Objectives

- Background and history of nomenclature project
- Rationale and Methods
- Application to nomenclature: controversies defining terms of the head and face
- Gestalt approach to face morphology
- Use of anthropometry
Why define phenotype variation?

- Syndrome indicator
- Statistical association with more serious internal defects, e.g. single central incisor
- Marker for study of teratogen
- Develop models for diagnostic reasoning, decision-making formulas, disease criteria
- Applied to computer programs and standard forms to aid diagnosis
- Scientific papers
Prominent nose and chin

Low-set ears with dysplastic helices
Short neck, pug nose

High eyebrows

Long philtrum, large earlobes
Flat philtrum  
Wide mouth
Hypertelorism, downslanting palpebral fissures, epicanthal folds
Mapping phenotypes to language: a proposal to organize and standardize the clinical descriptions of malformations

LG Biesecker
Clin Genet 68: 320-6, 2005
Attributes of an ideal standardized clinical genetics nomenclature

One-to-one correspondence of clinical terms to clinical manifestations

The confidence of the assignment of a feature should be codified

Terms should be linked to appropriate, validated qualifiers

Terms should not subsume multiple features if those features can occur alone

Descriptive terms should be coded in a form-driven manner and not recorded in prose

The terms should be versioned for updating and referencing to prior versions

LG Biesecker
Clin Genet 68: 320-6, 2005
The external ear: More attention to detail may aid syndrome diagnosis and contribute answers to embryological questions

Alasdair G.W. Hunter, Takatoshi Yotsuyanagi
Goals

- Reach consensus on usage and definitions of terms needed for phenotype analysis
- Obtain international “buy in”
- Facilitate accurate and standard descriptions in articles and databases
- Improve comparisons between syndromes and clinical data for studies of etiology, epidemiology and, ultimately, treatment
- Facilitate genotype-phenotype correlations
- Enhance our ability to train clinical geneticists and dysmorphologists
List of body regions
Sub-title: Naïve and ambitious

- Build and stature
- Face (including neurocranium, forehead)
- Eyes (including general, iris, pupil, lens, cornea, conjunctiva and sclerae)
- Periorbital tissues (including eyelids, borws, lashes, spacing, lacrimal apparatus)
- Nose
- Jaws (upper, lower, chin)
- Perioral (including mouth, philtrum, upper and lower lips)
- Intraoral structures (including voice)
- Teeth
- Ears
- Neck and shoulders
- Thorax (including ribs, mamma, nipple)
- Abdomen (including anus)
- Genitalia male
- Genitalia female
- Back (including sacrum, spinal cord, pelvis)
- Upper limbs
- Hands (including fingers, thumbs)
- Lower limbs
- Feet (including toes)
- Joints (including muscle, nerve supply)
- Skin (including hair, nails)
Brainstorming

- Concentrate on dysmorphic features
- Reduce project scope from entire list of LDDB terms (n=683)
- Start with craniofacies, hands and feet
- Divide that list into logical groups: eyes, nose, oral region, ears etc
- Set up a team to work on each region
- Team to decide first if any features should be removed or added?
- Agree on key list of features for each team

August 2005
Format

- Quantitative and qualitative traits
  - Variations in size: macrocephaly, microtia
  - Variations in shape: turriencephaly
  - Variations in position: low-set ears
  - Variations in individual anatomical parts: high anterior hairline, underfolded helix
  - Named anomalies: crumpled ear, cryptotia, Stahl ear
Teams

- **Judith Allanson**, Chris Cunniff, Gene Hoyme, Julie McGaughran, Max Muenke, Giovanni Neri
- **Les Biesecker**, Jon Aase, Carol Clericuzio, Fiorella Gurrieri, Karen Temple, Helga Toriello
- **John Carey**, Michael Cohen, Cyndy Curry, Koen Devriendt, Lew Holmes, Alain Verloes
- **Bryan Hall**, Susie Cassidy, John Graham, John Opitz
- **Raoul Hennekam**, Valerie Cormier-Daire, Judith Hall, Karoly Mehes, Michael Patton, Roger Stevenson
- **Alasdair Hunter**, Jaime Frias, Gabriele Gillessen-Kaesbach, Helen Hughes, Ken Jones, Louise Wilson

**Sponsorship:**
March of Dimes, CDC, NHGRI, University of Utah, John Wiley and Sons, Birth Defects Foundation [Newlife] UK, Catholic University Rome, Institute of Child Health UK
Expectations of each team:
Subtitle: Soft in the head

- Provide a definition for each term
- Present it in a standard format with synonyms and terms that have been replaced
- Describe how to measure or observe each feature
- Discuss and cite normal standards
- Include important anatomical or embryological details
- Provide good quality illustrations for each feature
- Achieve consensus and closure at a workshop in December 2005
Struggles

- Consensus among “experts”
- Avoidance of terms that imply an action: depressed, flattened
- Whether to include associated syndromes: NO
- Whether to include etiology/pathogenesis: NO
- Whether to include embryology: NO........or JUST A BIT
- Whether to include anatomy: YES where key
- Avoidance of bundled terms: included very few: “coarse”
- Use of radiographs for hands and feet: NO
- Open access to the published papers
- Wordsmithing and formatting
The future

- The project has taken 6 years from the original idea to publication
- Self-selected group and do not represent the international dysmorphology community
- We have not included the developing world yet we want the terms to be used world-wide
- Input from experts in other related disciplines: ophthalmology, dentistry, ENT
- International buy in
- Translation
- International nomenclature committee, similar to ISCN, Human Genome Variation Society nomenclature, with periodic discussion and revision
**Hairline, high anterior**

**Definition:** Distance between the hairline (trichion) and the glabella (the most prominent point on the frontal bone above the root of the nose), in the midline, more than two SD above the mean. *objective*

OR

Apparently increased distance between the hairline and the glabella. *Subjective*

**Comments:** This measurement is carried out with sliding caliper [Farkas 1981]. This feature gives the appearance of a tall forehead, and may or may not include reduction of hair in the temporal areas. This can be distinguished from male pattern baldness as the hairline is the superior boundary of the muscular forehead, which can be actively wrinkled, in contrast to the scalp where no wrinkling can occur. In addition, texture of the skin of the scalp differs from the texture of the skin over the forehead.

**Synonym:** Forehead, tall

Forehead, tall: see *Hairline, high anterior*
**Midface:** This is a region and not an anatomical term. It extends, superiorly, from the inferior orbital margin to, inferiorly, the level of nasal base. It is formed by the maxilla (upper jaw) and zygoma. Traditionally, the nose and premaxilla are not included in the midface.
Malar process (syn. frontal process): The most medial and superior part of the maxilla. It forms the medial border of the inferior bony orbit, and is contiguous with the lateral boundary of the nasal bridge.

Maxillae: these paired bones form, by their union, the upper jaw and contain the upper dentition. Each assists in forming the boundaries of three cavities – the palate, floor and lateral wall of the nose (frontal or malar process), and floor of the orbit. Each bone consists of a body and 4 processes – zygomatic, malar (frontal), alveolar and palatine.

Zygoma: the part of the temporal bone of the skull that forms the prominence of the cheek. It is also known as the zygomatic bone or arch, the malar bone (creating confusion with the malar process of the maxilla), the cheek bone and the yoke bone. The zygomatic arch is composed of the malar process of the maxilla, medially, the zygoma, centrally, and the temporal bone, posterolaterally. It forms part of the part of the lateral wall and floor of the orbit.
Ear rotation posterior angulation
Anatomical variation

- Triangular fossa
- Helix
- Scapha
- Antihelix, stem
- Cymba
- Concha
- Cavum
- Antitragus
- Lobe
- Incisura
- Crus helix
- Superior (posterior) crus of antihelix
- Inferior (anterior) crus of antihelix
- Tragus
**Nasal bridge:** A saddle-shaped area that includes the nasal root and the lateral aspects of the nose. It lies between the glabella and the inferior boundary of the nasal bone, and extends laterally to the inner canthi.

**Nasal ridge:** The midline prominence of the nose, extending from the nasal root to the tip (also called the dorsum of the nose).

**Nasal root:** The most depressed, superior part of the nose along the nasal ridge.
**Lips: Anatomy**

**Lips:** The structures that surround the oral aperture. In the central region their superior border corresponds to the inferior margin of the base of the nose. Laterally, their limits follow the alar sulci and the upper and lower lips join at the oral commissures. The inferior limit of the lips in the central region is the mentolabial sulcus. The surface of the lip is comprised of four zones: hairy skin, vermilion border, vermilion and oral mucosa.

**Philtrum:** A vertical groove in the midline of the upper lip bordered by two lateral ridges or pillars.

**Vermilion:** The red part of the lips.

**Vermilion border:** The rim of paler skin that demarcates the vermilion from the surrounding skin.
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