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Inherited Homeotic Midfacial Malformations in Burmese Cats

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During the past three decades, Burmese cats have been selected for a shorter muzzle and a more rounded face. Recently there arose a line of these animals that consistently exhibit such a brachycephalic appearance; unfortunately, approximately 25% of these kittens are born with a neonatal lethal midfacial malformation.

The abnormality is characterized by 1) agenesis of all derivatives of the medial nasal prominence; 2) lateral duplication of most derivatives of the maxillary process; including the canine teeth and whiskers fields; 3) telencephalic meningoencephalocele; and 4) secondary ocular degeneration. The anatomy, embryology, and pattern of inheritance of this unique midfacial malformation are described.

Key words: neural crest defects

INTRODUCTION

Studies of the mechanisms underlying craniofacial development using experimental embryological, teratological, and genetic methods have contributed greatly to our knowledge about the etiology of malformations and dysmorphologies of the brain and calvaria, sense organs, and the facial, palatal, and oral regions. However, each of these approaches has its own technical limitations, and our understanding of the development of these regions is incomplete.

This problem is especially acute in the midfacial area. While there exists a large body of observational [Couly, 1981; Kokich et al, 1982] and experimental [Adelmann, 1936; Evans et al, 1966] data pertaining to midfacial reduction defects, especially as related to various severities of holoprosencephaly [Lemire et al, 1981; Siebert et al, 1981; Cohen, 1982], less attention has been directed towards understanding how mesenchymal populations that form the frontonasal and maxillary prominences become spatially programmed and committed to particular species- and individual-unique patterns of development [see Opitz and Gilbert, 1982]. Lack of information is especially troublesome given the high frequency with which dysmorphologies of this region occur either alone or as part of syndromes [Barr, 1982; Cohen and Lemire, 1982; Siebert et al, 1985], which may have a genetic [eg, Toriello et al, 1985] or teratogenic [eg, Sulik and Johnston, 1983] basis.

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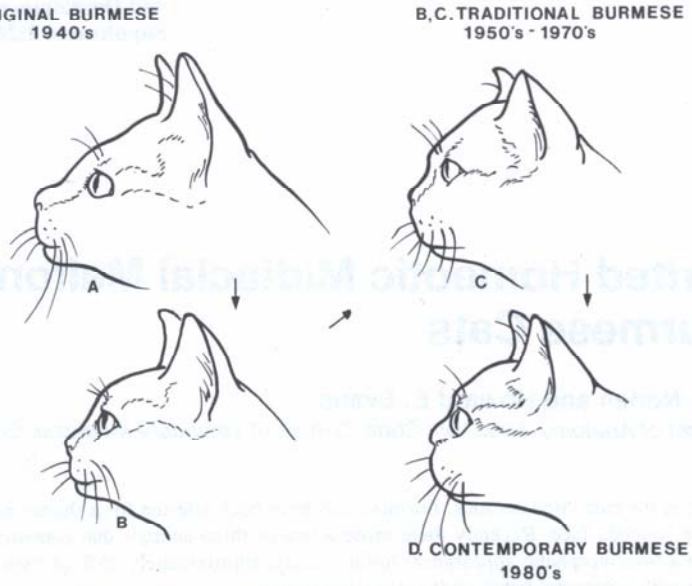


Fig. 1. Profiles of Burmese cats during the past four decades. The Contemporary phenotype is a round-faced, brachygnathic cat.

Mesenchymal cells that form frontonasal and maxillary prominences arise from the neural crest of the rostral midbrain and diencephalic regions. This has been proved experimentally in amphibians [Hörstadius and Sellman, 1946; Chibon, 1964] and birds [Johnston, 1966; Noden, 1975, 1978; Le Lièvre and Le Douarin, 1975; Le Lièvre, 1978; McKee and Ferguson, 1984], and the descriptive studies of Bartelmez and Evans [1926], Innes [1985], Tan [1985], and Nichols [1985] indicate a similar origin in mammals. The rostral neural crest disperses to form a continuous mesenchymal sheet that surrounds the prosencephalon. Later, invagination of the nasal placodes partially segregates the medial nasal and primary palatal regions from lateral nasal and periocular mesenchymal fields. Postoptic crest mesenchyme extends beneath the prosencephalon to the adenohypophyseal diverticulum [reviewed by Noden, 1982; Meier, 1982; Le Douarin, 1982].

The issue of how crest cells that invade the frontonasal, maxillary, mandibular, and hyobranchial regions become programmed to form regionally unique, species-specific skeletal structures has received less attention. Consider the differences in programming that must occur within this mesenchyme to create bulldog and collie facial dimensions [Stockard, 1941], for example, or the many reported frontonasal and medial nasal malformations in humans [Gorlin et al, 1976; Couly, 1981; Couly and Le Lièvre, 1983].

The close correlation between rostral prosencephalic abnormalities and midfacial mesenchymal malformations is well established [reviewed by Opitz and Gilbert, 1982]. However, many xenoplastic (between different species) and heterotopic (between different axial regions) transplantations by Hörstadius and Sellman [1946] and Wagner [1949, 1959] suggest that properties inherent to premigratory crest populations are critical for normal spatial development. This has been most clearly demonstrated for crest cells that seed the mandibular region of the first branchial arch and the second (hyoid) arch in avian embryos. If presumptive second arch neural crest cells are excised and replaced with a comparable population of presumptive first arch

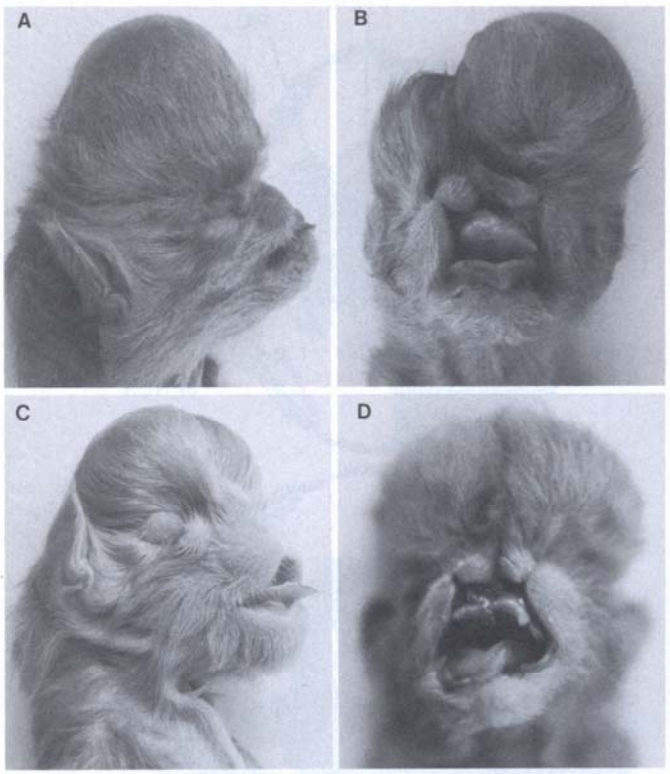


Fig. 2. Malformed neonatal Burmese showing encephalocele, anophthalmia, brachygnathia, and the presence of four whisker pads.

crest cells, host embryos develop with two sets of lower jaw structures, the normals and an extra set formed by graft-derived cells in the second arch [Noden, 1983, 1984; see Chapter by Noden, pages 15–32, this volume].

One enigmatic aspect of these recent grafting experiments is that when presumptive maxillary or frontonasal crest cells are similarly transplanted in place of the future second arch crest population, they too form a *mandibular* skeletal array; structures normally associated with maxillary, palatal, or frontonasal regions never appeared in ectopic locations. These data suggest that ectomesenchymal populations dispersing around the prosencephalon are not initially programmed to form specific mid- and lower facial structures.

The malformation in Burmese cats described in this report is linked to continuous selection over four decades for a rounded, brachycephalic facial appearance. This breed was first introduced to the United States in 1930 as a Siamese hybrid from Southeast Asia, but some of the progeny whelped from the original animal bred true for a dark, solid color and fine hair texture that are characteristic of the Burmese breed [Thompson et al, 1943; Levy, 1962]. These animals had an average muzzle (Fig. 1A), which was typical of the Siamese of the time but shorter than found in the Siamese of today. Beginning in the 1950's, breeders began to select for a more rounded head, with a full face tapering slightly to a short, well developed muzzle [Robie, 1967]. As is true with many quantitative, multifactorial aspects of inheritance, attempts to maintain lines with these craniofacial features were largely unsuccessful.

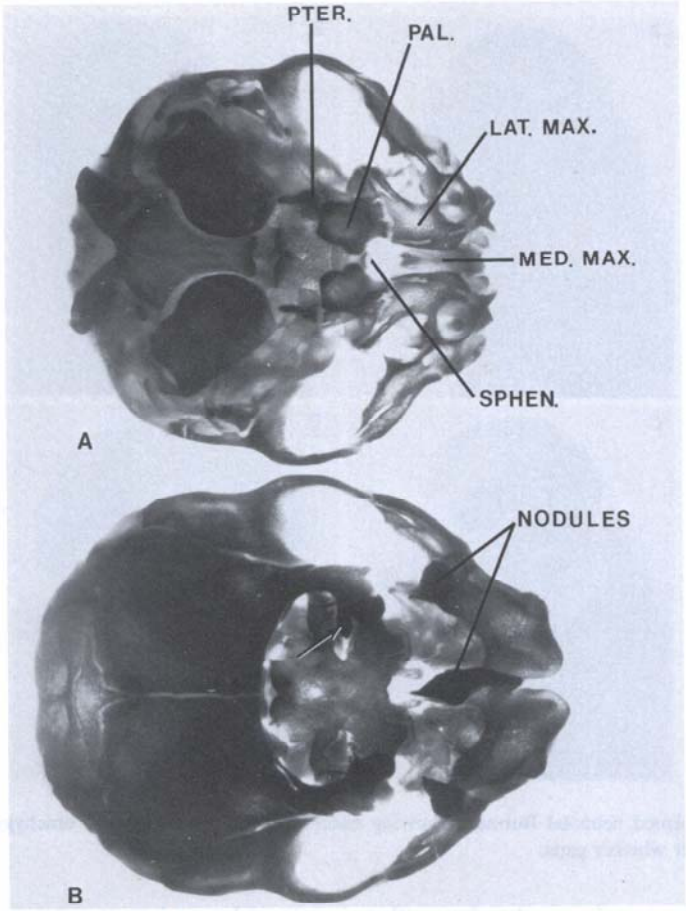


Fig. 3. Ventral (A) and dorsal (B) views of alcian- and alizarin-stained malformed neonates. The rostral tip of the sphenoid (SPHEN.) is marked. Arrow shows pigmented retinal tissue.

In the mid-1970's a line of Burmese cats became available that better fit the desired phenotype. This line is called the Eastern, "new look" or "Contemporary" strain of Burmese. They appear to be descended from a single male, and these cats have been enormously successful in competition. In addition to having rounded faces with distinctly heavy supraorbital crests (Fig. 1D), the contemporary Burmese cats typically have a more friendly demeanor.

Unfortunately, after these Contemporary Burmese had been introduced into colonies throughout the United States, breeders discovered that many litters from Contemporary crosses had one or more severely malformed live-born kittens, which died within a day of parturition. The malformation was initially described as either maxillonasal hypoplasia [Zook et al, 1983] or incomplete diprosopus, which has been reported occasionally in cats [Bissonette, 1933; Ellinger et al, 1950; Antin, 1956; Sekeles et al, 1985]. However, closer examination revealed that all normal derivatives of the median region of the frontonasal prominence were missing, and only two eyes and nostrils were visible [Noden et al, 1982].

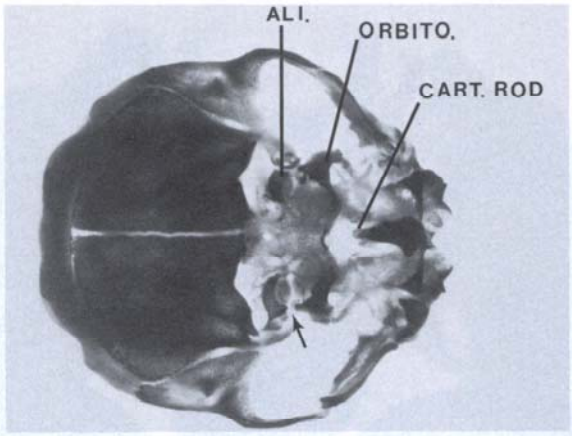


Fig. 4. Dorsal view of same animal as Figure 3A. The frontal bones have been removed to expose the sphenoid complex and optic canals (arrow). Note the absence of any median skeletal tissues articulating with the sphenoid rostrally.

NEONATAL ANATOMY

Neonatal Burmese kittens (n = 49) were obtained either by donation or from selected mating trials from 14 different cat breeders or veterinarians located throughout the United States. Breeding and ancestry records were available for 31 of these. Included in this total are six normal littermates used for comparative analysis. Five of the neonates received had anencephaly plus exophthalmos, which have been reported as occurring sporadically in both Burmese and Siamese breeds [Noden and de Lahunta, 1985]. However, there is no evidence that this condition is related to the syndrome in Comtemporary Burmese cats, and these animals were not included in the following analyses.

Affected kittens all have a telencephalic meningoencephalocele of varying severity (Fig. 2). In the worst cases, large, flaccid, fluid-filled vesicles have expanded over and covered the facial area; in these animals the forebrain is completely degenerated. There frequently is local alopecia over the encephalocele, and in a few cases an epidermal-meningeal anastomosis was apparent. The palpebrae are present but are convoluted and fused, and the animals appear to be anophthalmic.

The most unusual feature of these kittens is the appearance of the midfacial region. It is severely brachygnathic, and there are *two pairs of whisker pads*, with each pair surrounding a single external naris (Fig. 2B,D). Between each of the paired whisker pads is a deep furrow that, like the normal feline philtrum, opens ventrally. The two median whisker pads are joined in the midline by a shallow fissure.

The roof of the mouth is flat and ridged, with a distinct median furrow running caudally from the rostral margin of the oral cavity. There is no soft palate. The tongue protrudes from the oral cavity, but is not enlarged. In many animals there is a slight dorsal bowing of the lower jaw, which is typical of animals with maxillary hypoplasia and not unique to the Burmese syndrome. Postmortem examination of these kittens revealed no other gross congenital malformations.

Animals were received either in 10% formalin or frozen. In all cases the brain tissues were too necrotic to identify. Following dissection, 12 skulls were randomly

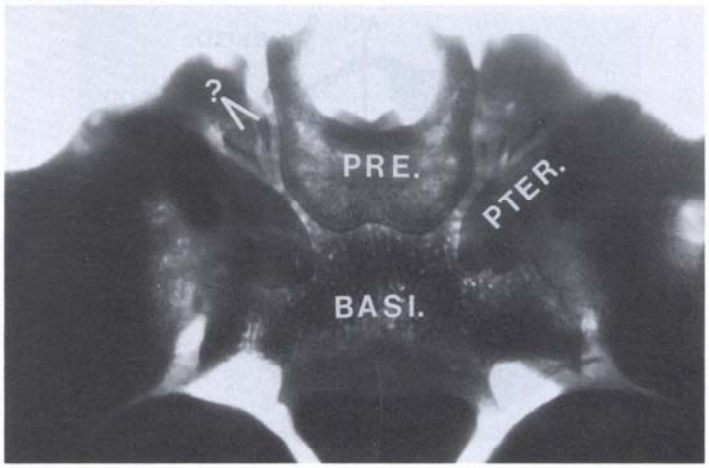


Fig. 5. Enlarged view of the floor of the basisphenoid (BASI.) region showing an abnormal presphenoid (PRE.) element and widely spaced pterygoid bones (PTER.).

chosen for clearing and in toto staining. Fresh or frozen specimens were skinned, and soft tissues were then immersed in 1.5% alcian blue in acidic ethanol for 1–2 days, rinsed in ethanol, then immersed in 0.5% potassium hydroxide until translucent. Following immersion in 0.01% alizarin red-S in 0.1% hydroxide for several days, the specimens were slowly dehydrated in a graded series of glycerol. The procedure for formalin-fixed material was similar except that the specimens were first washed thoroughly in running water, then stained in alcian blue, followed by treatment with 1% buffered trypsin until the remaining soft tissues were fully macerated [after Taylor, 1967; Watson, 1977].

Figures 3 and 4 present photographs of representative specimens. The cranioschisis is circumscribed by parietal and compressed frontal bones caudally and laterally. However, there are no skeletal tissues adjacent to the rostral margin of the opening, which is unlike a typical frontal cranioschisis. Occipital structures are normal.

The sphenoid complex is abnormal. The basisphenoid with temporal wings (alisphenoids) and that part of the presphenoid that bears large orbital wings constitute a single element (Fig. 3B). The length of this bone is approximately equal to the normal basisphenoid and half the presphenoid; its width is increased. The pterygoids articulate upon its ventral surface, and they are abnormally far apart. Underlying the sphenoid rostrally is a flat, horseshoe-shaped bone whose arms extend rostrally (Fig. 5). In some animals, these loosely contact the maxillae; in others they end freely. The rostral border of the body of the sphenoid is capped with cartilage but never articulates with other skeletal structures. All ethmoid and vomer elements are absent.

A ventral view of these skulls (Fig. 6) reveals a pair of widely spaced palatine bones with horizontal shelves that are heavily ossified and separated. The medial border of each shelf appears partially duplicated, with a distinct dorsomedial process not seen in normal neonatal cats; the perpendicular lamina and maxillary process are normal.

Extending forward from both the left and right palatines is a suture that separates a pair of large medial and lateral ossified structures. Each of these has a canine tooth and also a horizontal palatine process (Fig. 6). We have termed these the *lateral*

TABLE I. Contemporary Burmese Litters

Litter	Age (mm)	No. of: Normal	No. of: Malformed
1	21 d (9)	1	2
2	25 d (16)	6	0
3	30 d (30)	0	1
4	27 d (21)	5	0
5	22 d (10)	2	1[1]
6	30 d (29)	2	3
7	32 d (33)	3	2
8	27 d (20)	4	0
9	33 d (35)	3	0
10	25 d (16)	3	2[2]
11	26 d (18)	2	1

[1]Anencephalic fetus, not a typical Burmese syndrome.
[2]One fetus mummified

maxillary and *medial maxillary bones*. The two lateral maxillae have typical unerupted premolar teeth and normal zygomatic processes.

The medial maxillae are fused across the midline in the form of a rostrocaudally oriented pillar. In some animals, this median element is expanded dorsally and often has one or two osseous nodules resting on top of it without any articulation or suture, as in Figures 3B and 4. The midventral aspect of this median bone extends caudally toward, but never makes direct contact with, the sphenoid complex. Typically a cartilagenous rod is present in a shallow groove on the dorsal surface of this caudal extension. It is not possible to assign definitive identities to these structures.

Atop the caudodorsal zone of contact between the lateral and medial maxillae there appear one or two ossified nodules. In one animal these were attached to the dorsal median element by a dense connective tissue. It is not possible to assign identities to these various nodular structures. In no cases were nasal or premaxillary (incisive) structures present.

FETAL ANATOMY

In an attempt both to identify the ectopic skeletal structures described above and to unravel the etiology of this complex syndrome, fetuses were obtained from 11 queens (Table I). In all cases both parents displayed the Contemporary phenotype. Gravid uteri were obtained by spaying timed-pregnant animals either at the New York State College of Veterinary Medicine or at the owner's local veterinarian. Fetuses were exposed and immersed in either 10% formalin or 4% buffered glutaraldehyde. All specimens were photographed prior to subsequent processing.

Embryos displaying the Burmese syndrome were present in six litters. These were either cleared and stained with alcian blue and alizarin red (litter 6), dehydrated, critical-point dried, coated, and examined using an Hitachi HHS2R scanning electron microscope (litters 1 and 11), or dehydrated using a graded ethanol:butanol series, embedded in Paraplast, sectioned at 12 μm, and stained with H&E (litters 3, 7, and 10).

The oldest abnormal fetuses examined were at 30 and 32 days of gestation. These animals have a pronounced telencephalic encephalocele (Fig. 7). Optic tissues appear externally as a small, irregular mass rather than the distinct cornea, lens, and

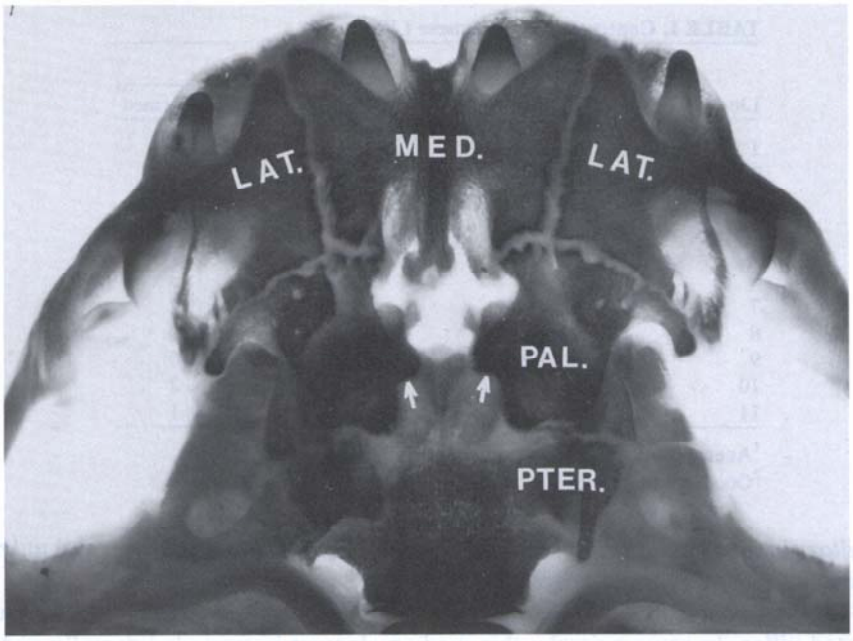


Fig. 6. The palatal and maxillary regions of a cleared, stained malformed Burmese kitten. The symmetric paired medial maxillae (MED.) and lateral maxillae (LAT.) each bearing a canine tooth and palatal process are shown. Arrows indicate sites of partial doubling of the shelves of the palatine (PAL.) bones.

pigmented retina visible in normal littermates. Maxillary prominences (processes) are present rostroventral to the eyes. Each is marked by two to four rows of whisker papillae, depending on the age, and forms the ventrolateral margin of the external naris.

In fetuses with the Burmese syndrome, the maxillary processes are located much farther apart than in normal littermates (compare Fig. 7A,B). The tissue masses between them appear as swellings located on both sides of the midline. In some embryos, these swellings have fused with the maxillary prominences ventral to the nares; in others, a cleft is still present. These paramedian prominences are characterized by the presence of three to four rows of whisker papillae (Fig. 8), a feature not normally found on medial nasal prominences. Both the normal and these ectopic whisker buds first appeared at 25 days of gestation. Based on this feature, I am calling these swellings the *medial maxillary prominences*. Between them in the midline is a shallow trough that extends into the oral cavity and has no distinguishing landmarks. It is important to emphasize that in none of the fetuses were there more than two external nares nor was there any evidence of a median optic vesicle.

Examination of cleared, alizarin red-stained normal 30-day (29 mm) embryos reveals well formed frontal, zygomatic, maxillary, incisive, palatine, and dentary bones (Fig. 9A); unossified mesenchymal aggregates forming the nasal and pterygoid bones could be recognized in the specimens. In Burmese syndrome fetuses the maxillae and palatines are abnormally far apart (Fig. 9B), but are otherwise identical with their homologues in normal fetuses. A pair of ectopic bones have formed, each rostral to the optic vesicle and slightly dorsal to the median part of the maxilla. The incisive, vomer, and nasal bones are absent.

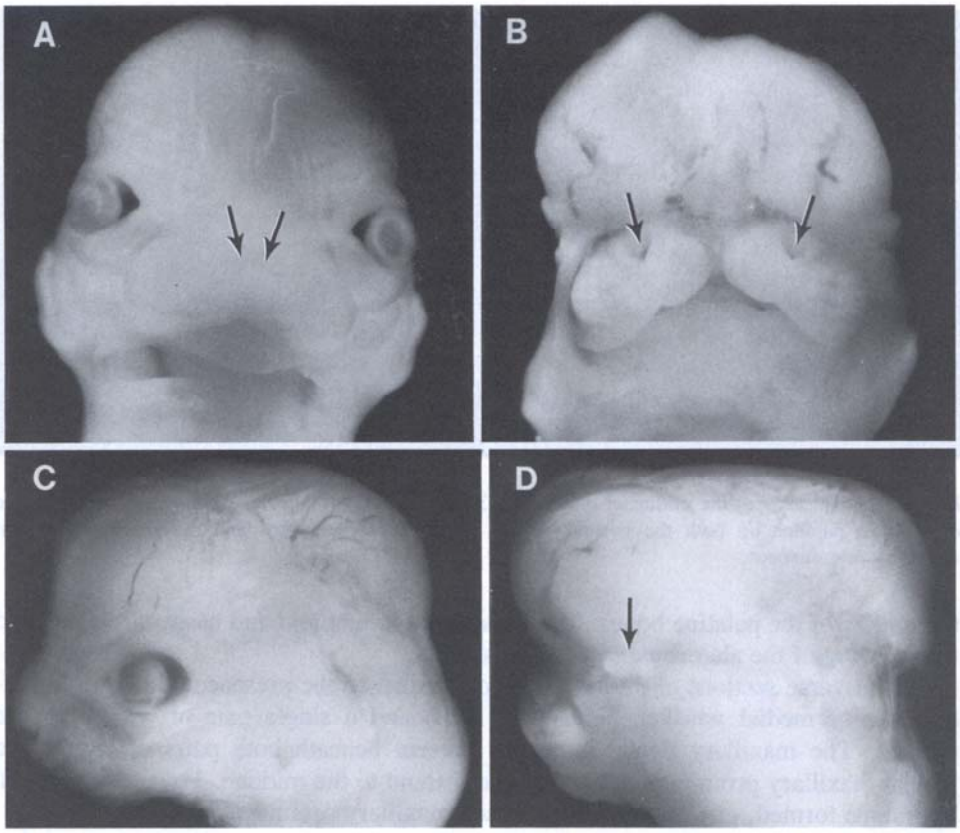


Fig. 7. Two 29-mm (30-day) Burmese fetuses. The abnormal littermate on the right has widely spaced nostrils (compare arrows in A, B), encephalocele, malformed midfacial swellings, and an abnormal solid tissue mass obscuring any evidence of optic structures (arrow in D).

The presumed frontals are present as small areas of chondrification caudolateral and occasionally rostral to the cranioschisis. This is unusual because the frontals normally form as intramembranous rather than as perichondral ossifications. It is possible that these cartilages are displaced portions of the orbital wing (ala orbitalis).

Across the rostral midline is a large, three-compartment, bilaterally symmetric dermal bone with one or two foramina in each lateral wing. Horizontal ossifying shelves project caudally from the lateral wings of this bone; these are adjacent to and in the same plane as the palatine processes of the maxillae. Also, a bony process projects caudally in the midline from the ventral margin of the median element of this complex. This fetal structure is the precursor to the medial maxillary complex described previously in the neonate.

The chondrocranium of these fetuses was examined using a modified dark-field illumination. In the malformed animals, the preoptic and metoptic roots of the orbitosphenoid are present, but the former project laterally in a transverse rather than an oblique rostral direction [see Terry, 1917; Evans and Christensen, 1979; Noden and de Lahunta, 1985, for descriptions of normal chondrocranial development]. The floor of the chondrocranium ends abruptly rostral to the optic canals at the level of

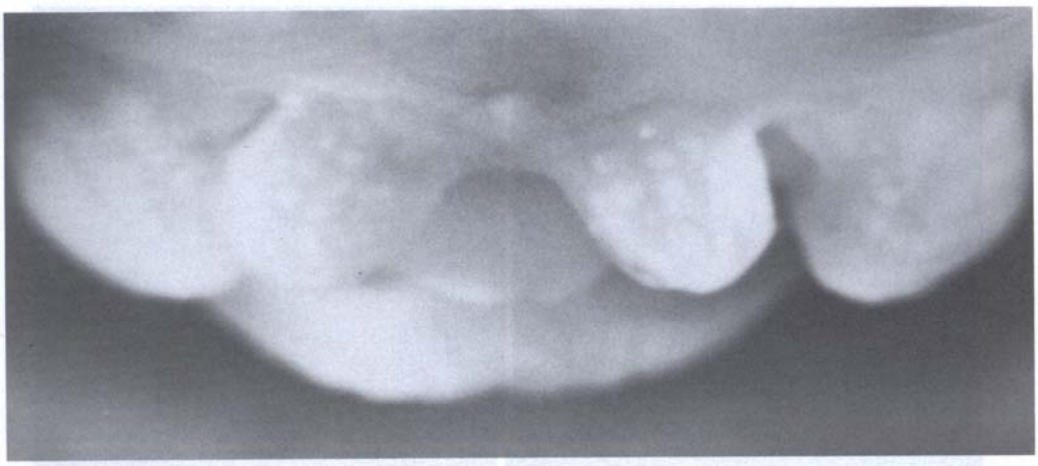


Fig. 8. Dorsal view of the midfacial region of a 33-mm (32-day) malformed fetus. Note the presence of whisker papillae on both the normal, lateral maxillary prominences and the abnormal, medial maxillary prominences.

the middle of the palatine bones. The nasal septum, ethmoid and nasal cartilages, and rostral wing of the ala orbitalis are all missing.

Transverse sections of 32-day embryos confirmed the presence of a supernumerary pair of medial whisker fields (Fig. 10B) and a single pair of widely spaced nostrils. The maxillary dental lamina is present beneath both pairs of lateral and medial maxillary prominences but does not extend to the midline. Four rostral dental buds have formed, one associated with each maxillary prominence.

The epithelial-lined nasal cavities extend caudally almost to the optic cups, but never establish contact with the oral cavity or nasopharynx. In contrast to normal embryos of the same stage, there are no cartilagenous capsular structures surrounding these nasal cavities, nor are conchae present. These cavities remain widely separated, with no nasal septum between them.

The mesenchyme between the nasal cavities has undergone intramembranous ossification to form the paired medial maxillary and median bony elements described above. Figure 10D and E illustrate that the horizontal shelves of this complex are adjacent to the palatine shelves of the normal (lateral) maxillae. These illustrations also show the presence of ectopic dorsolateral osseous and cartilagenous nodules located lateral to the nasal cavity.

There is a prominent rostrocaudally elongated cartilagenous nodule located in the midline dorsal to the caudal extension of the median rostral ectopic bone (Fig. 10C). In the absence of any vertical projection from this rod, it is not possible to claim it as homologous with the cartilagenous nasal septum.

Nasolacrimal ducts extend rostrally from the level of the median canthus to the lateral maxillae, but have no openings or connection at either end. A single wide choana located caudal to the palatine bones opens rostrally into a closed nasopharynx (Fig. 10F). This cavity extends beneath the sphenoid region of the chondrocranium, then narrows and opens again into the oral cavity. The rostral opening is located on a median fold that projects ventrally into the oral cavity (Fig. 10E). The mesenchymal partition that separates the short nasopharynx from the oral cavity has no evidence of

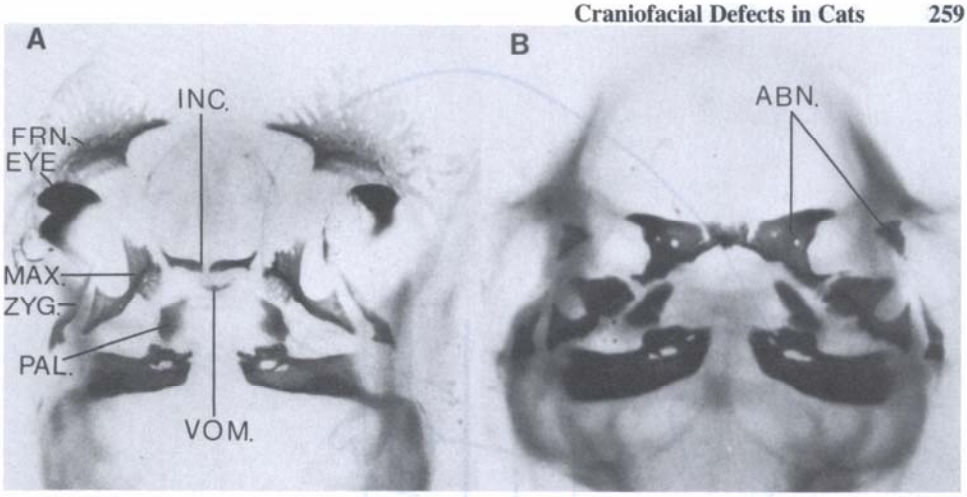


Fig. 9. Alizarin red-stained 30-day normal (A) and malformed (B) littermates. FRN., frontal bone; ABN., abnormal bones; INC., incisive bone; MAX., maxilla; PAL., palatine bone; VOM., vomer; ZYG., zygomatic bone.

a median fusion zone, which would normally be present at this stage if it had formed by the apposition and fusion of paired lateral palatine shelves.

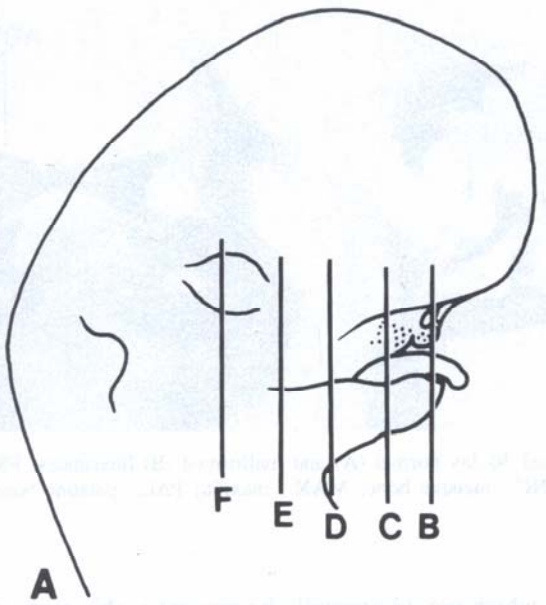
The eyes are present but degenerating. Neural retina and pigmented epithelial tissues extend laterally to the equatorial level of the hypertrophic lenses, and medially into the basal region of the diencephalon. No signs of an anterior chamber or cornea are to be found.

The youngest litter examined contained three 21-day embryos having 32–33 somites. In two of these embryos (Fig. 11B,C) the angle of cranial flexure is diminished compared to the third embryo, and the width of the prosencephalon is reduced, giving the rostral part of the head a convex wedge-shaped appearance. These two embryos are less developed than the third, although all had the same number of somites. A pair of optic vesicles (laterally) and two invaginating nasal placodes (rostrolaterally) are clearly visible in all these specimens. The third, wider embryo is identical with specimens obtained from two normal, mixed-breed cats. Thus, the narrower embryos appear to exhibit an early manifestation of the Burmese syndrome. Unfortunately there are no independent markers to verify this assumption.

GENETICS

To establish the mode of inheritance of this syndrome, an extensive series of test matings was organized and executed by the Burmese Cooperative Research Group, a group of Burmese cat breeders centered in California, in conjunction with several county 4-H organizations. Karyotyping of a contemporary female and three of her progeny, one of which had the Burmese syndrome, was performed, and all were normal 38XX or 38XY (Smith, in preparation). Table II summarizes the results of these mating trials. The sex ratios of progeny in this study were normal.

These data indicate that the lethal Burmese syndrome appears only when two Contemporary phenotype animals are mated. There was no correlation between the degree of severity of brachygnathia in one or both parents and the frequency of malformed offspring. Pedigree analysis indicates that the degree of relatedness of the



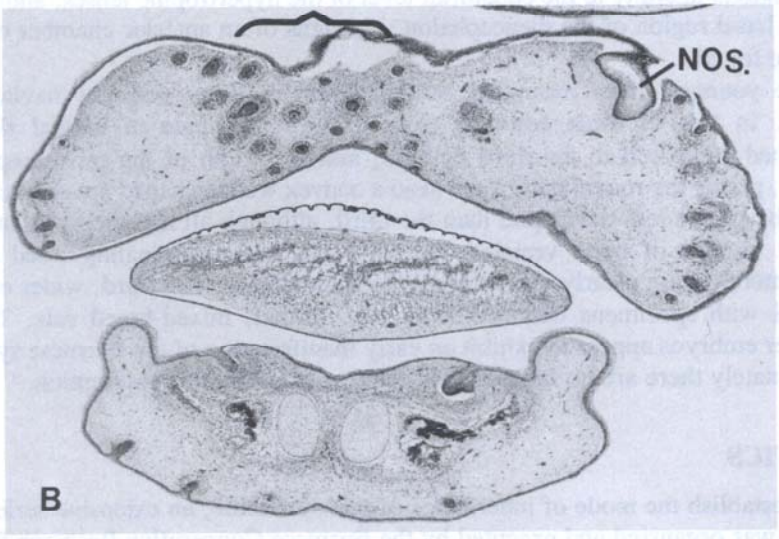
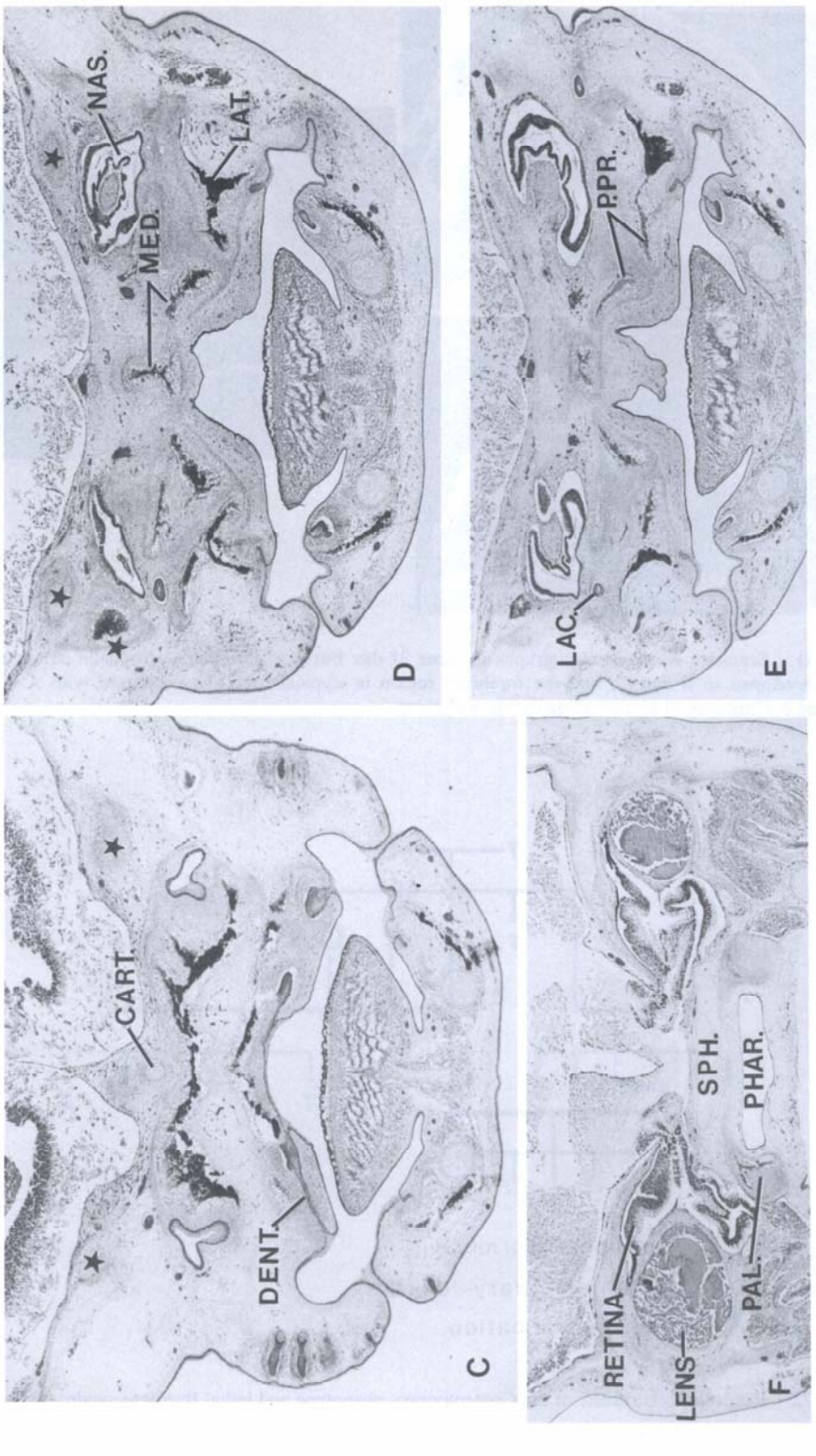


Fig. 10. Transverse sections through the midfacial region of a 32-day malformed embryo. Extra whisker tracts are shown in B (bracket), and medial maxillary ossifications are visible in C–E. Starred structures in C and D are ectopic cartilages and bones. CART., median cartilaginous rod; DENT., dental lamina; LAC., nasolacrimal duct; LAT., lateral maxilla; MED., medial maxilla; NAS., nasal cavity; NOS., nostril; PHAR., nasopharynx; P.PR., palatine process of maxillae; SPH., rostral cartilage of sphenoid complex.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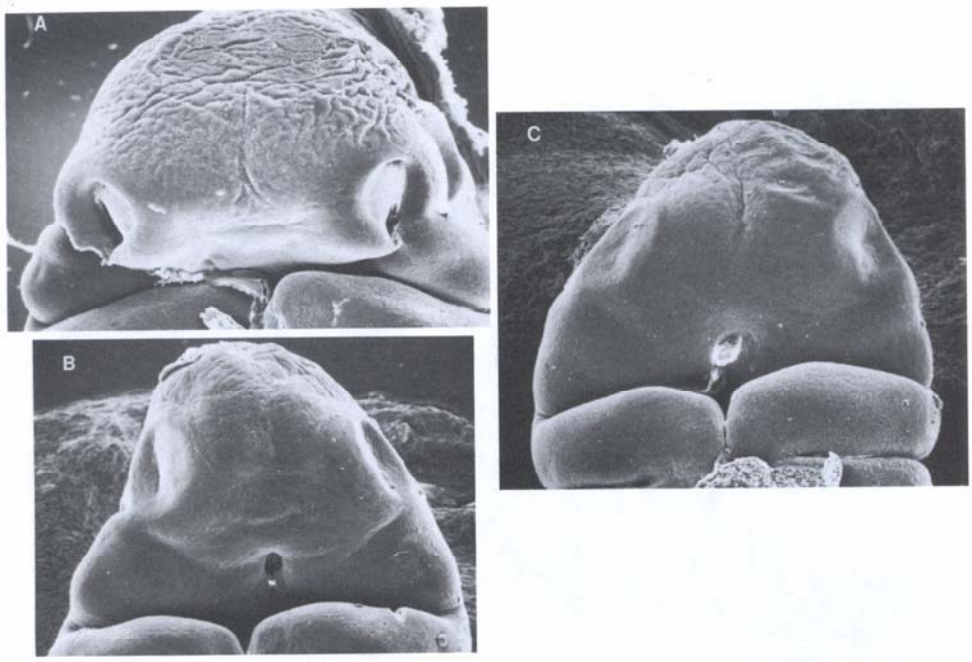

Fig. 11. Scanning electron micrographs of three 21-day Burmese littermates. Cephalic structures are less developed in B and C, and the forebrain region is atypically narrow compared with A or with normal cat embryos at similar stages of development.

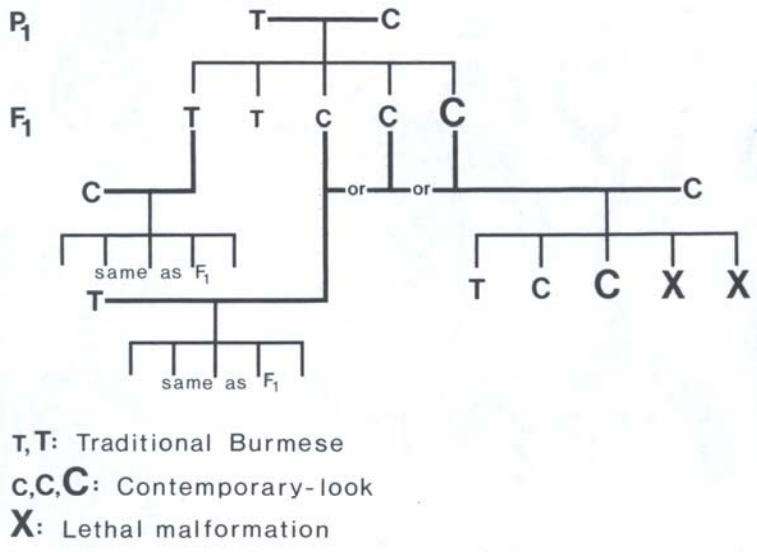

Fig. 12. Pattern of inheritence of the Contemporary phenotype and lethal Burmese-syndrome.

TABLE II. Breeding Results

	Traditional × Contemporary	Contemporary × Contemporary
Litters	26	40
Kittens	102	182
Average litter size	3.92	4.55
Malformed	8 (7.8%)	56 (30.7%)
Burmese syndrome	0	47 (25.8%)
Anencephaly	0	2
Gastroschisis	2	4
Ocular defects[1]	5	4
Cleft palate	1	0

[1]Includes dermoids, palpebral hypoplasia, and inflammation of the nictitating membrane.

parents also has no effect upon the incidence of this malformation (F. Smith, in preparation). The single consistent requirement for the appearance of abnormal kittens is a Contemporary phenotype in both parents.

DISCUSSION

After initial examination of malformed Contemporary Burmese neonates, three alternate explanations were proposed:

1. Incomplete diprosopus
2. Maxillary hyperplasia and field duplication
3. Transformation of the medial nasal part of the frontonasal process.

In the first scenario, twinning of rostral prosencephalon-derived and -dependent structures would occur concomitant with a loss of both frontonasal prominences. This is the most conservative hypothesis but is not supported by the observed embryonic anatomy. Only a single pair of optic and olfactory structures are present throughout the development of effected fetuses. Similarly, there is no evidence for more than two telencephalic hemispheres.

The second hypothesis suggests that the maxillary prominences might overgrow the frontonasal region. Then, as a result of the expanded maxillary field being divided by invaginating olfactory epithelia, each enlarged maxillary prominence would regulate to form two equivalent but smaller fields. During the period of facial process formation, the two medial maxillae were observed to develop within mesenchymal swellings that arise medial to the nostrils, in the region normally occupied by the frontonasal mesenchyme. The left and right maxillary processes develop normally, including fusing with lateral nasal prominences to form nasolacrimal ducts. These findings negate the second proposed explanation.

Finally, there is the appearance on day 25 of whisker papillae on the paired medial midfacial swellings, and the subsequent formation of intramembranous bones bearing canine teeth and forming horizontal palatine-like shelves. Also, all skeletal structures normally derived from the medial nasal prominence and adjacent dorsal mesenchyme, including nasal bones and capsule, the ethmoid complex, and the incisive and vomer bones, are missing. These data suggest that neural crest cells that disperse over the rostral surface of the prosencephalon are or become incorrectly spatially programmed. While not suggesting similar mechanisms, this phenotypic

transformation resembles the well described homeotic mutants in *Drosophila* [Postlewait and Schneiderman, 1974].

The width of the prosencephalon is abnormal at 21 days of gestation, by which time crest cells have circumscribed the future forebrain, diencephalon, and all but the anterior aspects of the optic vesicles. This suggests that the primary genetic lesion may operate on the rostral neural plate, which subsequently transmits incorrect spatial information to the overlying neural crest population.

As a practical matter for Burmese breeders, the breeding studies offer little solace. As summarized in Figure 12, the lethal malformation is inseparably linked to the Contemporary Burmese phenotype. Matings of Traditional with Contemporary phenotype Burmese typically produce both Traditional and a range of Contemporary phenotypes. Crosses among Traditionals or between these and other breeds of cats never produce the Contemporary phenotype. These results suggest that the Contemporary phenotype is inherited as an incomplete dominant, with heterozygotes expressing a range of facial dimensions. In some homozygotes a threshold is surpassed which results in the lethal malformation. All Contemporary phenotype Burmese cats are carriers of this set of defects.

Regardless of the arbitrarily defined advantages of this Contemporary phenotype, the lethal load exceeds 25%, which is unacceptable in any breed of domesticated animal. The history of other cat breeds (eg, Persian, Abyssinian) suggests that brachycephalic profiles can be selected for without such a lethal genetic load, although not without many ancillary problems such as malocclusion, dermoids, and nasolacrimal duct atresia.

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