

Past, present and future of molecular testing in haematology in Belgium

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1st June, 2006

Causes of the delay of introduction of molecular testing in haematological labs in Belgium

Discussion on:

1. Who is able to perform properly molecular testing
2. Which speciality is allowed to perform which molecular testing

Specialities claiming molecular testing in Belgium

1. Labs for human genetics from centres for hereditary diseases
2. Clinical biology labs
3. (Histo-) pathology labs
- [4. Labs performing neonatal screening for congenital diseases]

Working field of centres for hereditary diseases

- Defined by a Royal Decree in 1987 (article 1) as:
“Centres where diagnoses are made on”:
 1. the possibility that malformation or abnormalities, either mental or physical, are determined by heredity
 2. the nature of in (1) mentioned malformation or abnormalities
 3. the carrier state of hereditary properties
- In the explanatory memory of this Decree is stated that
“Activities of centres of hereditary diseases are often so complex, the investigated anomalies so rare making a limitation of numbers of such centres mandatory”.
- 7 University centres programmed in 1988; in 1989 addition of an 8th centre (“Institut de morphologie pathologique” of Loverval)

RIZIV/INAMI nomenclature on genetic testing (article 33) (1)

- Only 8 general items in the RIZIV/INAMI nomenclature. No diagnostic rules, 1 cumulation rule (588615 and 588652 may not be cumulated)
- Main numbers:
 - 588615/588652: karyotyping B8000 (298.96 €)
 - 588696: determination of genetic anomalies B8000 (298.96 €)
with a hybridisation method of DNA fragments
 - 588722/588794: dosage of intracellular enzymes
irrespective of the numbers, in order to detect
genetic anomalies B1050 (39,24€)

RIZIV/INAMI nomenclature on genetic testing (article 33) (2)

To allow tariffication important restrictions:

- test has to be performed by a recognised MD working in a recognised centre for antropogenetica
- test has to be prescribed by a MD working in the frame of genetic counselling in a centre for hereditary diseases recognised by the “high council for antropogenetica”

Working field of clinical biology labs

- Defined in a Royal Decree in 1999 – article 1-2: Clinical biology means: “the acts in the domains of biochemistry, haematology and microbiology including the utilisation of molecular biology and immunology, irrespective of usage of radio isotopes.
- In 2005 196 laboratories of clinical biology were recognised fulfilling the requirements of this Royal Decree

RIZIV/INAMI nomenclature or clinical biology testing (article 4 and 24)(1)

- *> 300 tests in the different fields of clinical biology*
- *testing in the field of haematology includes:*
 1. Bloodgroup – and tissue typing, both genetically defined
 2. Diagnosis and follow-up of benign haematologic disorders both congenital and acquired e.g.:
 - anaemias such as haemolytic anaemias: sferocytosis, thalassaemia, PK/G6PD deficiencies...
 - investigation for bleeding disorders: coagulation factor deficiencies
 - investigation for coagulation disorders: FV Leiden, FII mutation ...
 3. Tests for diagnosis and follow-up of malignant haematological disorders (with frequently acquired genetic abnormalities): cytologic and cyto-chemic or -enzymologic investigations, immunophenotyping.....

RIZIV/INAMI nomenclature on clinical biology testing (article 4 and 24) (2)

- ***> 80 diagnostic rules. Two examples in the field of haematology:***
 - ATIII, PC and PS testing (rule 20): only on patients < 45 yr with a thrombotic event, patients with a familial history of recurrent thrombosis or in case of diffuse intravascular coagulation
 - immunophenotyping (maximum 25 markers) (rule 68): only for diagnosis of acute haematological malignancies
- ***> 150 rules on cumulation/combination criteria***

RIZIV/INAMI nomenclature on (histo)pathology testing (article 32)

- *[no working field defined in a Royal Decree]*
- *main testings:*
 - histopathological examination of different organs/tissues (several numbers with a different tariffication)
 - histopathological examination during an operation by the freeze method
 - immuno-histochemical examination (maximum 4)
 - cytopathological examination (vaginal smears: max. 1/year)
 - access to eight examination numbers of the clinical biology nomenclature

Difficulties to introduce molecular techniques in haematological labs

- ***Main difficulty:*** claim of centres for anthropogenetica to restrict all molecular testing on human genome to genetic centres
- ***Other difficulties:***
 - lack of reimbursement (for all labs including genetic centres)
 - frequent improper use of RIZIV/INAMI code 588696 (hybridisation of DNA fragments) of article 33 by (some) genetic centres
 - [- difficulties of molecular techniques]
 - [- inadequate training (possibilities)]
 - risk of over consumption

Past, present and future of molecular testing: bloodgroup- and tissue typing

Present status

- 1999: introduction in article 24 of HLA-ABC/DR and DP/DQ testing “independent of the method used with the exclusion of a molecular biology technique”
- 2000: restriction “exclusion of a molecular biology technique” is removed
- [accreditation of HLA labs performed by European Federation of Immunogenetics (EFI)]

Future:

- all new molecular tests on bloodgroup- and tissue typing will probably be included in article 24 of the RIZIV/INAMI nomenclature

Past, present and future of molecular testing: benign haematological disorders

- *Past and present status*

- in 1998 during preceding negotiations molecular testing in benign haematological disorders was excluded from the task of the CMD/CDM (cf. malignant haematological disorders)
- till now not one test included in the nomenclature of clinical biology but several labs perform them

Past, present and future of molecular testing: benign haematological disorders (2)

- Introduction, however, is mandatory for two main clinical reasons:
 1. Additional molecular testing is sometimes needed for the differential diagnosis (and adequate therapy) in individual patients (e.g. with an (acute) haemolysis, bleeding, thrombosis...)
 2. Clinical haematologists (internal medicine, pediatry) are trained to give individual and familial counselling in congenital haematological disorders (e.g. haemochromatosis, haemophilia, sickle cell anaemia, thalassaemia...)
- explosion of cost (>10%/year) of genetic tests of article 33 will necessitate to review this nomenclature. Proposal of 2003 of working party of TGR/CTM is still in debate

Past, present and future of molecular testing: benign haematological disorders

- *Future*

- impasse due to rigid positions; impartial instance and approach urgently needed

- a study 2006-10 HSR on “Task and organisation of centres for human genetics” will be conducted by the KCE (kenniscentrum/centre d’expertise)

Past, present and future of molecular testing: malignant haematol. disorders

Past:

- Molecular testing performed in some genetic centres and clinical biology/pathology labs since early 1990's
- Three main reasons were quoted to delay introduction of molecular tests in clinical biology/pathology nomenclature:
 - molecular techniques too difficult to be performed in any lab
 - inadequate training of clinical biology/pathology staff
 - risk of overconsumption (mainly in field of microbiology)
- In 1998, as transient solution, CMD/CDM were set up

Past, present and future of molecular testing: malignant haematolog. disorders

- *Centres for molecular diagnostics (1998)*
 - only hospital clinical biology/ pathology labs (1/hospital)
 - prove of scientific expertise and knowledge in molecular testing
 - have to be associated with a centre for human genetics
 - limitative list of tests with possibility of yearly update (no tests on benign haematological disorders)
 - creation of a national committee (2 representatives of each CMD/CDM and 2 of the “High Council of Anthropogenetica”)

Past, present and future of molecular testing: malignant haematolog. disorders

- *centres for molecular diagnostics (1998)*
- tasks of national committee
 - * organisation of a quality control
 - * make proposals for introduction of molecular tests in the nomenclature
 - * give directives for requests and interpretation
 - * assignment to each CMD/CDM of part of the yearly budget (264 milj. BEF)

Past, present and future of molecular testing: malignant haematolog. disorders

- **2000-2003:** working party of haemato-oncology of CMD/CDM proposes several tests for introduction in the nomenclature. Accepted in 2003 by representatives both of clinical biology, pathology and centres for human genetics (in the commission clinical biology of TGR/CTM). Delayed due to lack of proposals in the field of microbiology
- **2005:** breaking of Royal Decree on CMD/CDM mainly because of exclusion of private labs
- **2005:** report of KCE on molecular testing in microbiology, haemato-oncology and oncology

Recommendations of the KCE report in molecular testing in microbiology and haemato-oncology/oncology (1)

Clear distinction between recommendation for microbiology and haemato-oncology/oncology

- Microbiology:

- * tests of proven clinical utility and greater frequency: introduction in existing clinical biology nomenclature
- * tests of low frequency: reference centre

- Haematology-oncology/oncology:

- * members of an oncology care programme and molecular/cytogenetic labs have to work out diagnostic schemes and reports have to be unified
- * different options for reimbursement inclusive nomenclature

Recommendations of the KCE report in molecular testing in haemato- oncology/oncology (2)

- Haematology-oncology/oncology:

- * the obligation to offer a complete spectrum of cytogenetic and molecular testing, to make service level agreements with the hospitals involved, and obligatory ISO accreditation, makes a further selection unnecessary
- * reimbursement for haemato-oncology/oncology via CME nomenclature has to be stopped

Recommendations of the KCE report in molecular testing in haemato- oncology/oncology (3)

- *Main remarks on recommendation for haemato-oncology/oncology*
 - * no referral to other techniques used in a diagnostic scheme e.g. morphology, immunophenotyping
 - * only very few tests with sufficient level of diagnostic utility
 - * linkage between cytogenetic and molecular testing unclear: one laboratory? agreements?

Past, present and future of molecular testing: malignant haematolog. disorders

Present and future:

- *temporary alternative financing* till introduction of molecular tests in the nomenclature or other way of financing :

new RIZIV/INAMI proposal for 2005-2006 with same principles as CMD/CDM except:

- * centres of genetics not involved
- * addendum list only contains haemato-oncology tests
- * no obligation to organise a quality control programme

Past, present and future of molecular testing: malignant haematolog. disorders

Present and future

- *Introduction of (haemato)-oncology tests in nomenclature based on CMD/CDM working party*

Main principles:

- * list of +/- 20 molecular tests including diagnostic and cumulation rules
 - * may be performed only in labs involved in a diagnostic and therapeutic oncology care programme
 - * ISO certification needed for all performed tests
 - * labs controlled by WIV/ISP
- *Other way of financing?*