

"Nothing oppresses the heart as much as symmetry"

Victor Hugo (quoted Fritsch, 1968, p.87)

"The (narwhale) is some sixteen feet in length, while its horn averages five feet, though some exceed ten, and even attain to fifteen feet ... it is only found on the sinister side, which has an ill-effect giving its owner something analogous to the aspect of a clumsy left-handed man".

Melville, Moby Dick

"Siegfried: And is that heart
 in the usual place,
 at the left of his breast?

Mime: Of course; dragons
 have hearts just like men".

Siegfried, II, 2 (translated by Andrew Porter)

*Note that in the original German text there is no reference to right or left.

11:1 Introduction

In this chapter I wish to discuss some disparate aspects of the biology of asymmetry. No attempt will be made to link the ^{separate} topics together in a logical order, nor to expound any of them in the completeness which they perhaps deserve - they are merely interesting data, or interesting theoretically, and should not be passed by without mention in a thesis on the biology of laterality.

11:2 Primary and secondary asymmetries: direct and indirect secondary asymmetries.

Man is a bilaterally symmetric organism. However this symmetry is not even skin deep for skinfold thickness is greater on the right side of the body than the left (Damon, 1965). Amongst paired organs there are large numbers of asymmetries, a summary of which appear in Table 11.1. Diseases of the paired organs also show a distinct asymmetry of occurrence, some of which are summarised in Table 11.2. It is hardly necessary to point out that the unpaired organs, particularly the thoracic and abdominal viscera, are grossly asymmetric. All such asymmetries cry out for an explanation; it is simply not satisfactory to say, as did Hass (1951) after reviewing 22,895 cases of congenital dislocation of the hip, of which 14,011 (61.19%) were on the left side ($X_1^2 = 114.8$, $p \ll 0.001$), that "It seems very probable that coincidence plays a

large part".

For some diseases there might well be particular mechanical factors which predispose one side rather than the other. The haemodynamics of the pulmonary circulation (Boyd, 1961) and the particular anatomy of the bronchial tree, (Brock, 1954) probably explain much of the right-sided predominance of primary (Blacklock, 1932) and secondary (Boyd, 1961) tuberculosis, carcinoma of the bronchus (Bignall, 1958), lung abscess (Brock, 1954) and lobar pneumonia (Tugwell and Williams, 1979). Similarly the relation of the iliac vessels to the loaded colon explains the left-sided predominance of ilio-femoral thrombosis (Negus, 1970). The cultural and metaphysical associations of 'right' (good, true, clean) and 'left' (bad, false, dirty, sinister) (Needham, 1973) might account for the predominance of hysterical paralysis (Brown-Sequard, n.d.) and conversion reactions (Stern, 1977) on the left, and perhaps also for other conditions such as mastalgia (Preece et al, 1976) as well as for patients' preference for treatments applied to the right side of the body (Ronn, 1976). The mechanics of right-handedness might explain the right-sided presentation of what is actually bilateral Parkinson's Disease (Klawans, 1972). Such explanations can however only form part of an infinite regress and one has ultimately to find an explanation for the asymmetry causing the asymmetries. As a general principle, asymmetric output must be a function

of asymmetric input. We must therefore examine the ways in which asymmetries may be related one to another, in order to find a succinct hypothesis to account for their inter-relations.

Firstly I would like to differentiate between primary and secondary asymmetries. Primary asymmetries are all uncorrelated one with another; secondary asymmetries are correlated. This simple distinction is of the utmost importance as if two asymmetries are uncorrelated it is extremely difficult to explain them by the same genetic mechanism. The asymmetries of handedness and viscera are primary in this sense as they are completely uncorrelated (Torgersen, 1950); hand-clasping and arm-folding may probably be added to this list (although as pointed out in chapter 9:5.4 the relationship with situs is unclear). Handedness and speech dominance are not both primary asymmetries, since they are clearly correlated with one another.

Secondary asymmetries may be direct or indirect. A direct secondary asymmetry is one in which there is a direct causal relation between one asymmetry and another; thus callouses on the hand may be a direct secondary asymmetry to handedness, the more frequently used hand developing the greater callouses. Indirect secondary asymmetries however would be linked only via their genetic control; thus both asymmetries would be consequent to an

earlier cause. The best example of this would be cerebral speed dominance; handedness and speech dominance, in the model described earlier, in Chapter 8, are linked only in so far as they are determinate in the DD genotype and have a random component in the DC and CC genotypes. Neither causes the asymmetry of the other.

Consider the viscera. The heart is almost always on the left side. It is one of the earliest viscera to develop and hence it is probably the primary asymmetry. In situs inversus the position of the heart is reversed; presumably here, as with left-handedness, all directional asymmetry has been removed and fluctuating asymmetry with canalisation forces the tissues one way or the other. In situs inversus totalis not only the situs of the heart but also of the liver, intestines, etc., is reversed. The implication is that these asymmetries are a direct consequence of the right-sided heart, for otherwise we would expect to find 50% of cases of situs inversus with a left-sided liver, etc. Presumably in this particular case there is a haemodynamic or other organising effect which causes the liver to be contralateral to the heart.

Within the details of the embryology of the heart, we may find evidence of direct and indirect asymmetries (see de la Cruz et al, 1969, 1971 for excellent accounts of the embryology). The direction of the apex, the position of the ventricles, and the trunco-conal morphology are

all indirect asymmetries since all possible combinations can and do occur. The position of the atria is directly linked to situs and apex position, since atrical inversion never occurs.

In order to see the relationship of direct and indirect asymmetries more clearly, let us consider the case of varicocoele, which almost always occurs on the left side.

The condition of varicocoele almost always occurs on the left side (Campbell, 1928). If this were directly related to cardiac asymmetry we would expect the incidence of left-sided varicocoele in situs inversus to be 0%; if it were indirectly related we would expect the left-sided incidence to be 50% (fluctuating asymmetry and canalisation); and if it were not secondary to cardiac asymmetry at all we would expect 100% on the left, as in situs solitus. In fact varicocoele in situs inversus is invariably on the right (Grillo-Lopez, 1971), and we may say therefore that there is a direct secondary asymmetry. Conversely consider osteoarthritis of the hands. This is about 12% worse in the right than the left hand of right-handers, mean scores for the hands being 2.555 and 2.274 respectively (Acheson et al, 1973). Let x be $L/(L+R)$, = 0.4709. If this left-right asymmetry were a result of mechanical stresses we would expect it to be directly linked to handedness and thus the value of x in left-handers should be $1 - 0.4709 = 0.5291$, i.e.

12% worse in the left hand. If the asymmetry were unrelated to handedness we would still expect the right hand to be the more severely affected, by 12%. If the asymmetry were indirectly related to handedness then using an additive model of inheritance we may calculate an expected value of $R/(L+R)$ of 0.49005 (i.e. 4.1% worse in the right hand) (for calculations see the table 11.3 where 0.49005 is the value of y). The actual figures for left-handers are right-hand 1.887, left-hand 1.835, a difference of 2.8% with the right hand being more severely affected. Osteoarthritis appears therefore to be indirectly linked to handedness, perhaps a surprising finding.

We may thus produce a general method of determining the type of control of asymmetry. Let x represent the degree of asymmetry in right-handers with situs solitus. The expectations under the various types of symmetry control are then shown in Table 11.3.

To summarise this section. All tissues show fluctuating asymmetries. Some also show directional asymmetries which may be primary, or directly or indirectly secondary to either of the known primary asymmetries of heart and brain. Tissues may be asymmetric at the organ level (e.g. in overall size) or even at the physiological level (e.g. in the asymmetric ability of sweat glands to concentrate sodium; Gibinski et al, 1971). A method is described for determining the type of the

asymmetry. Regrettably it is not possible to assess most of the known asymmetries in terms of this mathematical model since data on handedness and situs are simply not available. Similarly there is a lack of data on the inheritance of the asymmetries; one notable exception to this is carcinoma of the breast, for which there is evidence that the asymmetry is heritable (see McManus, 1977).

11:3 Hemihypertrophy

A fascinating condition which has not been discussed earlier in this paper is hemihypertrophy (Ringrose et al, 1965). Commonly associated with Wilm's tumours of the kidney, (Fraumeni et al, 1967) it presents simply as an accelerated growth of one side of the body over the other, usually to a degree which is immediately obvious on examination. It is commonly stopped by removal of the associated tumour. The mechanism of the condition raises several interesting questions for theories of symmetry. It implies that it is possible to make the tissues of one side of the body grow faster than those of the other, and that, as a result, tissues of the two sides may not be identical. Since the hypertrophy involves all of the tissues of one side we must assume that a systemic effect is occurring, and that possibly the tumour itself is secreting a 'dextrotrophic' or 'sinistrotrophic' substance; Wilm's tumours have been demonstrated to secrete growth promoting substances (Beierle et al, 1971).

A related condition, found usually in birds (Crew and Munro, 1937), but at least once in man (Brachetto-Brian et al, 1943), is that of hemi-hermaphroditism, in which once side of the body shows male and the other female secondary sexual characteristics. Once more it is tempting to speculate that perhaps cell receptors of one side are more sensitive to testosterone or oestrogen (an hypothesis which should be empirically testable). It also throws some light on the relatively high incidence of conditions in Table 11.2 related to the sexual organs.

11:4 The evolution of biological asymmetry

There are three distinct problems here; the evolution of molecular asymmetry; the evolution of morphological asymmetry in the form of situs; and the evolution of functional asymmetry in the form of handedness and speech dominance.

11:4.1 Molecular asymmetry

The well-known fact that the constituents of organic matter are usually only one of a pair of possible stereoisomers, was first demonstrated by Pasteur in 1848. In general biological systems use L-amino-acids and D-ribosides and D-sugars. Why this should be has provoked much speculation, often with a metaphysical tinge (e.g. du Noily's (1947) claim that it is apparent that God must have

made the first asymmetric molecule - see Gardner, 1967).

Two separate problems arise. Why only one type?
And why that particular type?

The evolutionary advantages of building complex systems out of only one of a pair of stereo-isomers are obvious. Imagine the inefficiency of a production line for cars in which each man assembling had beside him a racemic mixture of right and left-hand thread screws which he had to put into pre-threaded holes. Even if a 'wrong' screw were to be forced into a hole with the opposite thread, this would radically weaken the structure. The chemical analogues are readily found in synthetic polymer formation. Blout and Idelson (1956) showed that the formation of Poly- γ -benzyl-(L-/D)-glutamate was far quicker if the substance contained only L or D isomers. Furthermore the polymer became far longer if composed of purely one isomer.

Blout et al (1957) subsequently showed that pure L or pure D polymers were far more stable than polymers composed of both isomers.

The advantages therefore of having only one or other stereo-isomer seem clear. But the advantages of, say, just L-amino-acids are not so clear. One popular argument is that chance alone is the sole determining factor. Thus

one would start off with a racemic primordial soup; the first type of isomer to produce a self-replicating molecule (presumably a rare event) would then have an enormous advantage and would eliminate its competitor. The argument is put nicely by Wald (1957):)

"I once had the pleasure of discussing this matter with Albert Einstein. He had asked my opinion, and then said, "You know, I used to wonder how it comes about that the electron is negative. Negative-positive- these are perfectly symmetric in physics. There is no reason whatever to prefer one to the other. Then why is the electron negative? I thought about this a long time, and at last all I could think was, 'It won in the fight'". I said, "That's just what I think of the L-amino acids. They won in the fight"" (Wald, 1957).

All such theories however were conceived during that period when it was thought that the physical universe was completely symmetric. In 1957 Lee and Yang received a Nobel Prize for their demonstration of the non-conservation of parity. Recently attempts have been made to suggest that the primordial soup itself might have been asymmetric due to the asymmetric effects of the incident radiation. Garay et al (1974) have recently found that D-amino acids were more sensitive to destruction by β -particles. Kovacs and Garay (1975) showed that the precipitation rates of the two isomers of tartaric acid were different in the presence of non-polarised β -irradiation. Bonner et al (1975) found an asymmetric degradation of the stereoisomers of leucine with radiation. Norden (1977) showed that a racemic 'soup' of amino-acids became asymmetric

after only 60-80 hours of exposure to polarised light.

The implication of these experiments seems clear. The primordial broth may well have been asymmetric. But since, in no sense, could it be construed as consisting entirely of one isomer, or the other, all that happens is that we must set the a priori probabilities of, say, L-amino-acids, not at 0.5 but at some higher value less than 1. Nevertheless whilst chance may well still play a large role, it is possible as Morgan (1976) has suggested, that our basic asymmetries are a consequence of the inherent asymmetries of sub-atomic matter.

11:4.2 The evolution of Situs

The predominance of morphological asymmetries in the higher animals implies that there must be an advantage to such asymmetries. But as with optical asymmetry, we can conceive two separate questions; why is the system asymmetric, and why does it have this particular asymmetry?

The need for asymmetry of some sort is probably simple in the higher animals. When an organism is bilaterally symmetric then there reaches a stage of complexity at which it is no longer practical to control symmetric effectors. Thus imagine a vertebrate with two mirror-image hearts driving blood through symmetric arteries and veins. Before long, unless there were perfect synchrony between

the sides, the system would become out of phase, and one would find, for instance, that the systole of one heart would be opposing the diastole of the other, and exceptional pressure fluctuations would occur. Of course this could be avoided by having totally separate blood circuits; but then the immunity of one circuit would not transfer to the other side, with an obvious decrease in resistance to infection. The problem of running two hearts would be akin to the modern problem of knowing how to run computers with more than one central processing unit; the CPU's interact in awkward, unpredictable and unpleasant ways.

Once one accepts that it is preferable to have only a single, asymmetric heart it is obvious that it should, if possible, always be on the same side in different individuals. To return to the motor-car argument of the previous section, imagine a production-line producing both right and left-hand drive cars, the order of appearance being random. Each assembler will have two boxes of mirror-symmetric parts, each to be welded on to mirror-image symmetric positions. Clearly it would not be long before cars began to appear which had some right and some left-components; and before long such cars would reach a point in the production line beyond which they could proceed no further. The biological analogy of this process is what Waddington (1957) has called 'selection for repeatability'. It is better than the system has only

one known, and predictable, asymmetry, which it may then modify, and build upon, than that it should have the potentially increased variance due to two mirror-image phenotypes, but which will allow far more disasters to occur during development and modification. To sometimes have to turn right at an un-sign-posted junction, sometimes left, is a sure manner of losing one's way; better always to turn left, even if it means a detour, before certainly arriving at one's destination.

But such arguments do not justify a particular asymmetry. It is difficult to know what are the advantages of, say, a population with left-sided hearts, as opposed to a population with right-sided hearts. Once more, chance may be the major factor: the left-sided heart 'got there first'. The only moderately clear case of one of enantiomorphic phenotypes having an advantage, is that of the snail, Fruticola lantzi, in which the more common dextral form withstands starvation conditions far better (Gause and Smaragdova, 1940). It must of course be remembered that the selective advantage of an asymmetric phenotype may well have nothing to do with the asymmetry per se. Consider the case of Kartagener's Triad, in which as well as situs inversus (or rather, fluctuating asymmetry) there is ciliary dysfunction resulting in sinusitis and bronchiectasis. There is however also immotility of the spermatozoa, which results in infertility; clearly the latter produces sufficient of a reproductive

disadvantage to lead to the almost total loss of the gene from the gene-pool (Afzelius, 1976). In uncomplicated situs inversus there also appears to be a tendency to infertility (Arge, 1960). The predominance of a left-sided heart as opposed wto the predominance of a right-sided heart may well have as much to do with mitochondrial bio-synthesis as with the haemodynamics of the cardiovascular system.

11:4.3 The evolution of functional asymmetries

From sections 11:4.1 and 11:4.2 it should be clear that for any complex bilateral system there are clear functional advantages to developing some form of consistent lateral dominance, for then control will be easier. In the case of the functional as opposed to the morphological asymmetries this argument seems less strong, and, as has been argued, earlier in Chapter 10, it may well be that there are reproductive advantages to fluctuating asymmetry, whilst for hand-clasping and arm-folding I have argued, in Chapter 9,6 that what genetic factors there are can be explained simply in terms of genetic drift (that is, a total lack of advantages).

As to the question of why it is the left hemisphere that is dominant for speech, rather than the right hemisphere, there is simply no answer, and we may only return once more, to the null hypothesis that "it won the fight".

11:5 The season of birth of left-handers

Leviton and Kilty (1979) have recently suggested that in a survey of school-girls there was a significant excess of left-handers born around the month of November. Regrettably it is not easy to assess Leviton and Kilty's claim, since they give no actual data, merely the result of a statistical significance test. Nevertheless, since there were only 33 left-handed school-girls in their sample, each month-category can only have contained an average of 2.75 persons. Here I will describe results from my own larger study, other aspects of which have been reported in earlier chapters (i.e. surveys Ia, Ib and II).

In survey I a total of 948 students gave detailed information about their handedness. In survey II not only did 511 students give handedness information, but also their parents completed a handedness questionnaire. In the present report I have concatenated data from the two surveys and from parental and student generations.

Table 11.4 shows the sample size, for males and females, and for both sexes combined, for each particular month of birth. Before testing for seasonality of births of left-handers it is necessary to test for seasonality of overall births. Using the method of Edwards (1961), there are no seasonal trends in either males, females or the two sexes combined ($\chi^2 = 1.15$; $\chi^2 = 5.08$; $\chi^2 = 3.40$

respectively). Of the 1049 males, 134 (12.77%) were left-handed, whilst of the 706 females, 73 (10.34%) were left-handed. In the males there was no evidence of a seasonal trend in sinistral births ($\chi^2_2 = 2.17$, NS). Amongst the females there was no significant seasonal trend ($\chi^2_2 = 3.73$, NS), and in contrast to the data of Leviton and Kilty, the maximum incidence of sinistrality was around the month of July/August. Combining the male and female data, there was no evidence of a seasonal trend ($\chi^2_2 = 0.34$, NS).

In summary, the present analysis fails to support the hypothesis of Leviton and Kilty of a seasonal trend in sinistral births.

Table 11.1 Asymmetries in the paired organs of man and animals.

<u>Organ/Tissue</u>	<u>Species</u>
Humerus	Man
Humerus	Human Fetus
Radius	Man
Bone mass in hand	Man
Femur	Man
Clavicle	Man
Scapula	Man
Pelvis	Man
Skull: frontal and parietal bones	Man
: malar bone	Man
: Antero-posterior length internally	Man
: Position of falx	Man
: Mandible	Man
: Mandibular condyle	Man
: Jugular foramen	Man
: Incomplete pterygo-alar foramen	Man
Transverse process of cervical vertebrae	Chicken
Dystopia caudalis tuberculi anterioris	Mouse
Septal aperture of humerus	Rat
Rate of skeletal maturation	Man
Palmaris longus muscle	Man
Foramina transversaria imperfecta	Mouse
Polydactyly	Chicken
Polydactyly	Mouse
Heterodactyly with diplopodia	Chicken
Motor Cortex Betz cells	Man
Planum temporale of brain	Man
Areas 41 and 42 of auditory cortex	Man
Audiogenic seizure threshold	Mouse
Brachium of inferior colliculus	Man
Lateral lemniscus	Man
Gliae of lateral lemniscal nuclei	Man
n. mesencephalis lateralis pars dorsalis	Birds

Asymmetry

Larger on the right
 Larger on the right
 Larger on the right
 Greater on the right
 Larger on the left
 Heavier on the left
 Heavier on the right
 Heavier on the right
 Larger on the right
 Larger on the left
 Greater on the right
 Shifted to the right
 Longer on the left
 Longer on the right
 Larger on the right
 More common on right
 Longer on the left
 More common on the right
 More common on the left
 Greater on the left
 More common on the right
 More common on the left
 More common on the left
 More common on the left
 More common on the left
 More common on the right
 More cells on the left
 Larger on the left
 Larger on the right
 Lower on the left
 More fibres on the left
 More fibres on the left
 Greater number on right
 Larger on the left

Reference

Latimer & Lowrance (1965)
 Schultz (1926)
 Latimer & Lowrance (1965)
 Garn et al (1976)
 Latimer & Lowrance (1965)
 Lowrance & Latimer (1957)
 Lowrance & Latimer (1957)
 Lowrance & Latimer (1957)
 Woo (1930a)
 Woo (1930a)
 Hoadley & Pearson (1929)
 Inglessis (1925)
 Morant et al (1936)
 Morant et al (1936)
 Woo (1930b)
 Chouke (1947)
 Kawahara (1974)
 Grüneberg (1950a)
 Riessenfeld et al (1975)
 Torgersen (1951)
 Thompson et al (1921)
 Grüneberg (1950b)
 Bond (1920)
 Fortuyn (1939)
 Taylor & Gunns (1967)
 Lassek (1940)
 Geschwind & Levitsky (1968)
 Campain & Minckler (1977)
 Collins & Ward (1970)
 Ferraro & Minckler (1977a)
 Ferraro & Minckler (1977b)
 Ferraro & Minckler (1977b)
 Cobb (1970)

Table 11.1 continued/.....

<u>Organ/Tissue</u>	<u>Species</u>
Habenular Nucleus	Frog, newt, eel
Hypoglossal nucleus	Man
Optic Nerve and eye	Rat
Maturation of optic nerve	Rabbit
Unilateral microphthalmia	Rat
Cutaneous tactile sensitivity	Human neonate
Unilateral thyroid aplasia	Rat
Testis	Man
Testis	Human Fetus
Ovary	Human Fetus
Testicular artery arching over renal vein	Man
Displacement of pelvic ureter	Man
Intra-uterine position of fetus	Man
Polythelia	Mouse
Sodium concentration of sweat	Man
Skinfold thickness	Man
Digital dermatoglyphics: total ridge count	Man
Palmar dermatoglyphics: ridge count	Man
Palmar dermatoglyphics: ridge count	Man
Side of scalp hair-whorl	Man
Direction of scalp hair-whorl	Man
Length and area of striate cortex	Man
Noradrenaline concentration in the thalamus	Man
Height of the external ear	Owl
Depth of lingual fossa of 1st upper incisor	Man

Asymmetry

Double on left only
 Larger on the left
 Larger on the right
 More rapid on the right
 More common on the right
 More sensitive on the right
 More common on the right
 Larger on the right
 Larger on the right
 Larger on the right
 More common on the left
 More common on the right
 Left occiput more common
 More common on the left
 Greater on the left
 Greater on the right
 Greater on the right
 Greater on the left
 Greater on the right
 More common on the right
 More commonly clockwise
 Greater on the right
 Greater on the left
 Higher on the right
 Deeper on the left

Reference

Braitenberg & Kemali (1970)
 Tomasch & Etemadi (1962)
 Wang (1927)
 Narang (1977)
 King (1929)
 Hammer & Turkewitz (1974)
 King (1929)
 Chang et al (1960)
 Mittwoch & Kirk (1975)
 Mittwoch & Kirk (1975)
 Notkovitch (1955)
 Kabakian et al (1976)
 Steele & Javert (1942)
 Little & McDonald (1945)
 Gibinski et al (1971)
 Damon (1965)
 Holt (1953)
 Floris (1975)
 Pateria (1973)
 David & Osborne (1976)
 David & Osborne (1976)
 Cohn & Papez (1930)
 Oke et al (1978)
 Norberg (1968)
 Aas & Risnes (1979)

Table 11.2 Disease asymmetries in Man

More common on the Right side

Reference

: Conditions present at birth

Congenital unilateral third nerve palsy
Helical pit of the ear
Side of testis in hermaphroditism
Congenital inguinal hernia, in both males and females
Club foot
Radial aplasia
Infantile hemiolegia

Victor (1976)
Stannus (1914)
Polani (1970)
Packard & McLaughlin (1953); Atwell (196
Schnall & Smith (197
Schnall & Smith (19
Dennis & Whitaker (1977)

: Conditions presenting during childhood

Adolescent gynaecomastia
Retinoblastoma
Varicocoele
Hemihypertrophy

Nydick et al (1961)
Duke-Elder (1967)
Campbell (1928)
Schnall & Smith (19

: Conditions presenting during adulthood

Carpal tunnel syndrome
Mallet finger
Meningioma
Nephroptosis
Ovarian tumour
Post-encephalitic Parkinsonism
Adenocarcinoma of the kidney
Spontaneous pneumothorax
Testicular tumours
Trigeminal Neuralgia
Third molar impaction

Birkbeck & Beer (1
Abouna & Brown (19
Cushing & Eisen-Hardt (1958)
de Zeeuw et al (1977)
Seegar (1958)
Reynolds & Locke (1971)
Riches et al (1951)
Crimm (1948)
Ferguson (1965)
Rothman & Wepsic (1974)
Henry & Morant (1936)

Table 11.2 continued/.....More common on the Left sideReference: Conditions present at birth

Cleft lip, with or without cleft palate	Sanders (1933)
Congenital absence of a limb	Simmel (1961)
Congenital dislocation of the hip	Hass (1951)
Renal agenesis	Schnall & Smith (1974)
Polythelia	Schnall & Smith (1974)
Polydactyly	Schnall & Smith (1974)
Erb's Palsy	Bennett & Harrold (1976)
Hairy pinnae	Stern <u>et al</u> (1968)
Infantile hemiplegia	Dennis & Whitaker (1977)

: Conditions presenting during childhood

Neuroblastoma	Schnall & Smith (1974)
Hemifacial microsoma	Schnall & Smith (1974)

: Conditions presenting during adulthood

Acute optic neuritis	Bradley & Whitty (1967)
Carcinoma of the breast	McManus (1977)
Benign breast tumours	Ciambellotti (1961)
Adenoma of the epididymis	Beccia <u>et al</u> (1976)
Intra-cranial glioma	Denman & Smith (1954)
Osteoarthrosis of the hands	Acheson <u>et al</u> (1970)
Boerhaave's syndrome	Curci & Horman (1970)
Sprained ankle	Basur <u>et al</u> (1976)

Table 11.2 continued/.....More common on the left side: conditions presenting during adulthood

Renal artery stenosis	Schwartz & White (1964)
Subclavian steal syndrome	Santschi <u>et al</u> (1966)
Wallenberg's syndrome	Ask-Upmark & Bicker- staff (1976)
Herniated lumbar inter-vertebral disc	Kelsey (1975)
Atherosclerotic gangrene of the leg	Frohn (1976)
Aorto-Iliac artery thrombosis	Spiro & Cotton (1970)
Phantom breast following mastectomy	Weinstein <u>et al</u> (1970)
Conversion reactions	Stern (1977)
Hysterical paralysis	Hoadley & Pearson (1929)
Carcinoma of the Ethmoid sinus	Robin & Short- ridge (1979)
Deviation of the Nasal septum	Robin & Short- ridge (1979)

TABLE 11.3

<u>Handedness</u>		<u>Right</u>		<u>Left</u>	
		<u>Solitus</u>	<u>Inversus</u>	<u>Solitus</u>	<u>Inversus</u>
Primary asymmetry		x	x	x	x
Secondary to cardiac asymmetry	- Direct	x	1 - x	x	1 - x
	- Indirect	x	0.5	x	0.5
Secondary to handedness	- Direct	x	x	1 - x	1 - x
	- Indirect	x	x	y	y

- Note:
- i. In the last line of the table $y = (5 + 4x - \sqrt{16x^2 - 8x + 9})$
 - ii. If $x = 0.5$ then of course the situation is simply that of fluctuating asymmetry. Fluctuating asymmetry does not imply that other asymmetries cannot be directly secondary, but they cannot possibly be indirectly secondary.
 - iii. It is not necessary to know the incidence of a condition in left-handers with situs inversus to determine asymmetry type; this is fortunate since such individuals represent about 4 per million of the population.
 - iv. It is possible that the model above will suggest that an asymmetry is indirectly secondary to handedness; this of course could simply mean that it is directly secondary to cerebral speech dominance.
 - v. It has been assumed that the inheritance of situs is recessive and that of handedness is additive. These assumptions might require modification at a later date. Alternatively it is theoretically feasible that the expression of an indirect asymmetry may be additive for one particular asymmetry and recessive for another

Table 11.4 Shows, for males, females and males and females combined, the total number (N), and the number of left-handed (nL) subjects, born in each month of the year.

<u>Month</u>	<u>Males</u>		<u>Females</u>		<u>Males & Females</u>	
	<u>N</u>	<u>nL</u>	<u>N</u>	<u>nL</u>	<u>N</u>	<u>nL</u>
January	103	15	53	1	156	16
February	81	14	47	5	128	19
March	82	12	67	6	149	18
April	98	12	61	6	159	18
May	99	14	64	6	163	20
June	81	9	75	7	156	16
July	84	7	53	6	137	13
August	94	12	66	10	160	22
September	74	10	54	7	128	17
October	84	10	61	4	145	14
November	88	10	57	9	145	19
December	81	9	48	6	129	15
<u>Total</u>	<u>1049</u>	<u>134</u>	<u>706</u>	<u>73</u>	<u>1755</u>	<u>207</u>