	135	17	24

*Other organisms were as follows: anaerobes (4 episodes), propionibacteria (2), diphtheroids (2), micrococci (2), neisseria species (1), and *Campylobacter fetus* (1).

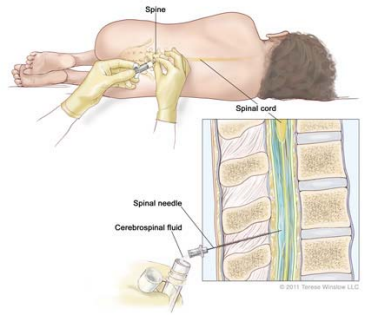
The NEW ENGLAND JOURNAL of MEDICINE

Durand ML et al. N Engl J Med 1993;328:21-28.

pain

hematoma

infection



Physical sign	Method of elicitation	Positive test
Nuchal rigidity	With the patient in the supine position, the resident gently flexed the neck, asking the patients to touch their chin to sternum	Resistance to flexion
Jolt accentuation of the patient's headache	The resident asked the patients to turn their heads horizontally at a frequency of 2–3 rotations per second	Worsening of the base line headache
Kernig's sign	With the patient in the supine position, the resident lifted the knee in flexed position until maximal hip flexion was obtained. The leg was extended at the knee and resistance was checked	Resistance to extension at the knee to >135° or pain in the lower back or posterior thigh
Brudzinski's sign	With the patient in the supine position, the resident flexed the neck, and looked for flexion of both the lower limbs	Flexion of the knees and hips

Objective

- Assess sensitivity and specificity of clinical signs in predicting CSF pleocytosis
- Assess diagnostic accuracy of physician's suspicion of meningitis

Method

- 2 inner city academic ER
- St Luke's Hospital and Roosevelt Hospital in Manhattan, New York (annual patient census 190,000)
- January 1, 2006 to December 31, 2009
- Inclusion: >=18 y/o + LP d/t suspected meningitis
  Exclusion: altered mental status, prisoner status (inability to consent)

Method

- by trained assistant: 8AM to midnight on university based calendar (60% of days annually)
- LP tray standby-> informed consent + physician interview (age, sex, symptoms, signs, suspicion of meningitis: either>50% or otherwise)
- CSF pleocytosis = WBC count >= 5cells/ HPF in 4th tube, with ratio of RBC/WBC <700
- Stata version 10

Result

Table 1
Demographic characteristics, subjects receiving LP

Characteristics	All patients
Age	
Age (y), mean (range)	40.2 (18-88)
No. of patients ≥60 years old (%)	28/230 (12.2%)
Sex	
Male	99/230 (43.0%)
Female	131/230 (57.0%)
Ethnicity	
White	82/230 (35.6%)
Black	70/230 (30.4%)
Hispanic	36/230 (15.7%)
Other/unknown[a]	42/230 (18.3%)

[a] Patients who during registration chose not to identify themselves by race.

Result

Table 2
Clinical presentation, subjects receiving LP

	All (n = 230)	No pleocytosis (n = 183)	Pleocytosis (n = 47)	P
Clinical characteristics				
Headache	197/230 (85.7%)	154/183 (84.2%)	43/47 (91.5%)	.20
Reported fever	90/230 (39.1%)	76/183 (41.5%)	14/47 (29.8%)	.18
Temperature ≥100.4°F	56/223 (25.1%)	49/176 (27.8%)	7/47 (14.9%)	.09
Reported fever or measured temperature ≥100.4°F	90/230 (39.1%)	76/183 (41.5%)	14/47 (29.8%)	.18
Jolt accentuation	37/197 (18.8%)	28/154 (18.2%)	9/43 (20.9%)	.66
Kernig sign	6/229 (2.6%)	5/182 (2.7%)	1/47 (2.1%)	1.00
Brudzinski sign	5/229 (2.2%)	4/182 (2.2%)	1/47 (2.1%)	1.00
Nuchal rigidity	43/229 (18.8%)	37/182 (20.3%)	6/47 (12.8%)	.30
Focal neurologic deficit	9/229 (3.9%)	8/182 (4.4%)	1/47 (2.1%)	.69
Vomiting	30/229 (13.1%)	28/182 (15.4%)	2/47 (4.3%)	.05
Rash	8/229 (3.5%)	7/182 (3.8%)	1/47 (2.1%)	1.00
Physician suspicion				
Bacterial meningitis	130/230 (56.5%)	109/183 (59.6%)	21/47 (44.7%)	.07
CSF results				
WBC count, mean WBCs/HPF	26.9 (n = 230)	0.7 (n = 183)	129.0 (n = 47)	.00
WBC count, median WBCs/HPF	1	0	44	-
Glucose level, mean mg/dL	64.2 (n = 228)	64.16 (n = 181)	60.49 (n = 47)	.15
Glucose level, median mg/dL	61	61	58	-
Protein level, mean mg/dL	49.8 (n = 229)	42.87 (n = 182)	76.77 (n = 47)	.00
Protein level, median mg/dL	42	39	66	-
Culture growth positive	8/230 (3%)	5/183 (3%)	3/47 (6%)	.21

Result

Table 3
Predicting pleocytosis among subjects receiving LP

	Sensitivity (0.95 CI)	Specificity (0.95 CI)	LR+	LR−
Headache (n = 230)	91% (88-95)	16% (11-21)	1.1	0.5
Fever (n = 230)	30% (24-36)	58% (52-65)	0.7	1.2
Jolt accentuation (n = 197)	21% (15-27)	82% (76-87)	1.2	1.0
Kernig sign (n = 229)	2% (0-4)	97% (95-99)	0.8	1.0
Brudzinski sign (n = 229)	2% (0-4)	98% (96-100)	1.0	1.0
Nuchal rigidity (n = 229)	13% (8-17)	80% (74-85)	0.6	1.1
Focal neurologic deficit (n = 229)	2% (0-4)	96% (93-98)	0.5	1.0
Vomiting (n = 229)	4% (2-7)	85% (80-89)	0.3	1.1
Rash (n = 229)	2% (0-4)	96% (94-99)	0.6	1.0
Physician suspicion (n = 230)	44% (31-59)	40% (33-47)	0.8	1.4

Abbreviation: 0.95 CI, 95% confidence interval.

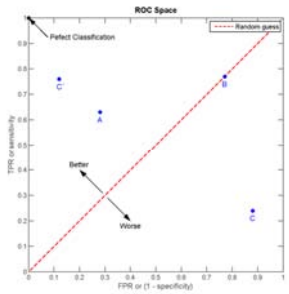
$$LR+ = \frac{\text{sensitivity}}{1-\text{specificity}} \qquad LR+ = \frac{\Pr(T+|D+)}{\Pr(T+|D-)}$$

$$LR- = \frac{1-\text{sensitivity}}{\text{specificity}} \qquad LR- = \frac{\Pr(T-|D+)}{\Pr(T-|D-)}$$

Table 4
Predicting moderate pleocytosis among subjects receiving LP

	Sensitivity (0.95 CI)	Specificity (0.95 CI)	LR+	LR−
Headache (n = 230)	80% (75-85)	14% (9-18)	0.9	1.4
Fever (n = 230)	27% (21-32)	60% (54-66)	0.7	1.2
Jolt accentuation (n = 197)	33% (27-40)	82% (77-88)	1.9	0.8
Kernig sign (n = 229)	7% (3-10)	98% (96-100)	2.9	1.0
Brudzinski sign (n = 229)	7% (3-10)	98% (96-100)	3.6	1.0
Nuchal rigidity (n = 229)	20% (15-25)	81% (76-86)	1.1	1.0
Focal neurologic deficit (n = 229)	0% (0-0)	96% (93-98)	0.0	1.0
Vomiting (n = 229)	7% (3-10)	86% (82-91)	0.5	1.1
Rash (n = 229)	0% (0-0)	96% (94-99)	0.0	1.0
Physician suspicion (n = 229)	56% (33-77)	43% (37-50)	1.0	1.0

Moderate pleocytosis = WBC >= 100 cell/ HPF



Discussion

2010, prospective, ER

2012, prospective, ER

Table 3. Diagnostic accuracy of Kernig's sign, Brudzinski's sign, and nuchal rigidity for patients with suspected meningitis who were examined for any of these 3 signs before lumbar puncture was done.

Sign	No. of patients: With meningitis[a]	Without meningitis	All
Kernig's[b]			
Present	3	8	11
Absent	63	163	226
Brudzinski's[c]			
Present	3	8	11
Absent	63	162	225
Nuchal rigidity[d]			
Present	24	69	93
Absent	56	148	204

NOTE. LR⁺, likelihood ratio for a negative test result; LR⁻, likelihood ratio for a positive test result.

[a] Defined as >6 WBCs/mL of CSF.

[b] Sensitivity, 5%; specificity, 95%; positive predictive value, 27%; negative predictive value, 72%; LR⁺, 0.97; LR⁻, 1.0; ratio of LR⁺ to LR⁻, 0.97.

[c] Sensitivity, 5%; specificity, 95%; positive predictive value, 27%; negative predictive value, 72%; LR⁺, 0.97; LR⁻, 1.0; ratio of LR⁺ to LR⁻, 0.97.

[d] Sensitivity, 30%; specificity, 68%; positive predictive value, 26%; negative predictive value, 73%; LR⁺, 0.94; LR⁻, 1.02; ratio of LR⁺ to LR⁻, 0.92.

Diagnostic Accuracy of Signs of Meningitis • CID 2002;35 (1 July) • 49

2014, prospective, ED

Table 3
Predicting pleocytosis among subjects receiving LP

	Sensitivity (0.95 CI)	Specificity (0.95 CI)	LR+	LR−
Headache (n = 230)	91% (88-95)	16% (11-21)	1.1	0.5
Fever (n = 230)	30% (24-36)	58% (52-65)	0.7	1.2
Jolt accentuation (n = 197)	21% (15-27)	82% (76-87)	1.2	1.0
Kernig sign (n = 229)	2% (0-4)	97% (95-99)	0.8	1.0
Brudzinski sign (n = 229)	2% (0-4)	98% (96-100)	1.0	1.0
Nuchal rigidity (n = 229)	13% (8-17)	80% (74-85)	0.6	1.1
Focal neurologic deficit (n = 229)	2% (0-4)	96% (93-98)	0.5	1.0
Vomiting (n = 229)	4% (2-7)	85% (80-89)	0.3	1.1
Rash (n = 229)	2% (0-4)	96% (94-99)	0.6	1.0
Physician suspicion (n = 230)	44% (31-59)	40% (33-47)	0.8	1.4

Abbreviation: 0.95 CI, 95% confidence interval.

No single symptom/sign as strong predictor.
Constellation of s/s remains possible.

Limitation

- Research assistant time frame
- Physican bias

Conclusion

- Jolt accentuation was poorly predictive of pleocytosis.
- Other symptoms/ signs are inconsistent predictor of presence or absence of meningitis.

Appraise

- 12 item CASP checklist for diagnostic questions
  - Clear question?
  - Diagnostic test appropriate?
  - All patient get diagnostic test?
  - Result influenced by the method of diagnostic test?
  - Disease clearly described? Comorbidity/ differential
  - Diagnostic test well followed?
  - Result presented with Sn, Sp, LR?
  - How sure inspect of the result? CI
  - Can result be applied to our population? Age/sex/ethnicity
  - Can test performed in our population? Skill/ cost
  - Could result change patient management? Improve well-being?
  - What is the impact of using the test on our population?

Level of evidence

Level 1
- Randomized controlled trial (RCT)
- Meta-analysis of randomized trials with homogeneous results

Level 2
- Prospective comparative study
- Meta-analysis of Level 2 studies or Level 1 studies with inconsistent results

Level 3
- Retrospective cohort study
- Case-control study
- Meta-analysis of Level 3 studies

Level 4
- Case series

Level 5
- Case report (a report of a single case)
- Expert opinion
- Personal observation

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Original Contribution

Pulmonary Embolism Rule-out Criteria vs D-dimer testing in low-risk patients for pulmonary embolism: a retrospective study☆,☆☆,★

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Introduction

- Europe guideline:
  - pre-test probability with Revised Geneva Score (RGS):
  - low to intermediate risk
    - -> d-dimer test (+)
    - -> CTPA , V/Q scan
- Pulmonary Embolism Rule-out Criteria (PERC):
  - high negative predictive value

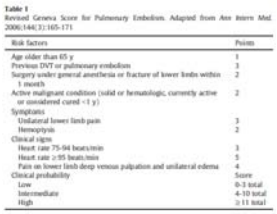

Table 1
Revised Geneva Score for Pulmonary Embolism. Adapted from Ann Intern Med. 2006;144(3):165-171.

Risk factors	Points
Age older than 65 y	1
Previous DVT or pulmonary embolism	3
Surgery under general anesthesia or fracture of lower limbs within 1 month	2
Active malignant condition (solid or hematologic, currently active or considered cured <1 y)	2
Symptoms	
Unilateral lower limb pain	3
Hemoptysis	2
Clinical signs	
Heart rate 75-94 beats/min	3
Heart rate ≥95 beats/min	5
Pain on lower limb deep venous palpation and unilateral edema	4
Clinical probability	Score
Low	0-3 total
Intermediate	4-10 total
High	≥11 total

Pulmonary Embolism Rule-out Criteria (PERC)

- Defined PERC as positive, if any positive of the following:
  - age above 49 years
  - pulse rate above 99 beats per minute
  - pulse oxymetry less than 95% on room air
  - unilateral leg swelling
  - history of hemoptysis
  - prior diagnosis of PE or deep vein thrombosis
  - recent surgery or trauma in the last 4 weeks
  - exogenous estrogen intake

Objective

- Rate of PE with D-dimer testing in PERC-negative patients
- Adverse events associated with: invasive imaging, anticoagulation treatment and unnecessary hospitalization for further testing

Method-population and setting

- 4 urban academic emergency departments in Paris metropolitan area (annual census of 45000 to 55000 ED visits each)
- from January 1, 2012, a 12-month period

Method-Inclusion/Exclusion Criteria

Inclusion criteria: all patient that had D-dimer testing

Exclusion criteria:

- PERC positive
- RGS intermediate to high
- incomplete chart PERC not available
- D-dimer test for other suspicion: DVT, septic coagulation screen...

Method-Data collection

Chart abstraction according to the recommendation of Gilbert et al.:

- Definition of every variable recorded
- Explicit protocols and criteria for selection and inclusion, or exclusion of screened patients
- Training of abstractors before the study starts with practice medical charts and examples
- Regular meeting between abstractors and study coordinators during the study, and after completion of data collection at each site
- Blinding initial chart reviews to the tested hypothesis, as PERC score was calculated prior to the collection of diagnosis

Method-Outcome

- D-dimers analyzed using ELISA with normal range under 500 ng/mL
- CTPA or V/Q scan interpreted by senior radiologist + second senior radiologist blinded to PERC score
- PE was diagnosed by one chart abstractor + principal investigator
- Cohen κ 1.0 = perfect agreement

Result

- 223287 ED visits

15/153 experienced adverse events:

- 2 allergic reactions to iodine contrast agent
- 13 started anticoagulation treatment with unnecessary admission

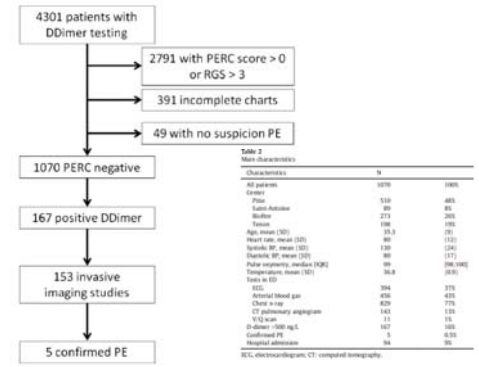

Fig. Flowchart. PERC: Pulmonary Embolism Rule out Criteria. RGS: Revised Geneva Score. PE: Pulmonary Embolism.

Conclusion

- D-dimer testing for PERC-negative patients led to 15% of irradiative imaging studies, for a rate of newly diagnosed PE of 0.5%, similar to prevalence
- The mortality rate of newly diagnosed PE was very low (0-1%)

Further D-dimer testing for PERC negative patients was not suggested

Discussion

- Kline et al: High sensitivity and negative predictive value
- Hugli O et al: pulmonary embolism rule-out criteria (PERC) rule does not safely exclude pulmonary embolism. *J Thromb Haemost JTH 2011;9:300–4.*

Discussion

- Retrospective = loss of follow up = no information on how many false-negative patients were discharged
  - Sensitivity, specificity and negative predictive values could not be calculated
  - Objective of this study is to determine the added value rather than sensitivity and specificity of the test

Appraise

- 12 item CASP checklist for cohort questions
  - Clear question?
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Level 3
- Retrospective cohort study
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Level 4
- Case series

Level 5
- Case report (a report of a single case)
- Expert opinion
- Personal observation

Question

- Newly diagnosed PE 0.5%, similar to prevalence?