



Research Annual Report 2009



Other research

Pharmacogenetics

Hospital pharmacy and clinical pharmacology

The allergic immune response and related allergic diseases

Determinants of falls and disability in older persons

Neurotraumatology and intracranial hydrodynamics

The urinary tract: Physics, function, epidemiology and reconstructive surgery

Pathophysiology and treatment of asthma, atopy and cystic fibrosis

Clinical affective neuroscience and psychiatric epidemiology

Biology and technology of oral and maxillofacial surgery

Diagnosis and treatment of disorders of the posterior segment and strabismus

Optimalising respiratory, circulatory and metabolic functions for improved (wound)healing after trauma and operation and infection in intensive care patients

Otorhinolaryngology and head & neck surgery

Addiction research

Philosophy of Medicine



Research Annual Report 2009



Other research

Palliative and supportive care

Surgery, non-programme associated

Pediatrics, non-programme associated

EMC OR-01-25-01 – Pharmacogenetics

Programme design in brief

The focus of this program is on molecular markers that can predict the effectiveness or the risk of adverse reactions of therapeutic interventions. In particular, the contribution of genetic factors in the drug metabolism is investigated.

Translational research is performed to define and evaluate the clinical significance of genetic polymorphisms in drug metabolizing enzymes (o.a. CYP450s, UGTs, TPMT and NAT genes), drug transporters (OATPS, OATS, ABC-Transporters) and drug targets (a.o. Folate-Dependant Emzymes). Drug classes include immuno-suppressives, anti-depressants, anti-cancer drugs, anaesthetics, anti-arrhythmics, anti-viral drugs, anti-coagulation drugs, proton pump inhibitors, opioids and anti-rheumatoid drugs. In addition, genetic and metabolic factors are investigated that determine the level of plasma homocysteine and its deleterious effect on methylation reactions

Key figures

| Department | SP1 | SP2 | SP3 | SP4 | SPtot | T1 | T2 | T3 | Ttot | IS | FS | OP | Ptot |
|--------------------|------|-----|-----|-----|-------|----|----|----|------|----|----|----|------|
| clinical chemistry | 3,63 | 0 | 0 | 0 | 3,63 | | | | | | | | |
| internal medicine | 0,3 | 0 | 0 | 0 | 0,3 | | | | | | | | |
| Total | 3,93 | 0 | 0 | 0 | 3,93 | 0 | 0 | 0 | 0 | 25 | 2 | 1 | 28 |

Article/Letter to the editor

Baker, S.D., Verweij, J., Cusatis, GA, Schaik, R.H.N. van, Marsh, S., Orwick, SJ, Franke, RM, Hu, S, Schuetz, EG, Lamba, V, Messersmith, WA, Wolff, A.C., Carducci, M.A. & Sparreboom, A. (2009). Pharmacogenetic Pathway Analysis of Docetaxel Elimination. *Clinical Pharmacology & Therapeutics*, 85(2), 155-163.

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Bijl, M.J., Schaik, R.H.N. van, Lammers, L.A., Hofman, A., Vulto, A.G., Gelder, T. van, Stricker, B.H.C. & Visser, L.E. (2009). The CYP2D6*4 polymorphism affects breast cancer survival in tamoxifen users. *Breast Cancer Research and Treatment*, 118(1), 125-130.

Bliek, J.B., Schaik, R.H.N. van, Heiden, I.P. van der, Sayed-Tabatabaei, F.A., Duijn, C.M. van, Steegers, E.A.P. & Steegers-Theunissen, R.P.M. (2009). Maternal Medication Use, Carriership of the ABCB1 3435C > T Polymorphism and the Risk of a Child With Cleft Lip With or Without Cleft Palate. *American Journal of Medical Genetics Part A*, 149A(10), 2088-2092.

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Driel, L.M.J.W. van, Eijkemans, M.J.C., Jonge, R. de, Vries, JHM de, Meurs, J.B.J. van, Steegers, E.A.P. & Steegers-Theunissen, R.P.M. (2009). Body Mass Index Is an Important Determinant of Methylation Biomarkers in Women of Reproductive Ages. *Journal of Nutrition*, 139(12), 2315-2321.

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EMC OR-01-34-01 - Hospital pharmacy and clinical pharmacology

Programme design in brief

Pharmacokinetics describe how the organism handles a drug, pharmacodynamics deal with the effects of the drug on the organism. Pharmacogenetics studies the genetic factors that contribute to variability in both pharmacokinetics and pharmacodynamics.

In our research programme we are active in all three topics. At present the focus of our activities is in the following areas of interest:

1. Transplantation. For several immunosuppressive drugs therapeutic drug monitoring is routinely applied. Pharmacogenetic studies aim to identify genes causing interindividual variability in drug exposure, population pharmacokinetic studies focus on non-genetic factors. Studies are ongoing in kidney, liver and heart transplantation. In kidney transplantation a multinational randomized trial investigating the value of therapeutic drug monitoring for mycophenolate mofetil is coordinated by our center. In 2005 a new PK/PD study was initiated, looking at IMPDH monitoring.
2. Oncology. Population pharmacokinetic studies are performed to identify patient factors that explain interpatient variability in exposure to anticancer drugs (e.g. docetaxel).
3. Psychiatry. Several anti-depressive and anti-psychotic drugs are critical dose drugs, for which dose adjustment based on drug levels is applied. In several clinical trials PK/PD analysis is part of the outcome parameters. In 2005 a prospective trial was started, to evaluate the impact of genotyping CYP2D6 before initiating imipramine therapy.
4. Pediatrics. Limited sampling strategies are developed to allow pharmacokinetic studies in neonates. Methods for determination of renal function in pediatric patients are evaluated.

Key figures

| Department | SP1 | SP2 | SP3 | SP4 | SPtot | T1 | T2 | T3 | Ttot | IS | FS | OP | Ptot |
|-------------------|-----|-----|-----|-----|-------|----|----|----|------|----|----|----|------|
| internal medicine | 0,1 | 0 | 0 | 0 | 0,1 | | | | | | | | |
| pharmacy | 2,3 | 1 | 0 | 2 | 5,3 | | | | | | | | |
| Total | 2,4 | 1 | 0 | 2 | 5,4 | 3 | 0 | 0 | 3 | 47 | 9 | 7 | 66 |

Thesis

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Article/Letter to the editor

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EMC OR-01-39-07 - The allergic immune response and related allergic diseases

Programme design in brief

The program is focused on the allergic immune response, the pathophysiological backgrounds of allergic disorders and the different forms of intervention. The induction of the allergic reaction by allergens is the basis of research to characterization of allergens, the relation between inhalant and food allergics and the modulation of the allergic reactions. Apart from classical pharmacotherapy and environmental control immunomodulation of the allergic response is the most promising form of intervention.

The main components of research comprise:

Occupational allergy. Erasmus MC has a unique location in a heavily industrialized environment, providing an excellent opportunity for research in occupational allergy.

This is reflected by research to allergy in horticulture and health professionals. Patient care in occupational allergy is organized in a multidisciplinary initiative instituted by the section of Allergology in collaboration with the departments of Dermatology, Pulmonology, ENT and Public health. There is a close connection between this initiative and our research. Currently, 2 large longitudinal studies among bell pepper and health care workers are being finalised. The focus of research is on the incidence of occupational disease and the effects of occupational disease on sick leave, work performance, costs and health related quality of life.

Food allergy. Research focuses on the optimization of diagnostic procedures.

Research objectives are closely related with patient care initiatives. In particular, the new initiative "Kinderhaven" - collaboration between Allergology, Pediatric Pulmonology and Pediatric Dermatology provides an environment for research to this topic.

Immunomodulation. The section Allergology is taking part in large scale RCT's to the effectiveness of sublingual immunotherapy. There is collaboration with the dept. of General Practice. A start has been made to the effect of biologicals on the allergic immune response. A promising pilot study is now followed by case-control study with sunitib in patients from the department of Oncology. Finally, a large cost-effectiveness study with regard to allergen immunotherapy has been started in 2009. The section of Allergology is taking the lead in this multi-center study financially supported by ZonMW.

Respiratory allergy and asthma. In 2009 we started to collaborate with the CHDR (Center for Human Drug research). One of their research directors has been sent on secondment to the section of Allergology. Together with the dept of Pulmonology of the Erasmus MC and the University Hospital in Gent we are establishing a new line of investigation focusing on the pharmacological modulation of the allergic response in rhinitis and asthma.

Key figures

| Department | SP1 | SP2 | SP3 | SP4 | SPtot | T1 | T2 | T3 | Ttot | IS | FS | OP | Ptot |
|---------------------|-----|-----|-----|-----|-------|----|----|----|------|----|----|----|------|
| family practice | 0 | 1 | 0 | 0 | 1 | | | | | | | | |
| internal medicine | 0,6 | 0 | 0 | 0 | 0,6 | | | | | | | | |
| otorhinolaryngology | 0,3 | 0 | 0 | 0 | 0,3 | | | | | | | | |
| Total | 0,9 | 1 | 0 | 0 | 1,9 | 0 | 0 | 0 | 0 | 6 | 2 | 2 | 10 |

Article/Letter to the editor

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Part of book - abstract

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EMC OR-01-39-08 - Determinants of falls and disability in older persons**Programme design in brief**

A - Determinants of falls

B - Drugs: effects and side effects, drug-related hospital admission, drug-related falls.

C - Vascular ageing.

D - Dementia - Co-morbidity in Alzheimer's disease

E - Delirium - Determinants and prognosis

F - Transmural projects with Stichting 'De StroomOpmaatGroep' in Rotterdam, Stichting Elisabeth in Breda and with the

Department of Industrial Design of Delft

Technical University

Key figures

| <i>Department</i> | <i>SP1</i> | <i>SP2</i> | <i>SP3</i> | <i>SP4</i> | <i>SPtot</i> | <i>T1</i> | <i>T2</i> | <i>T3</i> | <i>Ttot</i> | <i>IS</i> | <i>FS</i> | <i>OP</i> | <i>Ptot</i> |
|-------------------|------------|------------|------------|------------|--------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|
| internal medicine | 1,3 | 0 | 0 | 0 | 1,3 | | | | | | | | |
| Total | 1,3 | 0 | 0 | 0 | 1,3 | 0 | 0 | 0 | 0 | 15 | 0 | 2 | 17 |

Article/Letter to the editor

Blonk, M.I., Velde, N. van der, Cammen, T.J.M. van der, Stricker, B.H.C., Schaik, R.H.N. van & Bemt, P.M.L.A. van den (2009). Relatie tussen polymorfismen van CYP2D6*4, CYP3A5*3 en ABCB1 343ST en het risico op medicatiegerelateerde valincidenten bij ouderen. *PW*, 3, 187-190.

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Part of book - abstract

Velde, N. van der & Cammen, T.J.M. van der (2009). Drugs and falls. In S Jackson, P Jansen & P Mangoni (Eds.), *Prescribing for elderly patients* (pp. 429-433). Signapore: Fabulous Printers.

EMC OR-01-45-01 - Neurotraumatology and intracranial hydrodynamics

Programme design in brief

The program is devoted to experimental and clinical research in the field of traumatic brain injury (TBI) and hydrocephalus. The program on TBI focuses on three themes: 1) Trial methodology, guidelines and evidence based medicine, 2) Intensive care monitoring/therapy and neuroprotection, 3) Ethics and outcome. The program on intracranial hydrodynamics mainly concentrates on normal pressure hydrocephalus.

Head injury is the most common cause of death and disability in young adults in the Western world. As such it constitutes a major health and socio-economic problem. The initial trauma initiates complex pathophysiologic mechanisms, leading to secondary brain damage. Basic research has elucidated many of these mechanisms and has resulted in the development of promising neuroprotective agents.

Various of these agents are being tested in our in vitro model of experimental TBI. We have participated in the clinical evaluation of neuroprotective agents. This translational research has proved complex, and none of the randomised controlled trials on neuroprotective agents with demonstrated efficacy in the experimental situation, has shown convincing benefit in the overall population of TBI. Problems in clinical trial design and analysis, specific to the field of TBI may have contributed to this failure. Methodologic challenges are related to the heterogeneity of the population, outcome assessment, detection of treatment effects, the use of surrogate markers and interim analyses. These observations have prompted a significant research effort, organised as an international collaboration based on extensive analyses of data available from studies and trials in TBI encompassing approximately 10.000 patients.

International recognition of the importance of this study was illustrated by the receipt of a NIH RO1 grant for the period 2003-2006.

In the clinical situation cerebral ischemia is considered the central factor in the development of secondary damage.

Experimental and clinical programs focus on techniques for monitoring cerebral oxygenation and metabolism. Previous work has demonstrated the value of clinical monitoring of local brain oxygen tension in patients with TBI, and the current research focuses on possibilities to target therapy towards cerebral oxygenation

The third theme of the TBI program focuses on outcome assessment, including evaluation of cognitive functioning, and the development and evaluation of a disease specific scale for quality of life assessment in TBI. Ethical considerations are relevant to neuro-intensive care in general and particularly to the field of neuro-traumatology. The main focus of ethical research and evaluation concentrates on informed consent procedures in acutely incapacitated patients following TBI.

Normal pressure hydrocephalus is a treatable disease common to elderly patients with symptomatology often akin to Alzheimer's disease or vascular dementia. In this theme specific attention is paid to clinical diagnostic criteria and to shunt hydrodynamics. The department of neurosurgery currently co-ordinates a national multi-center study evaluating the use of a programmable shunt device for treatment of normal pressure hydrocephalus.

Key figures

| Department | SP1 | SP2 | SP3 | SP4 | SPtot | T1 | T2 | T3 | Ttot | IS | FS | OP | Ptot |
|--------------|-----|-----|-----|-----|-------|----|----|----|------|----|----|----|------|
| neurosurgery | 3,5 | 0 | 0 | 0 | 3,5 | | | | | | | | |
| Total | 3,5 | 0 | 0 | 0 | 3,5 | 0 | 0 | 0 | 0 | 4 | 1 | 0 | 5 |

Article/Letter to the editor

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EMC OR-01-49-02 - The urinary tract: Physics, function, epidemiology and reconstructive surgery

Programme design in brief

The program concentrates on physical and (neuro)physiological modelling of the urinary tract. Models are developed on the basis of measurements in single smooth muscle cells, muscle fibres and complete organ systems in vitro. Passive and active mechanical properties, electrophysiological properties and excitation-contraction coupling are described in this way. The innervation and function of the organ systems are studied in situ in guinea pigs and rats using morphological and neurophysiological methods. The models are applied for the development of diagnostic and therapeutic methods in a clinical setting. Epidemiological studies such as a longitudinal non-invasive study of changes in urinary bladder contractility secondary to benign prostatic hyperplasia, provide normative data that are important for modelling and clinical analysis as well. In this way function and dysfunction are described quantitatively and new treatment modalities are evaluated objectively. Automated analysis of clinical data and non-invasive diagnostic methods are important issues in the diagnostic field. In the therapeutic field, emphasis is placed on the development and evaluation of neural stimulation techniques to modulate organ (dys)function based on neurophysiologic principles and on stemcell therapy of incontinence

Key figures

| <i>Department</i> | <i>SP1</i> | <i>SP2</i> | <i>SP3</i> | <i>SP4</i> | <i>SPtot</i> | <i>T1</i> | <i>T2</i> | <i>T3</i> | <i>Ttot</i> | <i>IS</i> | <i>FS</i> | <i>OP</i> | <i>Ptot</i> |
|-------------------|------------|------------|------------|------------|--------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|
| urology | 2,4 | 0 | 0,67 | 0 | 3,07 | | | | | | | | |
| Total | 2,4 | 0 | 0,67 | 0 | 3,07 | 0 | 0 | 0 | 0 | 2 | 2 | 1 | 5 |

Article/Letter to the editor

Huang Foen Chung, J.W.N.C. & Mastrigt, R. van (2009). Age and Volume Dependent Normal Frequency Volume Charts for Healthy Males. *Journal of Urology*, 182(1), 210-214.

Idzenga, T., Pel, J.J.M. & Mastrigt, R. van (2009). Perineal sound recording for diagnosis of bladder outlet obstruction. *Indian Journal of Urology*, 25(1), 92-98.

Mastrigt, R. van, Pel, J.J.M., Huang Foen Chung, J.W.N.C. & Zeeuw, P.A. de (2009). Development and application of the condom catheter method for non-invasive measurement of bladder pressure. *Indian Journal of Urology*, 25(1), 99-104.

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Part of book - abstract

Mastrigt, R. van, Pel, J.J.M., Huang Foen Chung, J.W.N.C. & Zeeuw, P.A. de (2009). Niet invasieve meetmethoden voor obstructie. In *Handboek prostaataandoeningen* (pp. 107-112). Utrecht: De Tijdstroom.

EMC OR-01-54-02 - Pathophysiology and treatment of asthma, atopy and cystic fibrosis

Programme design in brief

This programme aims (1) to elucidate the etiology and pathogenesis of childhood asthma and asthma-like lung disease and allergy and determining the effects of chronic inflammation on the development and function of the respiratory system and (2) to determine the effects of therapeutic and preventive interventions in chronic inflammatory lung disease and atopy in children. Chronic lung disease, especially asthma, is one of the leading causes of chronic morbidity in children. Childhood asthma and other obstructive lung diseases predispose for obstructive lung disease in adults, an important health care issue with great socioeconomic impact. The search for causal and contributing factors, development of new diagnostic techniques and the determination of optimal treatment modalities for childhood asthma and allergy has the potential to improve morbidity and prognosis, and thus to reduce the burden of these diseases. In this respect, the development and validation of new techniques to measure lung function and airway inflammation in infants and young children has priority.

Infant lung function testing and new image analysis techniques using CT scan are developed as sensitive, objective endpoints for assessment of airway inflammation and damage. The development of structural lung damage is studied in a cohort of CF patients using CT and extensive lung function testing.

Inhalation of aerosolized medication is an important aspect of the treatment of lung disease, and poses specific problems in the pediatric age group. In this project, we examine the factors that determine lung deposition and effects of inhaled drugs in young children to optimize the effects of treatment.

The therapeutic and preventive intervention studies carried out within this project are important for specific patient groups (asthma, cystic fibrosis), and have impact for the treatment of childhood obstructive lung disease in primary and secondary health care practice.

The development of allergic diseases with age is studied in two large birth cohorts (Prevention and Incidence of Asthma and Mite Allergy, "PIAMA", and "Generation R"). These focus on interaction of genetic and environmental factors in relation to immunopathology and clinical phenotypes

Key figures

| Department | SP1 | SP2 | SP3 | SP4 | SPtot | T1 | T2 | T3 | Ttot | IS | FS | OP | Ptot |
|------------|-----|-----|------|-----|-------|----|----|----|------|----|----|----|------|
| pediatrics | 0,8 | 1 | 1,76 | 2 | 5,56 | | | | | | | | |
| Total | 0,8 | 1 | 1,76 | 2 | 5,56 | 2 | 0 | 0 | 2 | 30 | 4 | 8 | 44 |

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EMC OR-01-58-01 - Clinical affective neuroscience and psychiatric epidemiology

Programme design in brief

The research programme comprises two main projects:

I. Clinical affective neuroscience

II. Psychiatric epidemiology

Ad. I. This project combines psychiatric, psychometric, and psychophysiological measurements with pathogenetic neurobiological (neuroanatomical, neurophysiological, neurochemical, neurogenetics) investigations. Emotional and autonomic disturbances are investigated in relation to perceptual, motivational and psychomotor disturbances in adult patients with developmental mental disorders, psychotic disorders, depressive disorders or pre- and postpartum mental disorders. In addition, the effectiveness of neurobiological interventions, like psychopharmacological and electroconvulsive therapy, is investigated, related to pathogenetic mechanisms. A separate subproject focuses on the behavioural phenotypes in mentally retarded patients with psychiatric symptoms and/or behavioural abnormalities, with special emphasis on the relationship between genetic aetiology and dimensions of symptoms.

Ad.II. This project is part of O3, the Mental Health Research Centre Rijnmond. Prevalence, socio-economic determinants, development, persistence and interrelations of criminal or disruptive behaviour, social dysfunctioning, psychiatric disorders, and utilisation of mental health care are investigated, making use, amongst others, of the Psychiatric Case Register Rijnmond.

Key figures

| Department | SP1 | SP2 | SP3 | SP4 | SPtot | T1 | T2 | T3 | Ttot | IS | FS | OP | Ptot |
|------------|-----|------|-----|------|-------|----|----|----|------|----|----|----|------|
| psychiatry | 5,6 | 2,41 | 0 | 8,83 | 16,84 | | | | | | | | |
| Total | 5,6 | 2,41 | 0 | 8,83 | 16,84 | 1 | 0 | 0 | 1 | 33 | 5 | 39 | 78 |

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EMC OR-01-59-01 - Biology and technology of oral and maxillofacial surgery

Programme design in brief

General objectives

In Oral and Maxillofacial Surgery, the reconstruction of defects of either teratological, traumatological or pathological disposition, is always directly related to optimal function and esthetics of the face. The regeneration of hard and soft tissues can be initiated with the biological process of distraction osteogenesis. This process is utilized in a clinical setting and further elucidated in an animal study. The purpose of the projects is the development and evaluation of this process.

1. Various rhythms and forces in distraction osteogenesis: an animal experimental study. In a rabbit model different rhythms and forces are clinically, radio graphically (including micro-CT) and histologically tested to investigate ideal parameters for distraction osteogenesis.
2. Surgically-assisted rapid maxillary expansion: surgical and orthodontic aspects. In a prospective randomized clinical trial two surgical methods of widening the narrow maxilla are tested. The bone-borne distraction is compared with the tooth-borne distraction.
3. Orbital wall fractures: a prospective clinical trial. In a prospective randomized clinical trial two surgical endoscopic-assisted methods of orbital wall fractures are explored: autogenous bone from the iliac crest is compared with an alloplastic material.
4. Midface-hypoplasia: various peri-operative aspects. In patients with congenital craniofacial anomalies the severe hypoplastic midface can be corrected by means of distraction osteogenesis. In this study short-term and long-term results are evaluated including the usage of modern 3D-CT scanning.

Key figures

| Department | SP1 | SP2 | SP3 | SP4 | SPtot | T1 | T2 | T3 | Ttot | IS | FS | OP | Ptot |
|--------------------------------|------|-----|-----|-----|-------|----|----|----|------|----|----|----|------|
| oral and maxillofacial surgery | 1,05 | 0 | 0 | 1 | 2,05 | | | | | | | | |
| Total | 1,05 | 0 | 0 | 1 | 2,05 | 0 | 0 | 0 | 0 | 8 | 1 | 3 | 12 |

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EMC OR-01-60-01 - Diagnosis and treatment of disorders of the posterior segment and strabismus

Programme design in brief

Studies of cornea, uveal melanoma, macular diseases and strabismus

Ways are sought to prolong the survival of corneal grafts by local modulation of the immune response. Therefore, cellular and humoral immunity is examined in experimental corneal allograft rejection.

In a prospective and retrospective study of uveal melanoma patients the relation between chromosomal abnormalities and survival are analysed with molecular biology techniques. The detection of these chromosomal abnormalities in fine needle biopsies is validated with fluorescent in-situ hybridisation in collaboration with the Universities of Sheffield and Liverpool. Target genes like p16, p73 and pten are investigated. In a prospective study the control rate and complication rate is studied in uveal melanoma patients treated by stereotactic radiotherapy.

The pathogenesis of age-related macular degeneration (AMD) was studied in een group of very old. Macaque monkeys.

Molecular mechanisms that causes senescence in the retina, apoptosis and the expression of somatostatine receptor 2A are studied. Somatostatin receptor binding may inhibit angiogenesis in AMD. A pilot study was performed with octreotide treatment for the control of subfoveal choroidal neovascularisation in AMD in men. A two-center prospective randomized masked trial is initiated to investigate its clinical effect. The study of the effect of adjuvant hormonal treatment in surgery for macular holes is ongoing.

The study of strabismus consists of three multicenter and cohort studies: Together with the University of Heidelberg a study is organised to address the question whether children with congenital strabismus should be operated early or late, involving 54 European clinics (1992-2002). A second randomized study is organised that compares the two surgical techniques that are most commonly used in congenital strabismus, in 9 German and 4 Dutch clinics (1997-2002). A new microelectronic device has been developed that measures compliance in patch wearing in children with amblyopia; a cohort study has been initiated to measure compliance in the treatment of amblyopia

Key figures

| <i>Department</i> | <i>SP1</i> | <i>SP2</i> | <i>SP3</i> | <i>SP4</i> | <i>SPtot</i> | <i>T1</i> | <i>T2</i> | <i>T3</i> | <i>Ttot</i> | <i>IS</i> | <i>FS</i> | <i>OP</i> | <i>Ptot</i> |
|-------------------|------------|------------|------------|------------|--------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|
| ophthalmology | 1,7 | 0,4 | 0 | 3,07 | 5,17 | | | | | | | | |
| Total | 1,7 | 0,4 | 0 | 3,07 | 5,17 | 1 | 0 | 0 | 1 | 29 | 1 | 1 | 32 |

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Part of book - abstract

Simonsz, H.J. & Kolling, G.H. (2009). Best age for surgery for infantile esotropia: Lessons from the Early vs. Late Infantile Strabismus Surgery Group. In B Lorenz & MC Bordsky (Eds.), *Pediatric Ophthalmology, Neuro-Ophthalmology, Genetics; Strabismus - New Concepts in Pathophysiology, Diagnosis, and Treatment* (pp. 137-149). Berlin: Springer Verlag.

EMC OR-01-61-01 - Optimising respiratory, circulatory and metabolic functions for improved (wound)healing after trauma and operation and infection in intensive care patients

Programme design in brief

Intensive care is an indispensable health care provision. Mortality rates and morbidity typically are high. Every aspect of this specialism is continuously subject to new developments and views and opinions are subject to rapid changes. The developments are characterised by their multidisciplinary and technological nature. Recovery of intensive care patients requires optimal gas exchange and supply of nutrients to the tissues. The research efforts in a broader sense are aimed at technological improvements for optical tissue characterization for diagnosis and guidance of clinical procedures, non-invasive blood analysis, patient monitoring and rapid diagnosis of clinically relevant microorganisms for optimal patient treatment and infection control.

Key figures

| <i>Department</i> | <i>SP1</i> | <i>SP2</i> | <i>SP3</i> | <i>SP4</i> | <i>SPtot</i> | <i>T1</i> | <i>T2</i> | <i>T3</i> | <i>Ttot</i> | <i>IS</i> | <i>FS</i> | <i>OP</i> | <i>Ptot</i> |
|-------------------|------------|------------|------------|------------|--------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|
| Total | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 0 | 0 | 5 |

Article/Letter to the editor

Boncheva, M, Sterke, J. de, Caspers, P.J. & Puppels, G.J. (2009). Depth profiling of Stratum corneum hydration in vivo: a comparison between conductance and confocal Raman spectroscopic measurements. *Experimental Dermatology*, 18(10), 870-876.

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EMC OR-01-62-02 - Otorhinolaryngology and head & neck surgery

Programme design in brief

Can we improve early detection of disease?

Do prognostic models improve the quality of health care?

Head and neck cancer

Can we identify the role of organ-sparing strategies in head and neck cancer?

Do modern optical imaging and molecular biology add to the current diagnostic armamentarium?

What are key factors in optimal palliation of head neck cancer patients?

How can we improve Quality of Life in head and neck cancer?

Audiology/otology

Can we adequately describe epidemiology of hearing loss and can we identify etiological factors?

Can we improve diagnostics in hearing loss and central auditory processing disorders?

How can we effectively evaluate and optimise the result of Cochlear Implantation?

Speech

Is the Lidcombe programme for early stuttering intervention more (cost-)effective than the Demands and Capacities Model based treatment (Dutch standard) ?

Can risk factors for a Speech Sound Disorder (SSD) in preterm children at age 4 be identified? Is a short, parent based speech intervention programme for preterm children with a SSD at 2 years of age effective ?

Tissue engineering

Find methods to repair large tissue defects after oncologic surgery

Key figures

| Department | SP1 | SP2 | SP3 | SP4 | SPtot | T1 | T2 | T3 | Ttot | IS | FS | OP | Ptot |
|---------------------|------|------|-----|-----|-------|----|----|----|------|----|----|----|------|
| orthopaedics | 0,22 | 0 | 0 | 0 | 0,22 | | | | | | | | |
| otorhinolaryngology | 6,69 | 0,29 | 0 | 0 | 6,98 | | | | | | | | |
| Total | 6,91 | 0,29 | 0 | 0 | 7,2 | 3 | 0 | 0 | 3 | 40 | 3 | 5 | 51 |

Thesis

Borgstein, J.A. (2009, april 01). Surgical observations on atelectasis of the middle ear in children. EUR. Prom./coprom.: Prof.Dr. L. Feenstra.

Hakkesteegt, M.M. (2009, oktober 07). Evaluation of voice disorders, Dysphonia Severity Index and Voice Handicap Index. EUR. Prom./coprom.: Prof.Dr. L. Feenstra.

Tan, M.L. (2009, september 16). Cellular mechanisms of auditory processing in the inferior colliculus, an in vivo patch clamp study. EUR. Prom./coprom.: Prof.Dr. L. Feenstra & Prof.Dr. J.G.G. Borst.

Article/Letter to the editor

Al-Mangani, A., Tans, L., Rooij, P.H.E. van, Noever-Smit, I., Baatenburg de Jong, R.J. & Levendag, P.C. (2009). Hypofractionated radiotherapy denoted as the Christie scheme: An effective means of palliating patients with head and neck cancers not suitable for curative treatment. *Acta Oncologica*, 48(4), 562-570.

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Bever, Y. van, Gischler, S.J., Hoeve, L.J., Smit, L.S., Nauta, J. & Dooijes, D. (2009). Obstructive apneas and severe dysphagia in a girl with Townes-Brocks syndrome and atypical feet involvement. *European Journal of Medical Genetics*, 52(6), 426-429.

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- Part of book - abstract**
Gier, H.H.W. de (2009). Dysfagie. In SCF van den Borne & DJM Mateijns (Eds.), *KNO didact, handboek voor de huisarts*. Alphen aan de Rijn: Van Zuiden Communications.

EMC OR-01-65-03 - Addiction research

Programme design in brief

What is the prevalence and incidence of drug use, alcohol consumption and other lifestyles and addiction? Which factors are the determinants of lifestyles and addiction? What are the consequences of lifestyles and addiction in terms of health, quality of life, environment (a.o. nuisance). What is the quality, efficiency of addiction care, prevention and policy? What is the interaction of lifestyles and addiction with society

Key figures

| Department | SP1 | SP2 | SP3 | SP4 | SPtot | T1 | T2 | T3 | Ttot | IS | FS | OP | Ptot |
|--|-----|-----|-----|-----|-------|----|----|----|------|----|----|----|------|
| addiction research institute Rotterdam (IVO) | 1 | 0 | 0 | 3,5 | 4,5 | | | | | | | | |
| public health | 0 | 0 | 0 | 0,8 | 0,8 | | | | | | | | |
| Total | 1 | 0 | 0 | 4,3 | 5,3 | 3 | 0 | 0 | 3 | 9 | 0 | 18 | 30 |

Thesis

Baars, J.E. (2009, januari 16). Hard to reach?: hepatitis B vaccination among high-risk groups. EUR (159 pag.). Prom./coprom.: Prof.Dr. H. van de Mheen, Prof.Dr. H.F.L. Garretsen & B. Boon.

Kleinjan, M. (2009, februari 26). Dawning dependence : processes underlying smoking cessation in adolescence. EUR (273 pag.). Prom./coprom.: R.C.M.E. Engels, Prof.Dr.Ir. J. Brug & R.J.J.M. van den Eijnden.

Poel, J. van der (2009, december 16). Low-threshold care for marginalised hard drug users. EUR. Prom./coprom.: Prof.Dr. H. van de Mheen.

Article/Letter to the editor

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Research case

Schoenmakers, T.M., Baars, J.E. & Mheen, H. van de. Schatting van het aantal problematische harddruggebruikers in Den Haag voor 2008.

Straaten, B. van & Kleinjan, M. Een verkenning van onderzoek en geneesmiddelenontwikkeling op het gebied van stoppen met roken.

Straaten, B. van & Kleinjan, M. Priority Medicines. Een verkenning van onderzoek en geneesmiddelenontwikkeling op het gebied van alcoholische leveraandoeningen.

EMC OR-01-74-01 - Philosophy of Medicine

Programme design in brief

Are the obese the lepers of modern time? When is suffering unbearable? Is it okay to enhance one's memory by taking a pill? Can doctors still do the best for individual patients in health care systems organised by market principles? Is there an obligation to donate a kidney to one's close ones? Just some examples of questions we are working on now.

In our research the following themes play a central role:

Ethics and individual responsibility for health

Ethics, beauty and appearance

Ethics and fiction

Ethics and paediatrics

Ethics and technology assessment and professional morality

Ethics and transplantation

These are the themes that we have been working on for at least 5 years. More recent subjects we are working on are: medical decisions regarding the end of life, neuroethics and ethical aspects of pandemics.

We work in interdisciplinary contexts we; are not afraid of practical solutions, but also fascinated by underlying fundamental ethical issues. We strive for international cooperation, particularly via our EU projects, but we also participate in the Dutch debate.

Key figures

| Department | SP1 | SP2 | SP3 | SP4 | SPtot | T1 | T2 | T3 | Ttot | IS | FS | OP | Ptot |
|---|------|------|-----|------|-------|----|----|----|------|----|----|----|------|
| medical ethics and philosophy of medicine | 4,17 | 2,53 | 0 | 0,53 | 7,23 | | | | | | | | |
| Total | 4,17 | 2,53 | 0 | 0,53 | 7,23 | 0 | 0 | 0 | 0 | 12 | 7 | 40 | 59 |

Article/Letter to the editor

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External report

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EMC OR-01-86-13 - Palliative and supportive care

Programme design in brief

Palliative care aims to improve the quality of life of patients and their relatives in case of life-threatening disease. Because of the complexity of problems, multidisciplinary partnership is considered of utmost importance. When the underlying disease is still responsive to specific therapy, supportive care will be given to enhance the patient's quality of life by (symptomatic) treatment of concurrent disease- or therapy-induced complications. The research programme includes studies on the prevalence of symptoms and psychosocial problems in cancer patients at different stages during the course of disease, their needs and perceived quality of life and the development of clinical interventions to achieve symptom control in these patients. Specific attention is given to the development of effective interventions for chemotherapy-induced complications, medical and nurse-initiated interventions in pain and fatigue management, the use of a care pathway for the dying and end-of-life decisions.

Key figures

| Department | SP1 | SP2 | SP3 | SP4 | SPtot | T1 | T2 | T3 | Ttot | IS | FS | OP | Ptot |
|------------------------------------|------|------|-----|-----|-------|----|----|----|------|----|----|----|------|
| medical oncology | 0,67 | 0 | 0 | 0 | 0,67 | | | | | | | | |
| medical psychology & psychotherapy | 0,48 | 0 | 0 | 0 | 0,48 | | | | | | | | |
| palliative care | 0 | 0 | 0 | 1 | 1 | | | | | | | | |
| public health | 0,04 | 1,11 | 0 | 0 | 1,15 | | | | | | | | |
| Total | 1,19 | 1,11 | 0 | 1 | 3,3 | 1 | 0 | 0 | 1 | 10 | 3 | 5 | 19 |

Thesis

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Article/Letter to the editor

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Dooren, S. van, Duivenvoorden, H.J., Passchier, J., Bannink, M., Tan, M.B.M., Oldenmenger, W.H., Seynaeve, C. & Rijt, C.C.D. van der (2009). The Distress Thermometer assessed in women at risk of developing hereditary breast cancer. *Psycho-Oncology*, 18(10), 1080-1087.

Heide, A. van der & Rietjens, J.A.C. (2009). End of life decisions Doctors can be trusted. *British Medical Journal (International Edition)*, 339.

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Part of book - abstract

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EMC OR-02-47-12 - Surgery, non-programme associated**Key figures**

| <i>Department</i> | <i>SP1</i> | <i>SP2</i> | <i>SP3</i> | <i>SP4</i> | <i>SPtot</i> | <i>T1</i> | <i>T2</i> | <i>T3</i> | <i>Ttot</i> | <i>IS</i> | <i>FS</i> | <i>OP</i> | <i>Ptot</i> |
|-------------------|------------|------------|------------|------------|--------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|
| surgery | 0,9 | 1,3 | 0 | 2 | 4,2 | | | | | | | | |
| Total | 0,9 | 1,3 | 0 | 2 | 4,2 | 2 | 0 | 0 | 2 | 17 | 2 | 1 | 22 |

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Article/Letter to the editor

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| <i>Department</i> | <i>SP1</i> | <i>SP2</i> | <i>SP3</i> | <i>SP4</i> | <i>SPtot</i> | <i>T1</i> | <i>T2</i> | <i>T3</i> | <i>Ttot</i> | <i>IS</i> | <i>FS</i> | <i>OP</i> | <i>Ptot</i> |
|-------------------|------------|------------|------------|------------|--------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|
| Total | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 23 | 8 | 4 | 36 |

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