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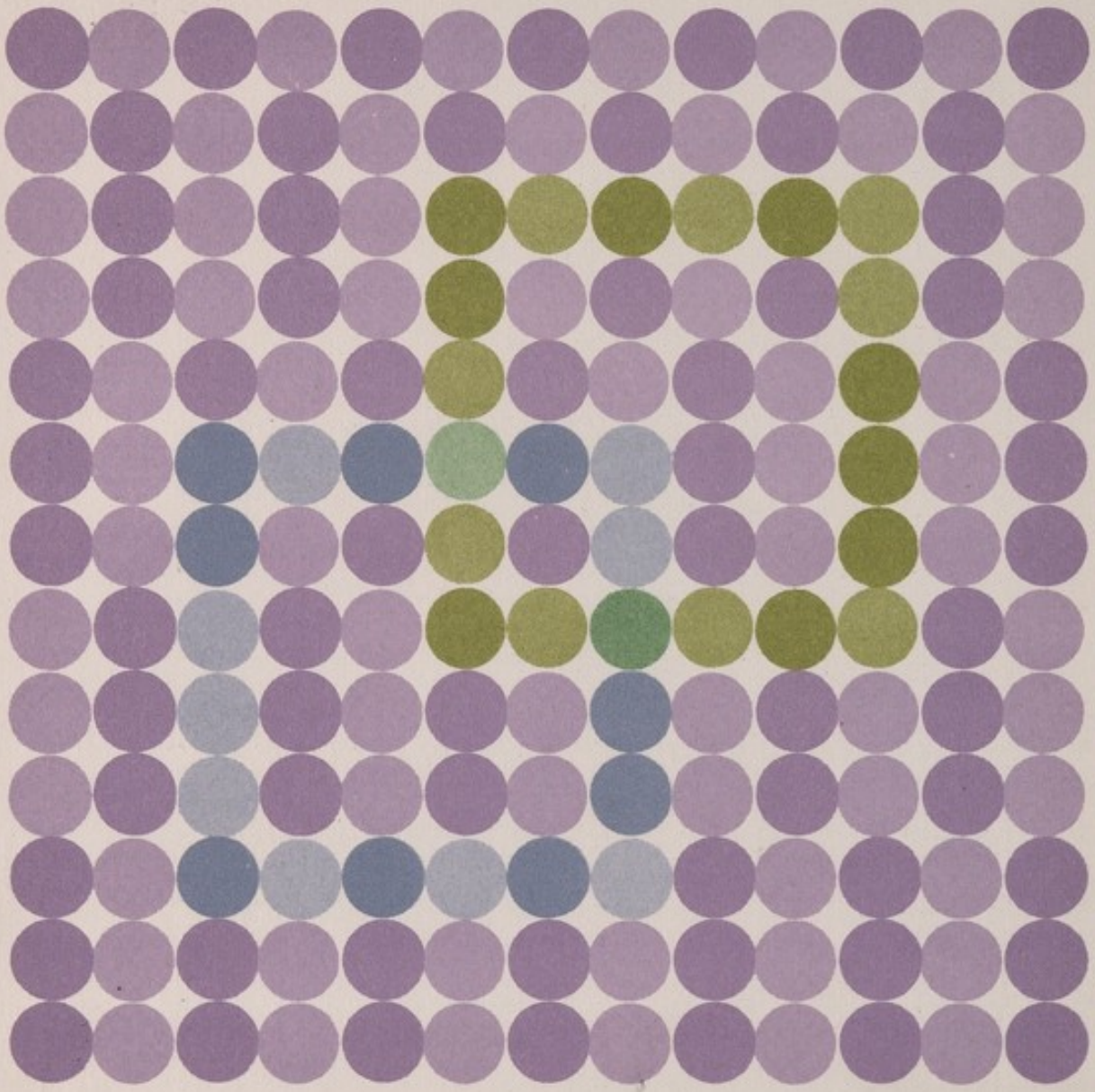

PLATE 1. Tritanopia plate.
1. Normal trichromats see two squares, but the green more clearly.
2. The complete tritanopes see only the blue square.
3. Tritanomalous people see the blue more clearly.

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(*Dean Farnsworth*)

DIAGNOSIS AND GENETICS OF DEFECTIVE COLOUR VISION

by

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PREFACE

DEFECTIVE colour vision, commonly called colour blindness, has since its discovery in the late eighteenth century attracted the attention of many theoreticians. Philosophers and psychologists were made to speculate on the nature of colour; linguists had to consider what colour names were appropriate in those circumstances; physicists, what external stimuli were implicated; physiologists searched among the various defects for clues explaining the mechanisms of normal colour vision, pathologists for the causes of the aberrations. Sociologists have pondered why these defects were so late in being discovered and artists what effect they have on painting.

The curious familial distribution of the common colour vision defects also aroused the interest of some early geneticists.

Practical interest in colour vision stems from its importance for the recognition of military and traffic signals and extends to all the arts and crafts which depend on normal colour discrimination; for instance, the printing of fabrics, mixing of pigments, sorting of electric cables, assessment of microscopic slides, colour titration and many other uses.

New practical and theoretical interests have been added to those older ones by recent developments in human genetics. These are first, the discovery of abnormalities in sexual development based on missing or supernumerary sex chromosomes or parts of them, in particular Turner's and Klinefelter's syndromes, in the elucidation of which defective colour vision has played some notable part. Secondly the discovery of additional and comparatively frequent sex-linked conditions, for instance of the G6PD deficiency which is the basis for primaquine sensitivity and favism, or of the Xg-locus which harbours a sex-linked blood group system; together with the haemophilias, muscular dystrophy of Duchenne's type and other rarer conditions, these have been tested for linkage with the various sex-linked colour vision defects.

One might also hope that recent considerable increases in our knowledge of defective colour vision will help the interpretation of certain human mosaics, deepen the understanding of nuclear sex, and finally help the speculations concerning the balance of the colour vision polymorphisms.

As there appears to be no modern comprehensive monograph on defective colour vision available in the English language, it is hoped that the present book will be useful.

Galton Laboratory H. KALMUS

CHAPTER I

SHORT HISTORY OF THE EXPLORATION OF DEFECTIVE COLOUR VISION

In her monumental monograph on the genetics of colour blindness, Julia Bell (1926) ascribes to Plato (*Theaetetus*) the first suggestion, derived possibly from Heraclitus, that individual colours do not necessarily appear the same to all people. The idea seems to have been lost and not further mentioned through antiquity, the Middle Ages and even the Renaissance.

In 1684 Dr. Turberville of Salisbury described a case of presumably acquired, most probably hysterical, colour blindness in "a maid, two or three and twenty years old who could see very well but no colour besides black and white". In 1688 Robert Boyle described at least one colour-blind person (Walls, 1956). These reports were again disregarded for almost a century.

Descriptions by Huddart (1777) of a family of sex-linked colour defectives, most likely protanopes, and by Scott (1778) concerning a similar family, fared somewhat better and were quoted in several publications; but sustained interest in defective colour vision was undoubtedly started 16 years later by the famous chemist Dalton (1794/1798), who was himself colour blind. To this day most French- and Spanish-speaking authors call defective colour vision "daltonisme" or "daltonismo". Elsewhere the unfortunate but ineradicable term colour blindness proposed by Sir David Brewster is widely used; some modern French authors tend to speak of *dyschromatopsie* and modern Germans of *Farbensinnstorung*.

In 1811 Wardrop recognized the lack of red and green perception, in the two common classes of dichromats, while Herschel in 1833 first suggested the term "dichromic vision".* Possibly in 1829, but certainly in 1837, Seebeck surveyed the literature and himself described a dozen colour-defective people. He introduced the method of making people match skeins of yarn of different colours and was the first to distinguish between protanopes and deuteranopes.

*In a letter to Dalton.

It took almost a century before the peculiar familial distribution of defective colour vision was widely recognized and Scott's (Fig. 21) and Huddart's pedigrees of protans were noticed. In 1876 Horner (Fig. 22) published an extensive pedigree of deuteranopes demonstrating its mode of inheritance long before the rediscovery of Mendel's laws. Another 34 years elapsed before Wilson in 1911 recognized that Horner's law and Mendel's laws might describe similar situations and, following Morgan, suggested that the genes responsible for the common defects of colour vision might be placed on the sex chromosome.

In 1877 Stilling invented and published the first pseudo-isochromatic charts (confusion charts) for the detection of colour defectives, the successors of which are still widely used. Lord Rayleigh (1881) demonstrated that monochromatic yellow light emitted by sodium (589 millimicron (mμ) wavelength) could be perfectly matched by a mixture in a definite proportion of monochromatic red light emitted by lithium (671 mμ) and monochromatic green light from a thallium source (535 mμ).

The formula connecting the quantities of yellow, red and green light is known as Rayleigh's equation. He also found that some colour defectives, the dichromats, accepted greatly varying proportions of red and green for their yellow matches basing their judgements on brightness only. The vast majority of people, however, the normal trichromats, agreed on a particular red–green match. Yet others, the anomalous trichromats, needed more green (deuteranomalous people) or more red (protanomalous people) than the majority to match the sodium yellow. Based on Rayleigh's experiments are the anomaloscopes (p. 41), still the principal tools for the classification of defective colour vision of which the first was constructed by Nagel (1907).

Acquired tritanopia was first described by König (1903), while several hereditary cases were fully explored by Wright (1952). Their incompletely dominant autosomal inheritance was established by Kalmus (1955). Sex-linked recessive tritanomaly had been discovered by Engelking (1925).

Allelism, localization and linkage of the genes responsible for sex-linked colour vision are now in the centre of interest and will be discussed later. The use of colour vision defects in the elucidation of the aetiology of sex chromosomally based sexual abnormality is also quite recent.

CHAPTER II

ESSENTIALS OF COLOUR THEORY

THE literature of colour theory is enormous and very confusing. For the purposes of this book, however, it is sufficient to clarify those points which are essential for the recognition and classification of defective colour vision.

To the naïve mind colour is an attribute of objects: violet is the colour of violets, orange that of oranges. In many languages the same words are used for colour and for paint. More sophisticated is the view that any particular colour is an attribute of a particular species of light characterized by its degree of "refrangibility" (Newton, 1672) or as we say today by its wavelength. Indeed visible radiation of a particular wavelength (monochromatic light) has in certain well-defined circumstances a characteristic colour for the normal observer. But the colour of some (e.g. brown) objects cannot be matched by spectral light of a particular wavelength while most naturally occurring colours (hues) whether red, yellow, green or blue may be produced by an infinity of mixtures of monochromatic radiations. The additive laws governing those mixtures we shall show (p. 4) to be fundamental for the understanding of normal and of defective colour vision. On the other hand, a colour sensation mediated by the impact of monochromatic radiation on the retina is greatly dependent on the radiation intensity (Purkinje, 1823–25), the size and localization of the affected retinal area (Maxwell, 1870), the illumination of neighbouring retinal areas (simultaneous contrast, Hering, 1878), and on previous conditions (successive contrast). We must thus conclude that there is no unique, and not even a simple, relation between wavelength and colour sensation.

In spite of these complexities it is not too difficult by using certain constraints and by standardizing the conditions of testing to establish individual differences of colour perception and to explore many aspects of this variability.

Normal observers can match the colour of any light—whether seen through an instrument or reflected from a surface—by mixing

(adding)* not more than three suitably chosen monochromatic radiations. This fact is the basis of the widely accepted trichromatic theory of colour perception (Young, 1801–2; Helmholtz, 1852) which postulates the existence of three kinds of colour receptors (cones) and which being the most suitable for expounding defective colour vision is adopted here. Quite recently Wald and Brown, as well as Dobelle and Marks (MacNichol, 1964) succeeded in measuring the absorption of single cones in human and primate retinas with a microspectrophotometer. Computation of these measurements showed three classes of cones with absorption peaks of about 430, 540 and 570 mμ. It should, however, be mentioned that Hering's four-colour theory (1878) which is based on certain antagonisms between complementary pairs (red, blue–green and blue–yellow) can also be applied to some cases of defective colour vision, though the phenomena it describes are probably not happening at the receptor level (pp. 54–55).

The trichromatic theory makes it possible to characterize colours (with certain exceptions) by their position in a triangle (Maxwell, 1871), in which the corners represent the colours of suitably chosen red, green and blue monochromatic light (Fig. 1).

The position of a colour C in such a *chromaticity chart* is fully determined by any two of the three colour coordinates, as the third is automatically fixed. Algebraically we can represent our colour by a match according to the equation

$$C = r.R + g.G + b.B$$

where C is the colour match and r, g, b are the "relative amounts" or colour coefficients—on an empirical scale—of red (R), green (G), and blue (B) monochromatic radiation.

It is interesting that the laws of colour mixing were formulated by the mathematician Grassmann (1809–1877), who was not himself an experimenter, but got interested in the work of Helmholtz. Based largely on Newton's observations he applied his "mathematics of dimensions" to the laws of colour mixing. He stated that (1) unlike lights mixed with like lights produce unlike mixtures, (2) like lights mixed with like lights produce like mixtures and (3) every mixture of light can be matched by a definite spectral mixture (Stiles, 1952).

Experience has shown that certain spectral colours, namely the blue and green ones, fall outside the area of colour triangles, which

* *The addition* (mixing) of lights must not be confused with the mixing of pigments, which is a *subtractive* process, because every pigment removes some radiation from the reflected light. Filters also are subtractive.

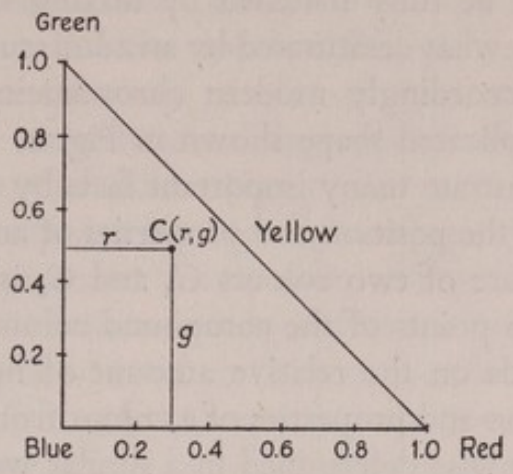

FIG. 1. The coordinates r and g define the position of a colour C on the area of the colour triangle, the corners of which are formed by blue, red and green light of specific spectral colours.

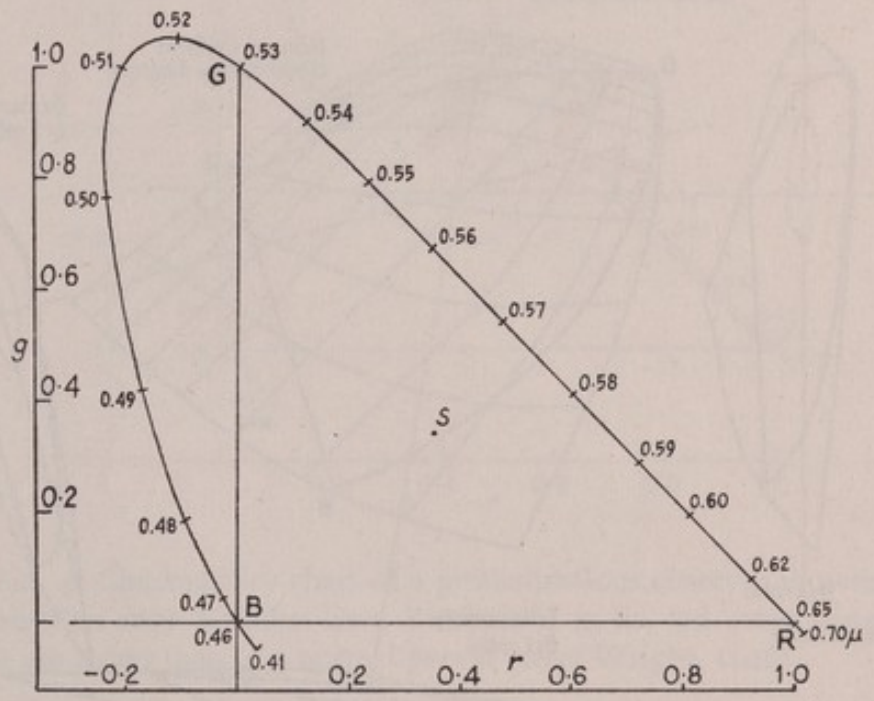

FIG. 2. Colour chart indicating the position of spectral colours, using 0·65, 0·53 and 0·45μ as matching stimuli. S indicates the position of "white". The straight contour joining red and green shows that pure spectral yellow can be perfectly matched by an addition of spectral red and spectral green, which is the basis of ordinary anomaloscopy. But the contour joining blue and green is steeply curved and mixtures of B and G are more desaturated than spectral blue–green (after Wright, 1946).

means they cannot be fully matched by mixing *G* and *B* radiation but have to be somewhat desaturated by an admixture of *R* (= monochromatic red). Accordingly modern chromaticity charts have the slightly more complicated shape shown in Fig. 2.

One can demonstrate many important facts by means of a colour chart. For instance, the position and properties of any colour *C* resulting from the mixture of two colours C_1 and C_2 is on a straight line connecting the two points of the compound colour, and the distance on this line depends on the relative amount of light from the two sources. The position and properties of a colour from a more complex mixture can be stepwise determined in a similar way.

Near the middle of the chromaticity chart lies a region of "white". According to different purposes different points may be selected in this region as representing an individual's neutral point (white). Two points on any straight line through any such neutral point connect *complementary colours* (Hering, 1878), that is pairs of colours such as

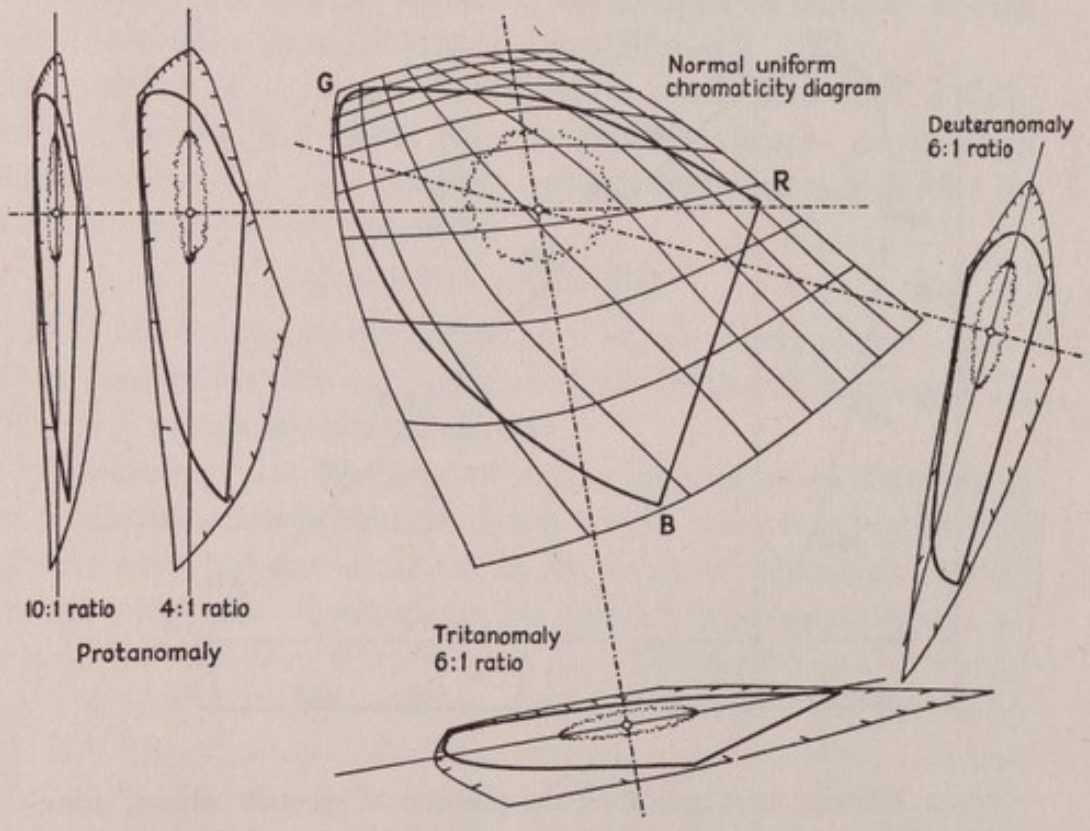

FIG. 3. Distortion of the normal chromaticity diagram for the three types of anomalous trichromasy. The ratios indicate the reduction of discrimination in a particular axial direction. The dotted circle and ellipses indicate the position of the colours of the Farnsworth–Munsell 100 Hue Test (p. 47) (after Farnsworth, 1943).

red and blue–green or blue and yellow, which added in suitable proportions produce a white sensation (Fig. 2).

The chromaticity charts of people—or eyes—with defective colour perception can be understood as "degenerate" versions of the normal chart; anomalous trichomats (see p. 42) are characterized by a diminished discrimination between light of certain wavelengths, e.g. between red and green or between blue and green (Fig. 3), and the resulting pairs of sensations can be represented as being nearer each other. This has been indicated on the chart by changes of scale.

In a different form of representation the scope and scales of the diagram are not altered, but the values of the scales are adjusted (Fig. 4).

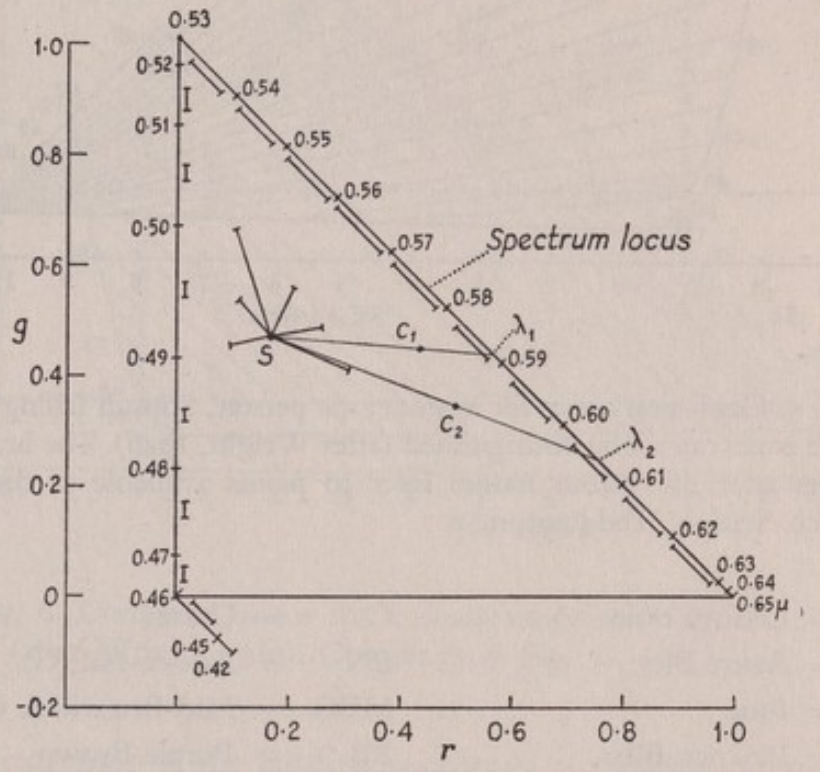

FIG. 4. Chromaticity chart of a protanomalous observer showing discrimination steps by short lines. Particularly in the red–green directions, these are larger than in a normal person (after Wright, 1946).

In protanopes the basic red sensation often is completely lacking and this can be represented in the form of confusion zones (lines) on the chromaticity chart (Fig. 5). These zones radiate from a point in the red region of the chart.

In deuteranopes all receptors are functional, but red and green are not recorded as different sensations but only jointly, subjectively as

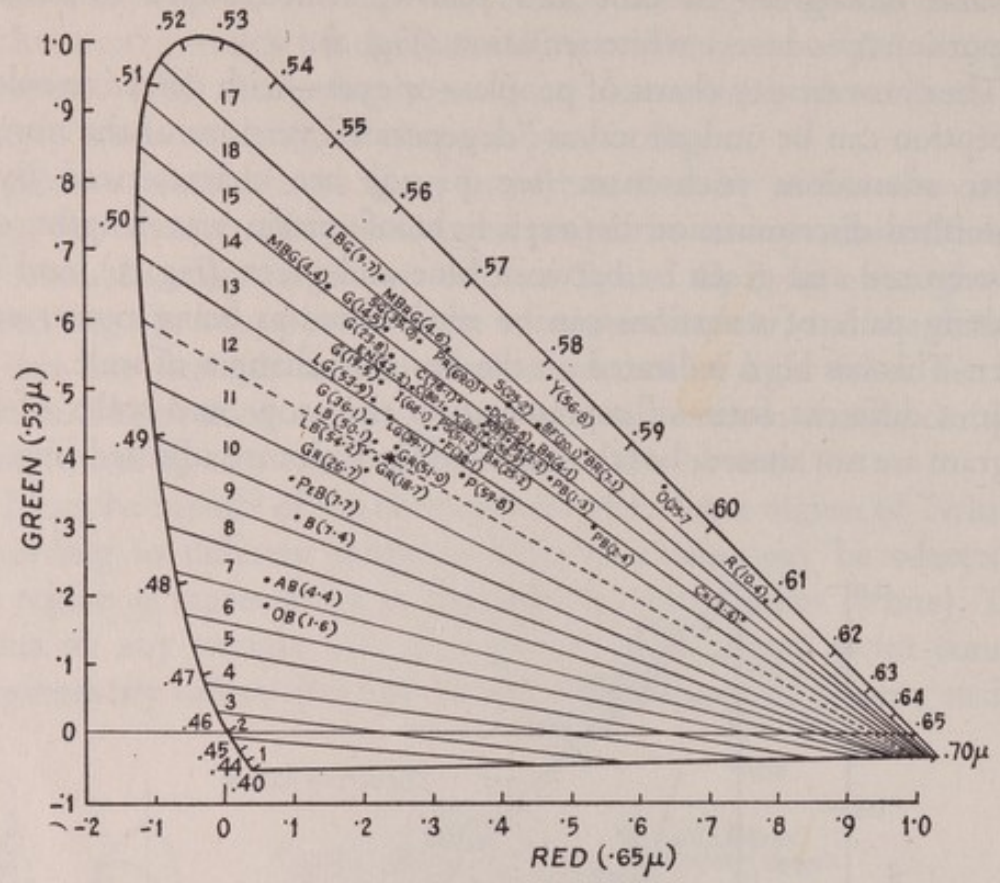

FIG. 5. Confusion zones for a protanope person. Stimuli falling in any of those zones cannot be distinguished (after Wright, 1946). The bracketed numbers after the colour names refer to paints available at the Paint Research Station, Teddington.

OB	= Oxford Blue	C	= Cream
AB	= Azure Blue	EN	= Eau-de-Nil (G)
B	= Blue	MBG	= Mid-Brunswick Green
PeB	= Peacock Blue	PB	= Purple Brown
Gr	= Grey	DC	= Deep Cream
LB	= Light Blue	SG	= Sea-Green
G	= Green	MBrG	= Mid-Bronze Green
LG	= Light Green	Pr	= Primrose
P	= Pink	Bf	= Buff
PS	= Portland stone	LBG	= Light Brunswick Green
F	= Fawn	Cr	= Crimson
I	= Ivory	Y	= Yellow
S	= Stone	O	= Orange
Br	= Brown	R	= Red

* = White

yellow (see p. 56). Accordingly the confusion zones of deuteranopes do not radiate but are parallel to the red–green axis (Fig. 6). Tritanopes which lack the blue sensation have again radiating confusion zones (Fig. 7), in this case originating from the blue corner.

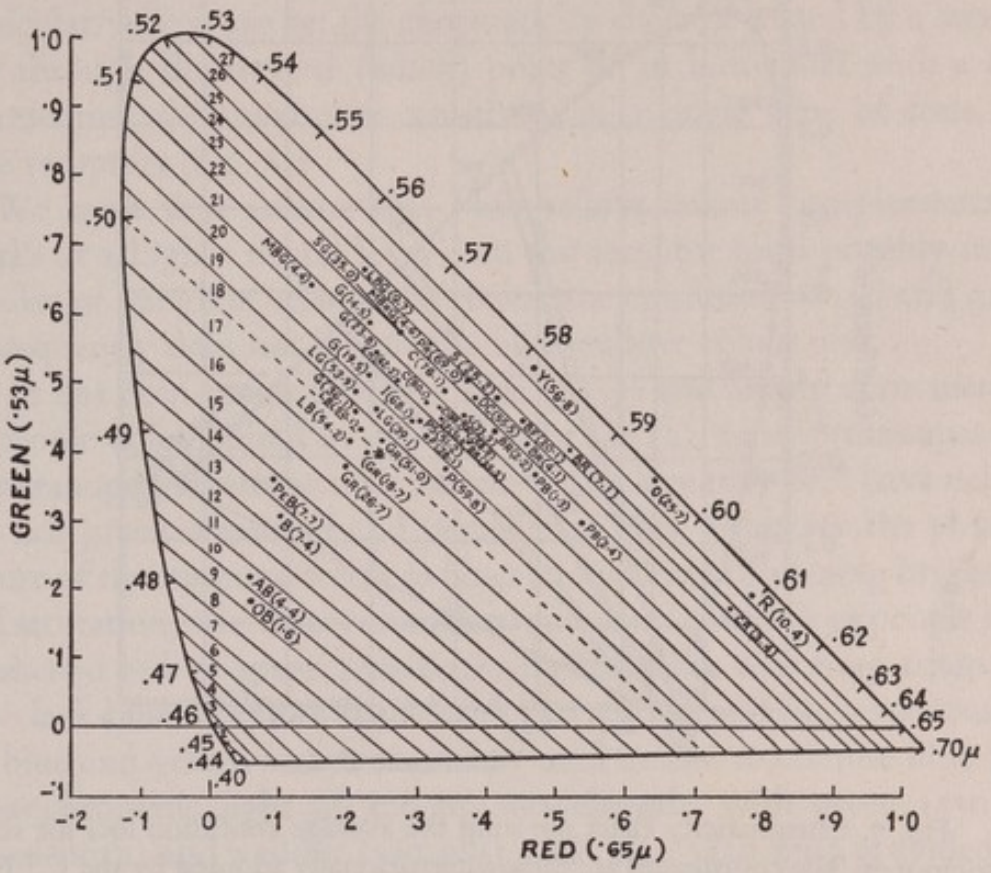

FIG. 6. Confusion zones for a deuteranope showing the iso-colour zones (after Wright, 1946). Colours as in Fig. 5.

The existence of the confusion colours as represented by the zones in these charts are the basis for most tests of defective colour vision with the exception of the anomaloscope.

The trichromatic theory postulates that in addition to the rods, which operate at low light intensities (scotopic vision, p. 20) and may at medium levels of illumination also be implicated in blue perception (p. 20), three kinds of cones operate at higher light intensities (photopic vision) the pigments of which have different maximum sensitivities in the spectrum and also different colour absorption (p. 28). It should be noted that the trichromatic theory does not require the existence of separate yellow receptors. The sensation "yellow" results from the simultaneous stimulation of red

and green receptors. Consequently yellow colours are represented by points on or near a straight line between the red and green corners of the chromaticity chart (see Fig. 2). This implies that by matching

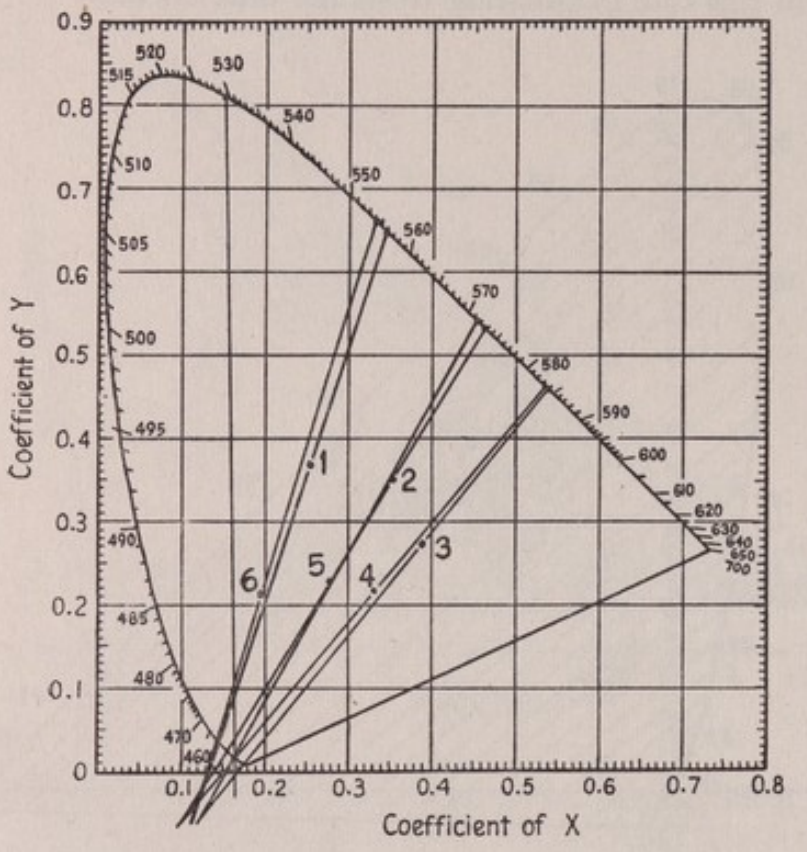

FIG. 7. Chromaticity chart showing the average confusion loci for six tritanopes. The coordinates are those internationally adopted by the C.I.E. (after Wright, 1952).

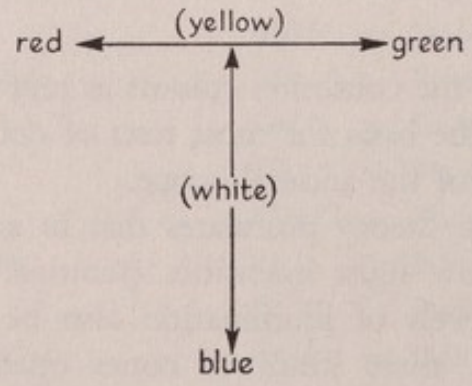

FIG. 8. Complementary colours according to Hering. In simultaneous or successive contrast experiments red provokes a green sensation and blue provokes a yellow sensation, and vice versa. Addition of red and green gives yellow. And addition of yellow (or red and green) and yellow gives white.

red and green to yellow—as is customary in ordinary anomaloscopy—no white light is needed for desaturation. Desaturation of the blue-green is, however, necessary, when matching it to a mixture of blue and green (p. 4).

The complementary colour sensation to yellow is blue and one particular yellow can on the chromaticity chart be joined by a straight line through the neutral (white) point of an individual with a blue representing the maximum sensitivity of a single type of cone, the blue receptors (Fig. 8).

We must thus assume that blue–yellow colour complementarity works at a higher neural level than the receptor level possibly in the bipolar or ganglion cells of the retina; the confusion of red and green consequently does not impair the blue–yellow colour axis.

As has been pointed out by Pole (1859) and amply demonstrated in people colour blind in one eye only (p. 12), most protanopes and deuteranopes, whatever their colour vocabulary may be,* have neither red nor green sensations and perceive colours, whatever the physical nature of the stimulus, solely as blues and yellows of varying brightness and saturation, while protanomalous and deuteranomalous people have weakened red or green sensations. By the same reasoning tritanopes who lack blue receptors should only have green and red sensations but no blue and yellow sensations. They tend indeed to confuse blue (e.g. monochromatic light of 420 mμ wavelength) with green (530 mμ wavelength) and yellow (580 mμ) with blue (430 mμ) provided the latter is a little desaturated with red of 650 mμ. However, the colour sensations of tritanopes have not so far been thoroughly investigated.

* It must be stated, that a minority of dichromats, especially some protanopes, can be credited with positive red and green sensations. A well-known example is that of Lenz (1963) who, on the strength of his anomaloscope readings and the Ishihara test, must be classified as a protanope and yet reports perfectly distinct red and also green sensations—incidentally subtending to quite small angles—when observing butterflies or flowers. Similar statements by several scientifically highly trained and colour-blind field naturalists have been made to the author while he tested their colour vision. Usually very saturated colours seem to be a prerequisite and also a "non-instrument" situation (see Land, 1959), where the integrative powers of the visual system are allowed fuller play. Green and red sensations have been also reported for deuteranopes (Ohkawa-Mascumi, 1951), when such observers view a continuous spectrum; the region which they describe as yellow is merely widened, but does not entirely cover the normally red and/or green regions.

CHAPTER III

SUBJECTIVE ASPECTS OF DEFECTIVE COLOUR VISION AND ITS SIMULATION

A MOST interesting description of the subjective aspects of defective colour vision has been rendered in a German paper by Ahlenstiel (1951) which, translated into English by Burnham, was printed privately by the Eastman-Kodak Company. But it is frequently accepted as an axiom, that normal people cannot experience what the world looks like to a colour-blind person and vice versa. In fact this is not quite so. It is perfectly feasible to simulate* for the benefit of the normal observer many aspects of a colour defective's subjective colour world, and there exist people who are colour defective in one eye only (pp. 57, 83) and who can compare normal and defective—or at any rate very different—sensations simply by closing one eye or the other. Colour blindness in one eye only has, since v. Hippel's (1880, 1881) once famous case, been described in a number of people and lesser degrees of divergent colour perception in the two eyes are probably fairly common after accidents or as concomitants of eye disease. By the testimony of such individuals we can indeed check our attempts at visualizing the various colour vision deficiencies. One such person—a young healthy woman, colour normal in her right eye and dichromatic† in her left eye—has provided more information in this respect than the several dozen cases of monocular defective colour vision previously described (Graham and Hsia, 1958), and the following description is based on her case.‡ Using her left eye she perceived

* Simulation of the sensations which colour defectives supposedly experience is, of course, clearly to be distinguished from fraudulent attempts by normal people at simulating colour blindness and from the efforts of defective people to appear colour normal.

† The left eye combined the features of deuteranopia with an unusually good discrimination in the violet.

‡ A film MN 8246 (*Colour Vision Deficiencies*) made by Cdr. Dean Farnsworth for the Research Division of the Bureau of Medicine and Surgery (Dept. of the U.S. Navy, Washington 25) shows, among other things, the colour worlds of this woman.

only three kinds of colour sensation, grey, yellow and blue. Shown a spectrum (see p. 31), any light of a wavelength above a neutral zone (wavelength 502 mμ) which she described as neutral or grey, and which to her normal eye was green, appeared to her left eye yellow, while any light of a shorter wavelength appeared blue. In particular she could match all the longer wavelengths (which to a normal eye range from green or yellow and orange to red) seen through her left eye to light of a wavelength of about 570 mμ perceived with her right eye and all the shorter wavelengths (green–blue–violet) with light of about 470 mμ. Altogether in her left eye she was *entirely lacking* any *green or red sensations* and everything appeared to her in the shades of yellow, blue or grey. When using both eyes this woman—in common with most similar people—perceived the normal full colour range and applied the appropriate normal colour vocabulary. But when using only the defective eye, red and green were absent and all sensations described in terms of grey, yellow and blue only. It was thus possible to manufacture visual environments, for example by furnishing a room entirely from grey, blue and yellow materials, which to her normal eye had the same appearance as similar objects covering the whole range of colours including red and green had for her defective eye. This colour-defective appearance of a room is shown in Dean Farnsworth's film, enabling us to see what the world looks like to deuteranopes. Protanopes—though different—usually also lack red and green sensations while the anomalous trichromats live in a world—also shown in the film—in which red and green are not entirely absent, but more or less weakened in intensity. One-sided colour-blind people having full normal colour perception in one eye can describe their sensations through their colour-defective eyes in terms of the colour-normal person. But people colour blind in both eyes cannot.

The use of colour fatigue for making a normal eye temporarily anomalous is described on p. 43.

CHAPTER IV

TYPES OF DEFECTIVE COLOUR VISION

CLASSIFICATIONS of defective colour vision vary according to the purpose for which they are designed and also according to theories of colour perception. All are more or less artificial and composite.

From the point of view of the pathologist (p. 52) two or three broad categories can be distinguished. First, acquired deficiencies of the colour sense which are either temporary or progressive and usually form only minor components of more serious defects or diseases of the eye or of the nervous system. A confusion between isolated "essential" cases of hereditary colour blindness and these acquired colour defects is not often experienced, because (1) the acquired forms are very often quite atypical, and (2) acquired deficiencies of colour vision forming part of morbid syndromes are usually late in appearance and are thus rarely observed in isolation. Cases of transient red–green blindness, following the taking of the drug iproniazid have also been reported (Greenblatt and Kahn, 1959). Large doses of JB516 had similar effects (Gillespie, Terry and Sjoerdsma, 1959).

Xanthopsia—a generalized yellow sensation following the intake of Santonine, an antihelminthic, has often been described in former times, but has little in common with colour blindness. Next are the deficiencies of colour sense forming part of hereditary diseases also showing other and usually more serious symptoms. Some of these are listed in Table 1. In a recent paper Jaeger and Grützner (1963) discuss these conditions.

A few remarks concerning the colour vision of albinos might be useful. About half of the autosomal recessive albinos show ocular symptoms. In some of these, nystagmus—probably caused by deficient macular development—makes reading difficult. This makes the assessment of colour vision rather difficult and the same applies to certain types of sex-linked recessive syndromes involving pigmentary dilution. Pickford (1958) reports, however, that the anomaloscope readings of three albinos—one woman and two men—were equivalent to those of protanomalous people and that the woman made 15 errors in a 24 chart Ishihara test.

An association between normal eye (iris) colour and hair colour on the one hand and defective colour vision on the other has in the past been suspected, and Burt (1945) as well as Vernon and Straker (1943, see p. 95) have indeed shown that in a large British sample population the frequency of colour defectives is positively correlated with the darkness of the iris and perhaps also with the pigmentation of the hair. This correlation—or rather the association between defective colour vision and pigmentation—is unlikely to be of a pleiotropic nature, but is probably a consequence of the heterogeneity of local

TABLE 1. EYE DISEASES IN WHICH DISTURBANCES OF COLOUR VISION OCCUR

Condition	Usual disturbance	Authors
Optic atrophy (dominant)	Blue–yellow and/or Red–green	Francois *et al.* (1961) Jaeger (1954)
Macular dystrophy	Red–green or Blue–yellow	Cox (1960) Grützner (1961)
Retinitis pigmentosa (rarely)	All colours	Weiner and Falls (1955)
Retinal detachment	Blue–yellow	Cox (1960) König (1897)
Toxic amblyopia (alcohol)	?	Cox (1960)
Trauma, concussion, brain tumour	Red–green or Blue–yellow	Many clinical papers

British populations in respect of both the pigmentation genes and the genes responsible for defective colour vision (see also p. 95). Pickford (1951) who searched for a correlation of defective colour vision with skin colour—but not eye colour—did not find it.

Finally there are the conditions which are remarkably stable throughout life* and as far as we know all not associated with any other symptoms and which are traditionally called hereditary colour blindness. Most of these are sex linked, but a few are not. These stable conditions form the main subject of this monograph. In addition to the genetically "pure" forms, composite forms exist, which complicate the picture and at the same time make it more interesting.

The classifications of hereditary defective colour vision have gradually emerged from the work of physicists, physiologists and psychologists and are largely, but not entirely, based on trichromatic theory

* Age has only a slight effect on the most frequently used colour vision tests (Lakowski, 1961). See also p. 53.

(see p. 4). Table 2 presents this classification in its most usual form.

TABLE 2. SIMPLE TYPES OF DEFECTIVE COLOUR VISION (FOLLOWING WRIGHT, 1957)

Monochromats	Dichromats	Trichromats	
		Anomalous	Normal
Cone monochromats (at high illumination)	Protanopes	Protanomalous Tr.	
	Deuteranopes	Deuteranomalous Tr.	
	Tritanopes	Tritanomalous Tr.	
Rod monochromats (at low illumination)			

While a fuller understanding of this system can only be gained by an appreciation of the diagnostic methods described in Chapter VII, it is useful at this point to explain the technical terms of the table and the principles of the classification. The main (physical) subdivision concerns the number of suitably chosen primary stimuli, for instance a red, a green and a blue monochromatic light, which suitably mixed are necessary to match *all* colour sensations of a person. Normal people (= normal trichromats), about 92 per cent of males and 99 per cent of females, need in general all three components for a colour match and there is little difference between such individuals concerning the relative intensities of these components. Other people (anomalous trichromats) may also need the three components for a general match, but the intensity of these components differs greatly from the intensity necessary for the normal trichromats. There are three kinds of these anomalous trichromats, namely protanomalous people who require more red stimulation, deuteranomalous people who require more green stimulation for their matches, and tritanomalous individuals who require more blue.

Dichromats need only two primary stimuli to effect all their colour matches. Their deficiency is more severe and it is said that they lack one of the fundamental sensations altogether. However, some people are dichromatic when matching small test areas, but are anomalous trichromats when matching larger fields (Jaeger and Kroker, 1952).* There are again three kinds of dichromats, namely the protanopes lacking a red sensation, the deuteranopes lacking separate red and green sensations, seeing yellow in place of both, and tritanopes lacking the blue sensation.

* To some extent this reflects differences between central and peripheral colour perception.

Monochromats are people who, using small test areas (see above and p. 45), can match any colour with any other depending entirely on brightness. They are sometimes considered to lack any colour sensation and have thus also been called achromats. Two kinds of monochromats exist: the majority are rod monochromats who, lacking photopic (cone) vision entirely or partially, have only the scotopic rod vision functioning at low intensities of illumination and at best some rudiments of colour perception (see p. 9). They are photophobic and their visual acuity is low. The other very rare type, the cone monochromats, have good vision also in bright light, but only vestiges of colour sensation. It is considered that they see scenes in the way colour-normal people see black and white photographs.

A fuller description and interpretation of these as well as a discussion of compound types will be attempted in Chapters VIII and IX. Here it should only be added that some exponents of the four-colour theory (see p. 9) have postulated the existence of yet another group of colour defectives, namely the tetartanomalous and tetartanopes; and have also predicted the symptoms of these defects. However, no tetartanope has been convincingly described and it is doubtful if such people exist; they must in any case be exceedingly rare.

The description and classification of the various types of defective colour vision is intimately connected with the methods of their detection and classification, and even their names cannot be properly understood without understanding these methods. Nevertheless, short preliminary descriptions based on a physiological classification (Table 2, across), must be given here, to make further discussion at all possible, while the methods will be described later on p. 28.

PROTAN DEFECTS (PROTANOIDS, PROTODEFECTS)

These people confuse red and green to a varying degree (see Fig. 5) and the severe types show a greatly decreased sensitivity to long wavelight. The types vary greatly in severity and are caused by sex-linked allelic mutant genes forming a graded series in the male hemizygotes, and showing a definite dominance relationship in the female heterozygotes: the normal allele is usually—though not always—dominant in women, while women carrying two abnormal alleles of different severity usually correspond in the severity of their defect to that of a man (e.g. a son) having the lesser defect (see p. 66). Three degrees of protan defects are commonly distinguished in the male, namely

protanopes, *extreme protanomalous* and *protanomalous* men; however, more than three abnormal protan alleles exist which result in a larger number of less different defects.

In terms of development protan alleles probably have similar effects—varying only in severity but acting on the same structures; thus the physicist's absolute (p. 16) distinction between dichromatic and anomalously trichromatic protans, i.e. between protanopic and protanomalous men, arbitrary from the point of view of the sense physiologist (pp. 52 ff.), becomes quantitative for developmental genetics. We shall see later that this distinction is in any case often dependent on the method of investigation, for example on desaturation of colours in the anomaloscope used or the size of the matching area (p. 45). However, different methods of testing will usually result in a sample of male protan defectives being arranged in the same order of severity. Protanopes lack the normals' red absorbing cone pigment (see pp. 28 ff.) which is supposed to be contained in special red sensitive cones, the *R* cones, and it is at present reasonable to assume that the protanomalous of whatever severity have less of this pigment and perhaps fewer of these cones in their retinae than people of normal colour vision; at least in the more central areas of the retina. The red sensitive cones of the colour-normal person may in protanopes be replaced by the green sensitive *G* cones (Walls and Mathews, 1952), or they may be missing or non-functional.

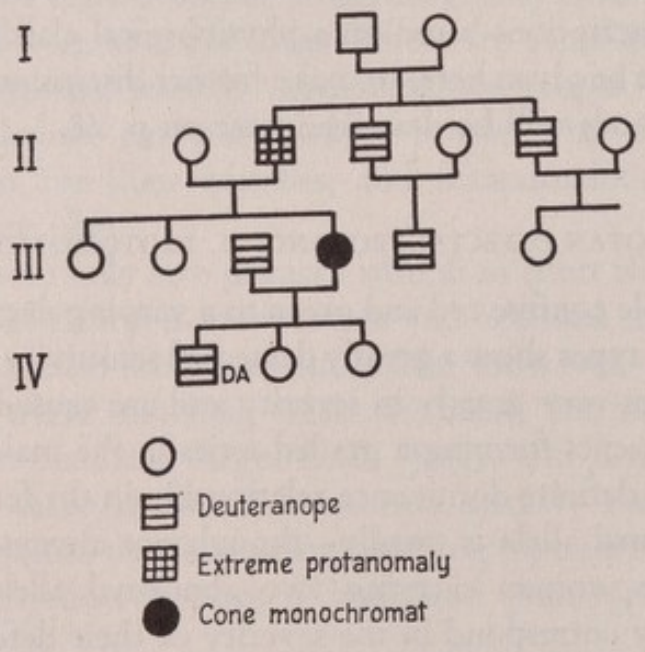

FIG. 9. A cone monochromat female in a pedigree of deuteranopia and extreme protanomaly (after Weale, 1953).

DEUTAN DEFECTS (DEUTEROIDS, DEUTERODEFECTS)

Deutans, though also unable to distinguish various shades of red and green (see Fig. 6), most certainly do not lack the normals' green absorbing pigment, nor probably the *G* cones. Their sensitivity to light of any wavelength is very similar to the normal sensitivity. The genes of the allelic series responsible for these defects are said to inhibit—to a varying extent—the differential development of separate *R* and *G* cones, with the result that a common cone type—possibly containing a mixture of both pigments—is produced either entirely (in deuteranopes) or more or less predominantly (in deuteranomals). If indeed there is only one type of "green+red cone" it is obvious that stimulation of such receptors cannot at a higher centre be separated into red and green sensations. It is, however, possible that the *R* and *G* cones of deutans are perfectly normal, but that the "wires are mixed up" only at the higher centre. As in protans three degrees of deutans are commonly distinguished, namely *deuteranopes, extreme deuteranomalous* and *deuteranomalous* people. But as in protans, more than three abnormal alleles exist causing defects of more finely graded severity in men and having definite dominance relationships in women (p. 66).

CONE MONOCHROMATS*

These rare individuals, as will be remembered, see well in the light and the dark and probably show Purkinje's phenomenon. Their naming of colours is quite erratic (Weale, 1953).

In bright light the red region of the spectrum appears lightest to them, as it does to normals, though, of course, they do not see it as red, whereas in dim light the blue region appears lightest. Bleaching experiments (see p. 28) have shown that the foveal retina of these people contains both the red and green sensitive pigments of the normal eye (Weale, 1959) and as brightness discrimination and visual acuity also are apparently normal, one might conclude that the deficiency is localized not in the cones but more centrally, perhaps in the brain centres where the colour sensations are computed from the "presensations" (see Fig. 19).

While cone monochromatism usually occurs in isolated individuals, colour defectives of other types are quite frequently found in some families of cone monochromats (Weale, 1953) (Fig. 9). This might

* See also p. 16.

support a possible compound nature of the defect (see pp. 23 ff.). However, in other pedigrees absence of colour defectives has been reported.

ROD MONOCHROMATS*

These, the more frequent monochromats, have even when corrected by glasses a very low visual acuity (20/200–20/70), maximal at rather low light intensities and cannot as a rule distinguish colours.† Furthermore, they do not show the Purkinje phenomenon; for them the relative brightness of the regions in the spectrum is the same at high and low intensities (Walls and Heath, 1957). All this amounts to an impairment of photopic vision and has been explained by a lack of function or even by the total absence of the cone apparatus.

However, Walls and Heath (1954) believe that in rod monochromats cones are present and normally distributed in the retina, but that they are all blue sensitive (*B* cones), and that the relative colour insensitivity associated with the condition is covered by some degree of macular degeneration, which may account for the avoidance of strong light and for the frequent nystagmus.

NIGHT BLINDNESS‡

Certain types of hereditary stationary night blindness are associated with defective blue sensation (Riddel, 1940). Night blindness has been explained by the non-functioning of the rod apparatus, e.g. by a defective retinene cycle, or even by its absence. The several genetical types (sex linked and autosomal) may differ somewhat in their developmental mechanics. The defect of the blue sensation (p. 9) of many night-blind people is interpreted as either showing that rods are implicated in blue perception or that *B* cones are perhaps functional in the dark (in scotopic conditions) (Willmer, 1949). That night-blind

* See also p. 15.

† Jaeger (1951) described a 49-year-old patient showing the classical symptoms of rod monochromatism (vision 5/35, nystagmus, photophobia, central scotoma, and a luminosity maximum at 520 mμ), who could match any small coloured field by a grey field; but who nevertheless correctly described the colour of areas exceeding a visual angle of 12°. He distinguished three areas in a projected spectrum (see p. 13): red–orange, yellow–green (which he perceived as grey) and blue–blue green. One must conclude that he could do so by means of a rudimentary cone system.

‡ See also p. 55.

people have no rods in their retinae seems rather doubtful. The defect more probably is in the more central layers of the retina or even in more remote brain regions. On the other hand in the mouse, which is said to have no cones normally, a mutant "rodless" exists which, in addition, greatly reduces the number of rods (Grüneberg, 1952).

TRITO DEFECTS (TRITANOPIA AND TRITANOMALY)

According to the three-receptor theory, one would expect to find not only protan and deutan defectives, but also people absolutely or relatively deficient in blue cones and exhibiting characteristic colour confusion in the blue–green and the orange–pink regions (see Fig. 7).

The first cases of this kind were found by König (1897); they were clearly acquired and not congenital. König (1894) also found that the fovea centralis of normal people is tritanopic and presumably lacking in blue receptors. This makes it possible to demonstrate tritanopia to normal people by the use of small areas (Willmer and Wright, 1945; Stiles, 1952; Kalmus, 1955).

Congenitally tritanopic and tritanomalous individuals, as well as some familial occurrences of the latter condition, have from time to time been described in the literature, but only comparatively recently have tritanopia (Judd, Plaza and Farnsworth, 1950; Wright, 1952; Cole *et al.*, 1964) and tritanomaly (Engelking, 1925; Jaeger, 1955) been more thoroughly explained.

Neither condition can be discovered with the Ishihara tables or the ordinary anomaloscope. Short of using a large spectral mixture apparatus, the special tables (Plate 1) devised for the discerning of tritanopia (Farnsworth and Kalmus, 1955, see p. 39) are the best means of discovering both tritan defects. The Farnsworth–Munsell tests (p. 47) can also be used.

Complications for the diagnosis of trito conditions, caused by the lens pigmentation, have been described on p. 53. Hereditary tritanopia has been shown to be an autosomal dominant trait (Fig. 20), with not quite complete manifestation (Kalmus, 1955; Henry *et al.*, 1963) and occurring in England with a frequency of between 1 in 13,000 to 1 in 65,000 (Wright, 1952; Kalmus, 1955). Tritanomaly has on several occasions been described as a more or less recessive sex-linked trait (Engelking, 1925; Oloff, 1935). Combinations of trito-forms with protans and deutans have been considered by Jaeger (1951) (Fig. 10), who discusses several such cases without reaching any firm conclusions.

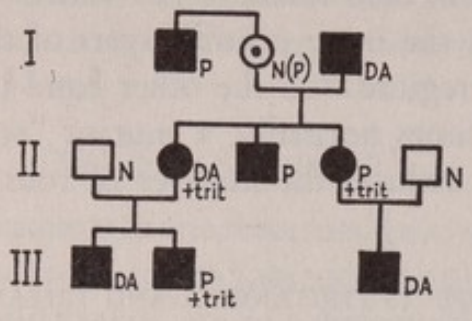

FIG. 10. Heterozygotes for non-allelic genes in a pedigree by Jaeger (1951). P—protanopic, N—normal, N(P)—heterozygote for protanopia, DA—deuteranomaly, trit—tritan factor.

When evaluating such situations one must bear in mind that in many red–green defectives a certain atypical impairment of the blue–yellow sense may occur, which, however, in no way represents a true trito defect (Jaeger, 1950). The existence of acquired (Oloff, 1939) and inherited trito defects in conjunction with diseases of the retina (Jaeger and Nover, 1954) and the optic nerve (Jaeger, 1954) must also be considered in this context.

CHAPTER V

COMPOUND DEFECTS AND INTERACTIONS

THE genetics of defective colour vision are still hampered by difficulties in classifying a minority of people of unknown genotype and even some of known genotype. Among the former, compounds undoubtedly are the most interesting; but unfortunately the imperfect understanding of the development and the physiology of the simple deficiencies makes difficult the formulation of very definite expectations concerning the properties of most of these compounds. The considerable frequency of the ordinary sex-linked colour-vision defects among the relatives of unique or rare types, seems to indicate the implication of the former in the aetiology of the latter, but it is difficult to exclude the possibility of a fortuitous coincidence in any particular pedigree.

FEMALE PROTAN–DEUTAN COMPOUNDS

The colour vision of simple female heterozygotes, most of whom are normal (p. 50), has been comparatively well investigated. Something is also known concerning women carrying a protan gene on one X-chromosome and a deutan gene on the other. Most such women are found by virtue of the fact that they have at least one protan and one deutan son; but occasionally they may be discovered in other ways, for example by having a protan father and a deutan son. Assuming the protans to consist of protanopes and protanomals and the deutans of deuteranopes and deuteranomals, not one, but four female protan–deutan combinations must exist according to the 1-locus hypothesis, while the more probable 2-loci hypothesis (p. 63) would let us expect 34 kinds of such compounds, some of which would be very rare and the characteristics of which would not easily be predicted and even more difficult to ascertain. If by recognizing a separate class of extreme deuteranomaly and one of extreme protanomaly one divides protan and deutan defects into three grades of severity each, (pp. 17, 19), the number of female compound types would be nine according to the 1-locus hypothesis and 117 if 2-loci exist. Only a small

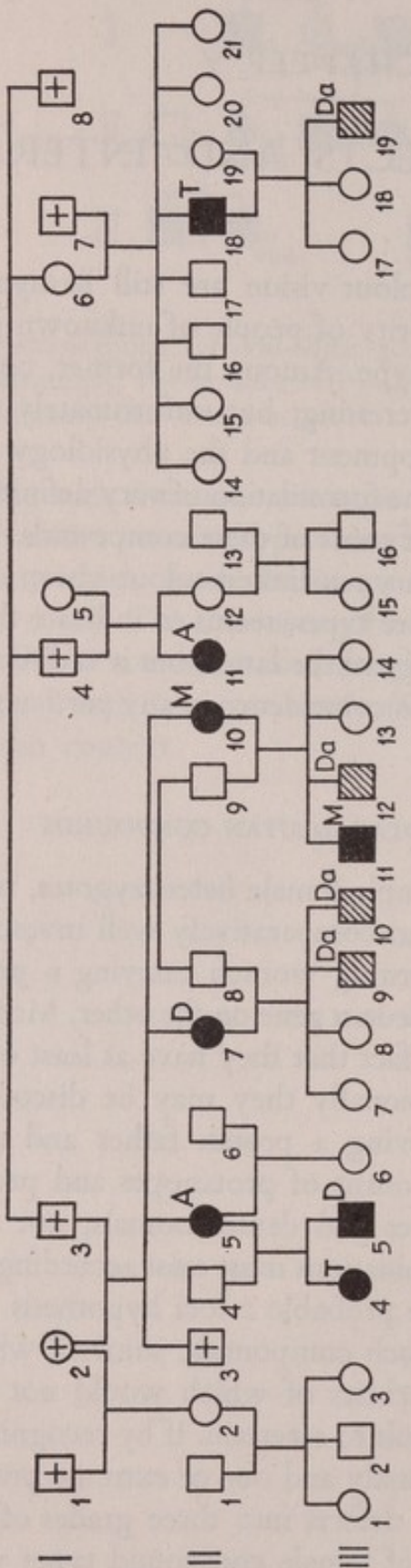

FIG. 11. Pedigree containing colour defectives of various types (after Crone, 1956).

A = colour weakness D = deuteranopia
Da = deuteranomaly M = monochromatism
T = trito defect

number of these compounds has ever been seen and even fewer adequately tested or described. Thus we do not know for certain what range of variation in colour vision they cover and how to evaluate some general statements concerning compound heterozygotes in the literature. According to Francescetti and Klein (1956) the colour vision of several of these female compounds is normal or nearly normal. This certainly indicates "complementation" and would favour the 2-loci hypothesis. But some kind of compensation can be visualized also on the basis of the 1-locus theory. However, several other authors (Walls and Mathews, 1952; Francois, 1961) report abnormal features in the colour vision of such women and Walls and Mathews (1952) assert that careful investigation may be expected always to reveal such features.

Jaeger (1951) described several non-allelic red–green compound heterozygotes, some of whom showed practically normal colour vision, while others were quite abnormal. He was also the first to record the colour vision of a woman whom he had reason to suspect of combining sex-linked red-green defects with one or the other trito defect. Crone (1956) described a pedigree, in which two cases of trito defect, two of deuteranopia and four of deuteranomaly occurred in addition to two cases of cone monochromatism and two cases of reduced colour discrimination covering the whole spectrum: and he considers the last four people to be combination forms of trito defects and red–green defects (Fig. 11). In this context the ideas concerning the genetics of cone monochromatism (see p. 19) are, of course, very relevant.

As even simple heterozygotes often show slight abnormal features (p. 50), the unpredictability of the compound heterozygotes is not really surprising. The situation unfortunately does not contribute to clarity. Tables 3 and 4 indicate the theoretical frequencies of the various protan–deutan compounds in a European population according to the 1-locus and 2-loci hypotheses.

MALE PROTAN–DEUTAN COMBINATIONS

According to the 1-locus hypothesis such males do not exist. If, however, separate loci are postulated for protan and deutan defects, four kinds of abnormal compound hemizygotes can be expected—assuming two grades of each defect—or nine kinds assuming three grades. Table 4, left, gives the overall theoretical frequencies for two

TABLE 3. THEORETICAL FREQUENCIES OF THE 15 POSSIBLE FEMALE COMBINATIONS, ASSUMING 5 ALLELES WITH THE FREQUENCIES 0·92 (NORMAL), 0·01 (PROTANOPE), 0·01 (PROTANOMALOUS), 0·01 (DEUTERANOPE) AND 0·05 (DEUTERANOMALOUS)

Combination	Frequency	Symbols
normal, normal	0·8464	cv^+, cv^+
normal, protanope	0·0184	cv^+, cv^P
normal, protanomalous	0·0184	cv^+, cv^p
normal, deuteranope	0·0184	cv^+, cv^D
normal, deuteranomalous	0·0920	cv^+, cv^d
protanope, protanope	0·0001	cv^P, cv^P
protanope, protanomalous	0·0002	cv^P, cv^p
protanope, deuteranope	0·0002	cv^P, cv^D
protanope, deuteranomalous	0·0010	cv^P, cv^d
protanomalous, protanomalous	0·0001	cv^p, cv^p
protanomalous, deuteranope	0·0002	cv^p, cv^D
protanomalous, deuteranomalous	0·0010	cv^p, cv^d
deuteranope, deuteranope	0·0001	cv^D, cv^D
deuteranope, deuteranomalous	0·0010	cv^D, cv^d
deuteranomalous, deuteranomalous	0·0025	cv^d, cv^d
	1·0000	

grades. Very little is known concerning the phenotypes (colour vision) of those various compound hemizygotes.

Walls and Mathews (1952) have described a pair of brothers of the protanope–deuteranopia kind, whom they described as atypical protanopes. Pickford (1962) reports a similar pedigree in which a simple deuteranomalous woman has three sons showing different types of defect, namely, simple deuteranomaly, simple protanomaly, and extreme deuteranomaly, respectively, and considers that the simple protanomaly–extreme deuteranomaly compound is in effect an atypical protanomal. The same author also suggests that presumed simple protanomaly–simple deuteranomaly hemizygotes in two of his families may have had normal colour vision. The effect of one-chromosome combinations of the colour-vision genes in even more complicated female heterozygotes are at present quite conjectural.

TABLE 4. THEORETICAL FREQUENCIES OF THE 9 X-CHROMOSOMES AND THEIR 81 COMBINATIONS IN FEMALES ASSUMING TWO ALLELIC SERIES WITH PERCENTAGES 98, 1, 1 IN THE PROTAN LOCUS and 94, 1, 5 IN THE DEUTAN LOCUS. (THE ENTRIES IN THE MAIN TABLE MUST BE MULTIPLIED BY 10^{-4}.)

Paternal X-chromosomes			Maternal X-chromosomes										
Protan locus	Deutan locus	Per cent	cv_1^+	cv_1^+	cv_1^+	cv_1^P	cv_1^P	cv_1^P	cv_1^p	cv_1^p	cv_1^p	Protan	locus
			cv_2^+	cv_2^D	cv_2^d	cv_2^+	cv_2^D	cv_2^d	cv_2^+	cv_2^D	cv_2^d	Deutan	locus
cv_1^+	cv_2^+	92·12	8486·0944	90·2776	451·3880	86·5928	0·9212	4·6060	86·5928	0·9212	4·6060		
cv_1^+	cv^D	0·98	90·2776	0·9604	4·8020	0·9212	0·0098	0·0490	0·9212	0·0098	0·0490		
cv_1^+	cv_2^d	4·90	451·3880	4·8020	24·0100	4·6060	0·0490	0·2450	4·6060	0·0490	0·2450		
cv_1^P	cv_2^+	0·94	86·5928	0·9212	4·6060	0·8836	0·0094	0·0470	0·8836	0·0094	0·0470		
cv_1^P	cv_2^D	0·01	0·9212	0·0098	0·0490	0·0094	0·0001	0·0005	0·0094	0·0001	0·0005		
cv_1^P	cv_2^d	0·05	4·6060	0·0490	0·2450	0·0470	0·0005	0·0025	0·0470	0·0005	0·0025		
cv_1^p	cv_2^+	0·94	86·5928	0·9212	4·6060	0·8836	0·0094	0·0470	0·8836	0·0094	0·0470		
cv_1^p	cv_2^D	0·01	0·9212	0·0098	0·0490	0·0094	0·0001	0·0005	0·0094	0·0001	0·0005		
cv_1^p	cv_2^d	0·05	4·6060	0·0490	0·2450	0·0470	0·0005	0·0025	0·0470	0·0005	0·0025		

CHAPTER VI

THE DETECTION OF DEFECTIVE COLOUR VISION

In spite of a great deal of work, no single instrument or test has as yet been proved infallible in the detection of defective colour vision. Even less can a single procedure scale its degree or determine its special kind. Several methods must be used according to the circumstances as in other clinical investigations and it is the main justification for this little book to enable the reader to select the most useful methods and to apply them properly.

OBJECTIVE TESTS

To date, the only objective difference between normal and one class of colour-defective people is that discovered by Rushton (1955, 1958), who showed that light reflected from the normal eye fundus indicated the presence of two foveal cone pigments.* Reflected light from the protanopic and the severely protanomalous fundus showed abnormal absorption (Fig. 12). Partial bleaching with intense red or blue light gave identical difference spectra in protan eyes, but different spectra in normal eyes, indicating the absence of one cone pigment in the former. No similar difference can be shown for deuteranopic or deuteranomalous eyes. Microspectrometric measurements on single cones (see p. 4) in the retina of a colour-blind person have as yet not been made.

An interesting half-objective method for the demonstration of dichromasy (protanopia and deuteranopia) has been invented by Fincham (1953); using an optometer he could show that the accommodation of the lens when an observer looks at a small object depends on the colour of the light used. This depends on the difference of refraction of monochromatic light of different wavelength and the reaction is actuated by colour fringes at the edge of the retinal image

* The fovea centralis of the normal eye is tritanopic, lacking blue receptors (see p. 21).

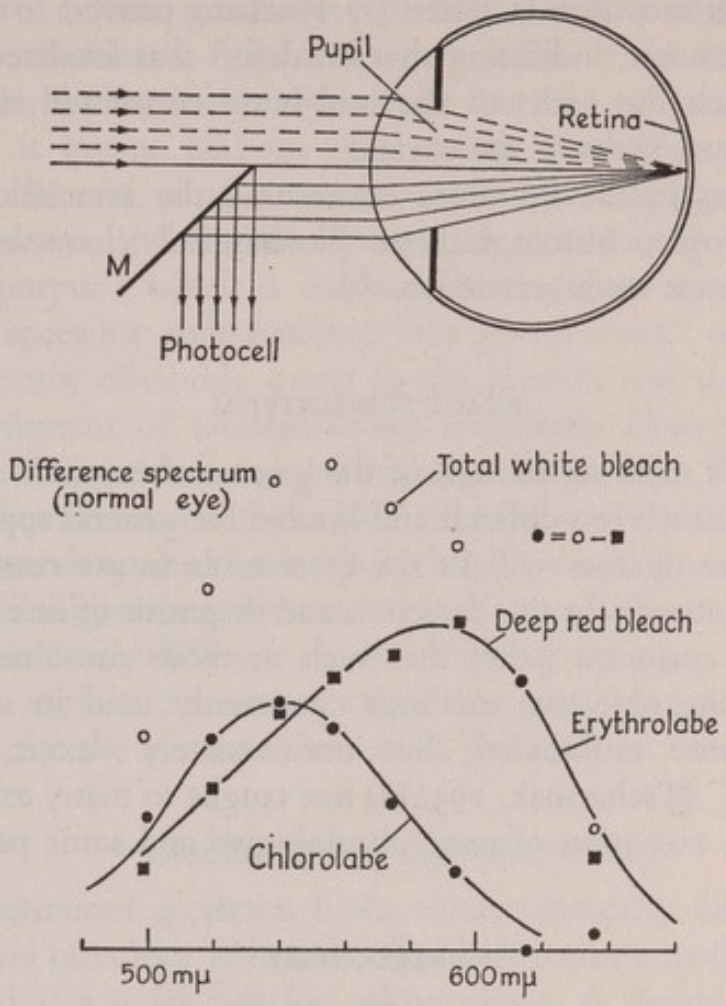

FIG. 12. Arrangement for recording light reflected from the retina (top). Pigments in the normal and protanopic eye analysed by bleaching with colour lights. The chlorolabe curve corresponds to the green absorption of the normal, but also represents the total absorption of the protanope (after Rushton, 1958).

due to chromatic aberration. The accommodation is operated by retinal stimuli reaching the superior colliculus where the ciliary reflexes are controlled and is independent of the cortex.

This chromatic accommodation is complicated by another form of accommodation not dependent on colour, but its existence can be shown by alternatively using monochromatic light and a heterochromatic mixture matching it.

In normal trichromats who have two kinds of cones in the fovea centralis the chromatic adaptation can be always demonstrated, but it is absent in protanopes and deuteranopes, who have only one type of cone—or one kind of cone group—in the fovea centralis (see p. 21, Willmer, 1949).

A cone monochromat tested by Fincham proved to react like a normal trichromat, indicating that his defect was localized above the zone at which the paths to the mid-brain concerned with reflexes leave the visual paths to the cortex.

Statements in the literature concerning the association of other ophthalmoscopic, histological or biochemical characteristics with colour blindness seem erroneous.

EXACT SUBJECTIVISM

Rushton's method, though of the greatest theoretical importance, is at present much too difficult and limited for general application and genetical investigators will in the foreseeable future continue to use subjective methods for the detection and diagnosis of defective colour vision. The common belief that such methods must necessarily be inferior to the objective methods commonly used in science is in any case quite unfounded; but unfortunately "exact, measuring subjectivism" (Tschermak, 1932) is not taught to many experimentalists with the exception of sense physiologists and some psychologists.

VERBAL TESTS

Contrary to much "scientific opinion" colour naming can be most informative and useful in many situations, provided it is used critically.

The pitfalls of simply accepting the correct naming of a colour as proof that a subject has normal colour sensations are obvious. Many blind-born people have an excellent colour vocabulary but certainly have no colour sensations. Colour defectives, who are somewhat better off in this respect, will also accept and use the colour designations of the normal majority irrespective of the quality of their own sensations. Moreover, having never experienced the normal sensations they are often quite unaware of their deficiency. The author found among 107 "colour-blind" male students no fewer than 21 ignorant of their peculiarity. It is also well known that some people, irrespective of their sophistication, decline to believe in their own colour deficiency.

While the correct use of colour adjectives in familiar situations cannot in itself prove normal colour sensations it may do so in experimental situations, and simulation apart, the use of "wrong" colour names is a strong indication for a defect, especially within the

investigator's culture group (see p. 100). Certain points, however, have to be considered; first, usage may differ in the same language; some people, for instance, may call the hue of a turquoise blue while others call it green, without there being any difference in colour perception. Second, similar words in different languages can denote different colours: the English "purple" is much more blue than the German "purpur" which is redder. Third, colour names are prone to assume specialist connotations: "the green livers" of some pathologists are not obviously green to the layman and the eyes of the "Cherry" mutant of *Drosophila* not manifestly cherry coloured to everybody. Colour defectives misname colours more frequently and their mistakes are more significant in situations where neither the context nor secondary clues, principally brightness, help. Such situations arise when a subject is confronted with identical objects (paper, wool, blocks) which only differ in colour. Naming of colour of individual dots in the various colour test charts (see p. 5) also provides useful indications for the existence, and even the kind, of colour defect.

DESCRIPTION OF THE SPECTRUM

The continuous spectrum looks characteristically different to the various types of colour defectives. If a dark room is available this fact can be used as a quick test for colour vision. A sizeable spectrum is projected on a screen and the investigator asks for a verbal description of its various regions (see also p. 13).

Provided the subject is not intent on deception and at the same time fairly knowledgeable, his description will, if he is colour blind, be faulty and up to a point indicative of the kind of defect. Many protanopes will, for instance, not see the red end of the spectrum and describe it as black. Table 5, which combines information from the literature with the author's own observations, lists the kind of answers which one can expect in this type of test. The method can be sharpened by the use of a black mask carrying a narrow slit which can be moved across the spectrum (Collins, 1925).

LANTERN TESTS

Colour naming is still widely used in lantern tests, for the strictly practical purpose of determining a candidate's suitability for jobs involving the recognition of signal lights, usually red, green, amber and white. The colour, size and intensity of the lights as well as the

TABLE 5. NAMING OF PORTIONS OF A CONTINUOUS LUMINOUS SPECTRUM BY COLOUR DEFECTIVES OF VARIOUS DESCRIPTIONS. SIMILAR RESULTS CAN BE OBTAINED BY MOVING A PIECE OF PAPER CONTAINING A NARROW SLIT OVER A PRINTED PICTURE OF A SPECTRUM. (METHOD BY COLLINS, 1925.)

Normal description	Black	Dark red	Red	Orange	Yellow	Yellow–green	Green	Blue-green	Blue	Violet	Black
Protanopes	black	dark grey	brown	dirty yellow	yellow	yellow-brown	grey	grey	blue	dark blue	black
	dark blue	brown	red	dark yellow	yellow	dirty yellow	grey	blue-green	blue	black	black
	black	dark red	red	orange	yellow	dirty yellow	orange	grey–green	blue	purple	dark red
Protanomalous people	black	dark red	red	orange	yellow	light green	grey–green	green	blue	violet	black
	black	dark brown	dark red	orange	yellow	brownish yellow	green	bluish	blue	dark	black
Deuteranopes	black	brown	red	green	yellow	orange	brown-green	bluish green	blue	red	black
	black	dark brown	red	orange	yellow	dirty yellow	green	blue-green	blue	dark red	black
Deuteranomalous people	black	dark red	red	orange	yellow	orange	greenish	blue	greenish blue	dark violet	black
	black	brown	red	green	yellow	green	greenish	blue	blue	grey	black

Normal description	Black	Dark red	Red	Orange	Yellow	Yellow-green	Green	Blue-green	Blue	Violet	Black
Tritanopes	black	dark red	red	pink	grey	grey-green	green	green	blue-green	violet	black
	black	dark red	red	orange	yellow-grey	yellow-green	green	blue-green	blue	dark	black
Tritanomalous people	black	dark red	red	orange	grey-yellow	green-ish	green	blue-green	blue	blue-purple	black
	black	dark red	red	mauve	prob. yellow	yellow-green	green	green–blue	blue	dark	black
Cone monochromats	black	dark	dark	grey	light	light	grey	grey	grey	dark	black
	black	dark	red	red	grey	light	grey	grey	grey	dark	black
Rod monochromat											
small area	no colour named specifically										
large area	black–red				yellow–grey–green				green–blue		black

viewing conditions (general level of illumination) can be raised so as to simulate practical conditions as nearly as possible. Lantern tests are employed by the Services of many nations and also by transport enterprises where they serve quite well in eliminating colour defectives. Genetically they are of little use and the simultaneous screening of mass audiences by lantern tests is to be deplored.

An example is the New London Navy Lantern (Farnsworth and Foreman, 1946). This is an instrument in which nine pairs of colours (all possible of white, red or green) are made visible through an aperture. The pairs are presented at three aperture sizes and the subject is asked for the name of the colour on the top and on the bottom. The efficiency of this test has been favourably compared with the efficiency of other lantern tests.

MAXWELL'S SPOT

An entoptic and subjective phenomenon in which normal and colour-defective persons differ is Maxwell's spot (Walls and Mathews, 1952). When looking at a large white card illuminated by incandescent light, using alternatively a spectrally unselective grey filter and a purple gelatine filter transmitting only short wave (violet and blue) radiation and long wave (red) radiation, most observers see through the dichroic filter a pattern of circular shape and varying internal structure, subtending about 3° (Judd, 1953) (Fig. 13). The colour of this "spot" first seen by Maxwell (1849) depends on the type of colour vision as follows:

Normal: Red or pink
Protanope: Blue or dark
Deuteranope: No spot, hence no colour
Protanomalous: Blue or red or dark
Deuteranomalous: Mostly no spot, hence no colour, occasionally red or violet, or orange or dark.

Maxwell's spot can also be demonstrated in an after image. Its interpretation is controversial. Some regard it as a consequence of special macular pigmentation and others as caused by the different receptor distribution near the fovea centralis.

PSEUDO-ISOCHROMATIC CHARTS

With the possible exception of lantern tests, which because of their similarity to colour signals are popular with the armed forces of several

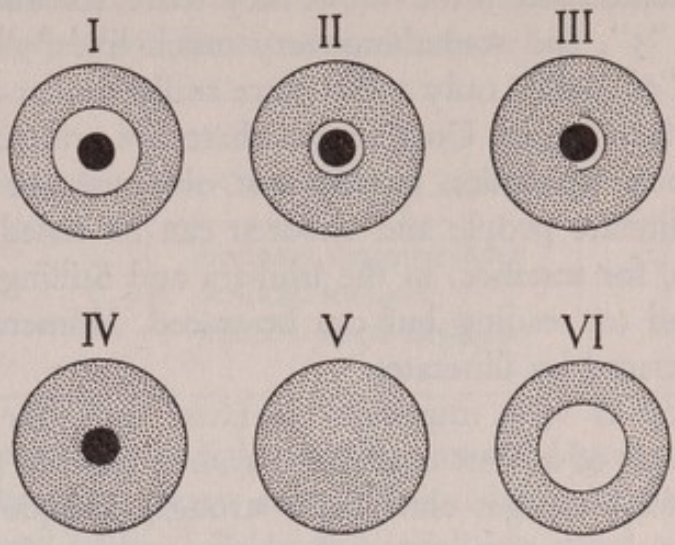

FIG. 13. Patterns of "Maxwell's spot" as it appears to normal observers.

I : halo, clearing, central spot
II : halo, narrow clearing, central spot
III : halo, cut-up clearing, central spot
IV : halo, no clearing, central spot
V : homogeneous disc
VI : halo, clearing, no central spot
(from Izobe, 1955).

nations, pseudo-isochromatic charts are the most frequently used screening device for the detection of defective colour vision.

These "confusion charts" (Wright, 1957) are based on the existence of iso-colour zones (pp. 8–10) and consist of patterns of variously coloured dots, containing some number, letter or other shape which the subject is asked to read, or if illiterate or a child, to trace; most of the charts of any series are read by colour normals but not by colour defectives or by certain classes of them. In several series of these charts some are contained which colour defectives read more easily or read differently from normals.

The relative merits of the various collections of these charts—some of which will be described later—have been compared, but such evaluations are unfortunately not too useful because successive editions of the "same" charts have been shown to differ in their colours.

Great caution is required in the special interpretation of readings. Thus the German style of the numbers in Stilling's tables differs somewhat from the English shapes; Spanish-speaking people make systematic mistakes when reading the Ishihara tables. More seriously, Arab people use numerals which are entirely different from the

"arabic" numerals used in the West: they write, for instance, "o" for our numeral "5", and something very much like "5" and "7" for our "2" and "6", while only 1 and 9 are really similar in both European and Arab numerals. Until special charts are printed for the Arab people European confusion charts must obviously be applied with great care. Illiterate people and children can be tested with the aid of patterns as, for instance, in the Ishihara and Stilling charts which do not depend on reading but can be traced. Numerals, of course, may also be traced by illiterates.

Illumination is very important in chart tests (see p. 39). The various pigments of a chart may differ in their gloss so that a colour-defective person may get clues from strongly oblique light; diffuse light or light impinging perpendicularly on the charts from the direction of the observer must therefore be used.

The most important source of error in the use of confusion charts is a wrong choice of illuminant. Chart tests must never be undertaken in direct sunlight, nor during dawn or dusk, nor in rooms with strongly coloured walls. Most important of all the charts must not be used in artificial light except as specified below.

Waaler (1928) noted, for instance, that adult deuteranopes could more correctly read a greater number of Stilling charts under incandescent light than under daylight; similar observations have often been made since.

Though daylight varies considerably (Farnsworth and Reed, 1943), diffuse daylight of sufficient brightness is in practice almost invariably used and for genetical purposes chart readings in the open either in the shade or under an overcast sky will seldom be misleading; nor will be reading in a room where the subject has its back to a north window (in the Northern Hemisphere).

If more stringent conditions are desired, for instance in comparative studies or if testing in the above daylight conditions is impossible, artificial standard illuminants must be used. The most important characteristic of these is "colour temperature", that is the absolute temperature of a radiant "black body" which would produce light corresponding to the illuminant's spectral composition. It should be mentioned that a high colour temperature corresponds to "cold" (greenish–bluish) light, while a low colour temperature produces a "warm" (yellow–reddish) illumination. Standard illuminants may be produced by combinations of incandescent lamps with filters or by fluorescent light.

Various standard illuminants have been defined from time to time and a few models will be mentioned below:

Standard illuminant	Corresponding light source	Colour temperature °K
A	ordinary tungsten lamp	2850
B	artificial sunlight	4800
C	artificial north skylight	6500

Ordinary tungsten light enables many deutans to read many pseudo-isochromatic charts correctly; it is less misleading for protans. Similarly most artificial lights will invalidate wool tests, Farnsworth tests and all others depending on pigments and reflected light. An illuminant-stable colour vision test consisting of six charts which may be read in daylight or incandescent light has been devised by Ellis Freeman (1948). But its efficiency in other respects has not been fully tested.

Viewing distance also affects chart readings as colour matching depends on field size (Horner and Purslow, 1947–48; Jaeger and Kroker, 1952). The effects of very small fields producing tritanopic vision are described on p. 21. Therefore, charts should be used at ordinary reading distance or at the distance stated; refraction errors should be corrected by wearing glasses, but these must not be tinted.

Nagel's Charts (Bergmann, Wiesbaden, Germany)

The working of these charts depends on colour naming. First published in 1898, each of the charts carries a circle of 23 coloured dots of various hues, some of them being more or less red. In a preliminary run the subject is shown all the charts and asked whether each contains a red dot. People not making any mistakes are judged to be normal, but a single mistake makes a person suspect of defective colour vision and he is then retested and asked additional questions according to instructions. The charts are not suited for mass screening, but allow some subclassification.

Stilling's Charts (20th edition by Hertel, Leipzig)

These, the first widely used colour charts (1878), are still used on the continent of Europe and in Latin America. It has been stated that they are less efficient in discovering and classifying colour defectives than more modern charts. On the other hand, unlike the other col-

lections they incorporate tables for the discovery of tritans (groups VIII–XV). Of these, group XV has been found to be effective (Kalmus, 1955), though it is occasionally failed by older normal people (see p. 97). The diagnostic power of Stilling's tables has been discussed by Trendelenburg and Meitner (1941).

Ishihara Charts (Kanehara, Tokio and Nippon Isho Shippranco, H. K. Lewis, London)

These are at present the most popular charts in use. Unfortunately the various editions differ considerably so that validation data for one edition do not necessarily apply to others. Only protans and deutans, but not tritans, are discovered. Numbers or patterns for illiterates are laid out in various shapes and in the confusion colours: yellow, green, orange, red, brown, pink and grey. In some editions four and in others two are incorporated with one red and one purple number against a grey background. Most protanopes cannot read the red figure while deuteranopes do not as a rule see the purple one. However—as Wright (1957) remarks—some protanopes who are slightly insensitive to blue (perhaps owing to lens pigmentation, p. 97) miss the purple numbers as well as the red ones, making the diagnosis less certain. Distinction between protanomalous and deuteranomalous trichromats by means of these charts alone is even more uncertain, and anomaloscopy should be used if at all possible.

Pickford (1949), investigating a 25-plate Japanese edition of these charts, concluded that by applying certain numerical criteria they could be used to distinguish satisfactorily between major red–green defectives and the rest, but that they fail to distinguish with any certainty between extreme and moderate defects and cannot be used to detect minor deficiencies in colour vision. One may, however, object to these conclusions.

It is not usually realized that the diagnostic power of individual charts in a collection varies a great deal and that in the Ishihara charts in particular some are almost useless when considered in isolation, while a few do most of the discriminatory work.

This fact, though well documented by von Planta (1928) and Sloan and Habel (1956), has been frequently overlooked, and additive test scores have been used in consequence instead of properly weighted ones. The latter authors, giving the misclassification of normal people as colour blind three times the weight of the other misclassifications, published the following empirical sequence of efficiency for an un-

dated Japanese edition. The figures in brackets are what the author presumed to be the correct readings: 6 (5), 4 (29), 13 (45), 3 (6), 12 (97), 2 (8), 16 (16), 9 (74), 10 (2), 5 (57), 17 (73), 8 (15), 7 (3), 11 (6). Unfortunately this ranking does not strictly apply to other editions.

The Ishihara charts reading 26, 42, 35 and 96—occurring in all editions—can be used for a tentative distinction between protans and deutans. Protanopes read only the digits on the right (6, 2, 5 and 6) while deuteranopes often read 2, 4, 3 and 9. Anomalous trichromats tend to err in the same direction as the corresponding dichromats. A few severely defective people cannot read these four charts at all. The use of the Ishihara tables has been extensively discussed by Cavanagh (1955, 1956).

Colour Charts of the American Optical Society

These are also widely used, especially in the Western Hemisphere. Their efficiency in detecting defective colour vision is about as good as that of the Ishihara charts.

The original test charts of the American Optical Company were hastily compiled early in the last war from the then unavailable German Stilling charts and Japanese Ishihara charts. They were considerably improved by Hardy, Rand and Ritter (1946) and in 1955 were published as the American Optical Company H–R–R–polychromatic plates and have since been republished with slight alterations. Their efficiency has been tested by Walls (1959) and Habel (1956).

Dvorine Test

Another American chart test is the Dvorine test (second edition 1953). It works under the light from a cheap daylight fluorescent tube (6500°K) and does not require the expensive Macbeth Easel lamp designed for pseudo-isochromatic tests (Walls, 1959). Its diagnostic value has been studied by Peters (1953, 1959) and Walls.

Comparative studies concerning the discriminatory power of the various pseudo-isochromatic charts have been published among others by Kettesy (1955), Frey (1958) and Walls (1959).

Tritanopia Charts★

While only the Stilling charts contain any designed for the detection of tritanopia, other series lack those entirely and must be supplemented

★ See Plate I opposite p. 22.

by special charts if one wants a test for tritans. However, these charts are not commercially available. The periodical *Die Farbe* has distributed such a chart to the members of a colour conference in Germany and some copies may be available on application. Recourse can be had to publications by Stiles, 1952; Kalmus, 1955; Farnsworth, 1956. It is also possible to make such charts from Munsell papers as specified by Kalmus (1955).

Coloured Wool Tests

These are now little used and by most people considered obsolete. They are, in fact, not very efficient. However, matching and grouping dyed skeins of wool is a method well suited to test infants as such activities have been shown by the Montessori movement to develop quite spontaneously during play. Two well-known wool tests are the one by Holmgren and the Loken's Nela test.

STABILITY OF TEST RESULTS

Repetition of the diagnostic tests described in this chapter produces practically identical results in the genetically colour blind; indeed the very stability of these conditions throughout life makes them such valuable genetical markers. Claims that these conditions can be cured or that colour vision can be improved by training have so far all been spurious (Chapanis, 1949). They may, however, be connected with slight nycthemeral, lunar and seasonal changes of spectral sensitivity (Dresler, 1941). A particular test procedure can, of course, be learned and fraudulent stimulations or dissembling of defective colour vision has succeeded when the tests were administered by inexperienced people or through carelessness. But this should not happen when proper care is taken. Significant changes in test performance, which are indicative of pathological changes over longer periods, are, however, experienced in acquired or transient deficiencies of colour vision, when they may be either improvements or deteriorations (see p. 15), and in progressive and more generalized eye conditions when they show increasing deficiency.

CHAPTER VII

DIAGNOSIS OF TYPE

THE classification of defective colour vision is based on matching ability (p. 40) and it would seem only logical that the type of any individual's defect should be best determined by matching devices. Of these the most useful ones are the anomaloscopes. Sometimes where the use of these is impracticable—as in very remote places or where children or people unused to any form of instrument are concerned—certain procedures resembling games with colour blocks have proved quite efficient.

As in other fields of medicine, diagnosis of a special kind of colour defect implies a deficiency of a more general kind: if anomaloscopy shows a person to be deuteranomalous, he is obviously colour blind. If by anomaloscopy one could easily and unfailingly discover all kinds of colour defectives, these instruments would be the most useful not only for the typing but also for the discovery of colour defectives and one could dispense with preliminary chart screening. However, as we shall see, dichromats— and in particular deuteranopes—accept a multiplicity of green–red mixtures when matching yellow, which they do predominantly by brightness; and as many of them also accept the "normal" match, these can easily escape discovery when the anomaloscopy is done by an unskilled person. It is therefore safer—and in the end quicker—when exploring a population's colour vision to use confusion charts first and only test those suspect of a colour defect by anomaloscopy. Even then one should realize that one's methods must be considered as rather crude, considering that one single measurement only is applied to gauge very crudely a specific fault of one of the most complex systems in existence, namely that of the eye, the visual integrative pathways and the cortex.

ANOMALOSCOPES

Colorimetric devices for the subjective matching of any colour by mixtures (additions) of two or more spectrally pure lights are the most

powerful tools for purposes of general colour physiology and colour pathology (Wright, 1946). However the bulk, cost and rarity of these instruments puts them quite out of reach for routine genetical purposes. For these, much simpler special instruments with more modest aims exist which are called anomaloscopes. The first of these, constructed by Nagel (1907), was based on Rayleigh's (1881) equation (p. 2), uses spectral light and is still widely used. A few simpler models mostly using colour filters will be described below:

A subject confronted with an anomaloscope observes a small circular or square field, subdivided horizontally or vertically into equal halves (Fig. 14). One of these halves is illuminated by pure yellow

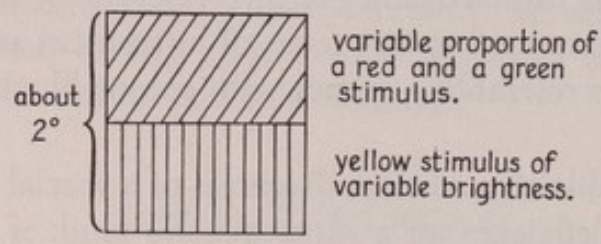

FIG. 14. Appearance of the matching field in an anomaloscope for testing red–green defects. Additive mixtures of red and green stimuli are matched against yellow of variable brightness. For tests of other colours different mixtures can be matched against particular stimuli. The colour of one or the other half of the field can also be desaturated by addition of a small proportion of white or other light.

light either from a spectrum or through a filter, the intensity of which can be varied by the subject himself or by the investigator; the other half is illuminated by a mixture of red and green pure lights, the proportion of which can again be varied at will. To effect a match the normal observer primarily uses his powers of colour discrimination, but the colour defective relies—more or less in proportion to the severity of his defective or even mainly—on a brightness comparison. Thus the demand to match the two halves of an anomaloscope area is ambiguous to him and it is not surprising that some abnormal observers cannot find a satisfactory match at all.

As their name implies, anomaloscopes are primarily designed to classify and sometimes to detect *anomalous trichromats*.* They are not primarily designed to classify dichromats, though they can often be also used for this purpose (see p. 43). Among the anomalous tri-

* For the measurement of tritanomaly a mixture of spectral blue and green lights would have to be matched against blue-green desaturated with a little red.

chromats, the protanomalous people will not accept the red–green mixtures matching the yellow half of the field for normal trichromats —and which vary only within narrow limits—but will match the yellow with mixtures containing more red light; on the other hand, deuteranomalous people will produce matching mixtures which to the normal eye appear decidedly too green.

It is possible for the sake of demonstration to induce temporarily conditions resembling anomalous trichromatism. This can be done by looking at a bright light through a coloured filter. For instance one can set an anomaloscope—with a vertical dividing line—so that the two fields match and then fatigue the left eye by looking for ten seconds through a red or a green filter at a bright light. A piece of black cardboard is then held so that it separates the two halves of the anomaloscope's field and also the two eyes. The red–green mixture which previously was perfect will then no longer match the yellow (see p. 12).

Dichromats are also classified by anomaloscopy. Some of these people are characterized by accepting a multitude of red–green mixtures—including also the normal one—and by making their matches by varying the brightness of the "yellow" half of the anomaloscope field or the red–green proportion. For the effects of field size and distance see p. 44.

Anomaloscopes are often used incorrectly; of several correct procedures one combining Wright's (1946) use of mid-matches and Pickford's (1949) consideration of matching ranges is as follows: the red–green half of the test field is set at pure red and the subject is asked to match* this red by altering the intensity of the yellow. This, trichromats, whether normal or anomalous, are unable to do. But a dichromat will be prepared to produce or to accept such a match. The matches of dichromats will be of two characteristic and very different kinds. To the protanopes, the "red" field is of very low intensity and they require only a small amount of yellow to accomplish a match, whereas to the deuteranopes the "red" field appears as bright as to a normal observer and thus deuteranopes require much more yellow for matching the red.

To confirm dichromasy and to distinguish it from anomalous trichromasy† the investigator then sets the yellow half in succession at different brightnesses and asks the subject to match them with red–green mixtures.

* Most subjects will not express any doubt, whether to match for colour or for brightness. But occasionally more specific instruction is demanded.

† The differences between protanopia and protanomaly and between deuteranopia and deuteranomaly are discussed on p. 16.

Dichromats may match every brightness setting of the yellow with a different mixture of red and green, but anomalous trichromats will neither produce nor accept matches to very light or very dark yellow, but only a much narrower range of matches at intermediate values of yellow. Within these limits they will produce repeatable red–green mixtures somewhat varying with brightness. Protanomalous people will produce mixtures within a range decidedly too red for the normal person while deuteranomalous people produce matches which are too green. To assess the defect of a colour-blind person it is necessary to consider both the mid-point and the range of his matches (Willis and Farnsworth, 1952).

Anomaloscope readings provide respectable measurements by which to assess the degree of both anomalies; but these are not unequivocal. As a rule anomalous trichromats making more severely erroneous matches also perform more poorly on chart tests than those with a more nearly normal performance; but as this is not always so, anomaloscope readings cannot by themselves uniquely grade the degree of trichromasy. On the other hand anomaloscope readings remain constant characteristics of an individual and are also very similar in the affected members of a family (for females, however, see p. 50) when they are caused by the same gene.

Before describing some typical makes of anomaloscopes a few general remarks concerning their use are necessary. Tests may be performed in the dark or in moderate illumination, but not in the sunshine or in competition with glaring lights. The surrounds of the matching field and eye pieces, if they are used, should be black or neutral grey and the size and distance of the viewed area standardized. The visual angle of the matching area in the instruments with a fixed viewing distance varies a great deal—between 2°15, in the "Hecht–Schlaer" and 9° in the "Double Dichroid Polaroid" (Willis and Farnsworth, 1952). On an instrument having a circular matching area of 18 mm diameter, which can be viewed from different distances, Horner and Purslow (1948) showed that the relative amount of red and green light needed by several observers to match the yellow changed considerably from a distance of 50 cm (corresponding to about 2 degrees) to 4 metres (corresponding to about 15 minutes): while viewing at 50 cm most observers have very similar matches, but when viewing from greater distances they differ in the amount of the green component which they have to add to their original match. The addition of green light could, however, be greatly reduced by

inserting a 3 mm artificial pupil in front of the eye, when the red–green ratio appears to depend on field size (angle) only and not on distance. The difference between these matches may be due to the Stiles–Crawford effect (1933). The practical conclusion from these observations should be that the matching field of an anomaloscope, which can be freely viewed, should not be more than 50 cm from the eye (corrected for refraction) and should not be smaller than 2 or 3°, corresponding to field diameters of 17·5 or 26·2 mm at 50 cm viewing distance. Very large matching areas (angles) are also unsuitable, as shown by Jaeger and Kroker (1952). They showed in experiments using colour tops, that some dichromats—but not all—find their own small area (1°15) matches quite unacceptable over large areas (22°); using large areas a majority of protanopes would be classified as protanomalous and a minority of deuteranopes as deuteranomalous (see the discussion on p. 16).

Nagel's Anomaloscope

This, the most widely used instrument, is a combination of a spectroscope and a comparison polarimeter and was first described in 1898–9. It has subsequently been improved and a model 2 is being built by Schmidt and Haensch. The observer looking through an eyepiece sees a circular field, half of which is illuminated by yellow light from a narrow spectrum produced by a prism and the other half by an adjustable mixture of narrow spectral regions in the red and the green. Description of the instrument can be found in papers by Nagel (1907), Rosmanit (1914), Verrey (1926) and Wright (1947). Other spectral anomaloscopes are Rayleigh's original apparatus (1871, 1881, 1890), the instrument by Houston (1922) and the large instrument of Wright (1947).

Filter Anomaloscopes

In these instruments light from narrow-range colour filters is used instead of light from a prism. The red and green filters may be arranged in many ways; for example, as sectors of a circular disc which can be turned relative to a diaphragm, to transmit red and green light in controlled and reproducible proportions. Slit devices, optical wedges or neutral polarizing filters (Hecht, Shlaer and Peskin, 1943–49) are also used for intensity control. The mixing may be effected by dioptric means or by diffuse reflection inside a white sphere. The intensity of

the light from the yellow filter may be similarly controlled or regulated by means of a diaphragm or a wedge. Filter instruments are as a rule cheaper and simpler in construction and use, but less efficient in separating normal from anomalous people. A considerable number of investigators have built their own versions and a few of these have been described (Crawford, 1951; Hecht and Shlaer, see Walls and Mathews, 1952; Horner and Purslow, 1947–48; Schmidt, 1936; Pickford and Lakowski, 1961; Pitt, 1944; Jobesee, Bausch and Lomb in Willis and Farnsworth, 1952).

Dichroic Filter Anomaloscopes

These employ filters produced by the Polaroid Company containing microscopic crystals which selectively transmit light of different wavelength, for example red and green, dependent upon the direction of the plane of polarization of the differently coloured light. This removes the necessity for two separate light sources for the red and green light, so that altogether only two light filters are required instead of three and the optical parts are almost reduced to one prism. The red and green mixture is simply controlled by rotating a neutral polaroid filter. Filter instruments are commercially produced in several countries and most of them are reasonably useful for diagnosis. But no single model has as yet been widely used.

A comparison of the performance of several anomaloscopes has been attempted by Willis and Farnsworth (1952). It would be very desirable for reasons of comparison if geneticists and anthropologists could internationally agree on the choice of one anomaloscope and on the procedure to be followed when using it. Until then definitions of the various classes of colour-vision defects in terms of mid-matching points and matching ranges as read on any particular instrument are not comparable and therefore no details are given here. An attempt at comparing different anomaloscopes has, however, been made by Willis and Farnsworth (1952).

Rotating Discs

Additive colour mixture can also be produced by means of rotating discs, a development from Maxwell's (1855) colour top. The procedure is based on the fact that two light stimuli alternating above a certain frequency will not be separately perceived but will merge, as if superimposed. Rotating discs made up from reflecting coloured surfaces

are nowadays little used in the production of additive colour mixtures for matching purposes, but rotating filter discs continue to be of value for this and for measuring the critical flicker-frequency of light stimuli differing in spectral composition.

FARNSWORTH–MUNSELL 100 HUE TEST FOR COLOUR DISCRIMINATION

(Munsell Color Cie, Baltimore, Maryland)

The test material consists of a case, manual and plotting charts (Farnsworth, 1943, 1947).

In its revised form the test series consists of 85 colour caps made from Munsell papers and covering at roughly equal steps a closed circle of unsaturated colours. The caps are contained in four separate racks (boxes) in each of which two end caps are permanently fixed, while the others are loose and can be randomized by the experimenter. The subject is asked to rearrange these loose caps "in their natural order". Each box is opened separately and put on the table in front of the subject under suitable illumination (see pp. 36 ff.). Care must be taken to allow any person the same time for each of the racks to be put in order, but different people may—according to age or skill—require different times, usually between one and two minutes for every box. The box is then closed, turned round and opened again so that the numbers on the inside of the caps become visible and can be recorded.

Subjects of high colour aptitude will arrange all caps in their correct order or perhaps make one or two mistakes, while inferior aptitude will lead to more mistakes. However, these are only symptomatic for specific defects of colour vision when they occur in characteristic parts of the colour circle. For diagnosis the mistakes are recorded in a simple cumulative way on a circular diagram (Figs. 15 and 16). Against every cap number the sum of the differences—irrespective of sign—between this number and that of the number put on either side is entered and marked on the diagram. If, for instance, the reading goes " . . . 23, 26, 22, 24 . . .", $3 + 4 = 7$ is entered against 26. The smallest possible entry in a region without mistakes is, of course, 2. Figure 15 shows each of the three forms of dichromasy as characterized by failure in two opposite regions of the diagram; these are different for protanopes, deuteranopes and tritanopes and are usually sufficient for diagnoses. The three types of anomalous trichromats collectively make similarly

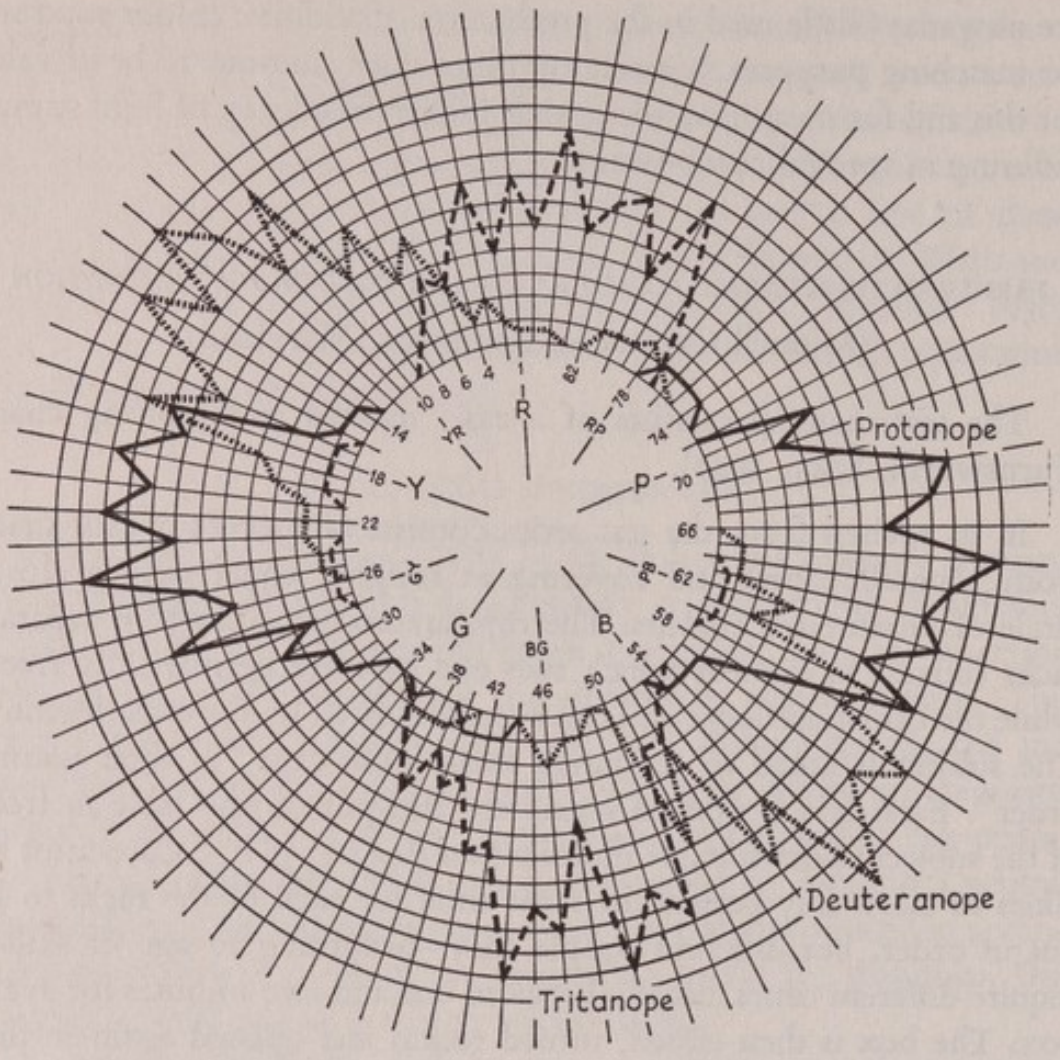

FIG. 15. Average scores from two trials on the Farnsworth–Munsell 100 hue test of a protanope, a deuteranope and a tritanope.

located mistakes as the respective dichromats but fewer of them, consequently their individual classification into protanomalous, deuteranomalous and tritanomalous trichromats is rarely possible (Fig. 16).

The 100 hue test is rather time-consuming and therefore not suitable for the screening of great numbers, but it is useful when applied to people who have been found colour blind by other screening tests, particularly when an anomaloscope is not available or cannot be used and when the reading of those colour charts which ordinarily differentiate between protan and deutan defects is not informative.

FARNSWORTH DICHOTOMOUS TEST FOR COLOUR BLINDNESS (Farnsworth, 1947)

As this is derived from the 100 hue test it is mentioned here,

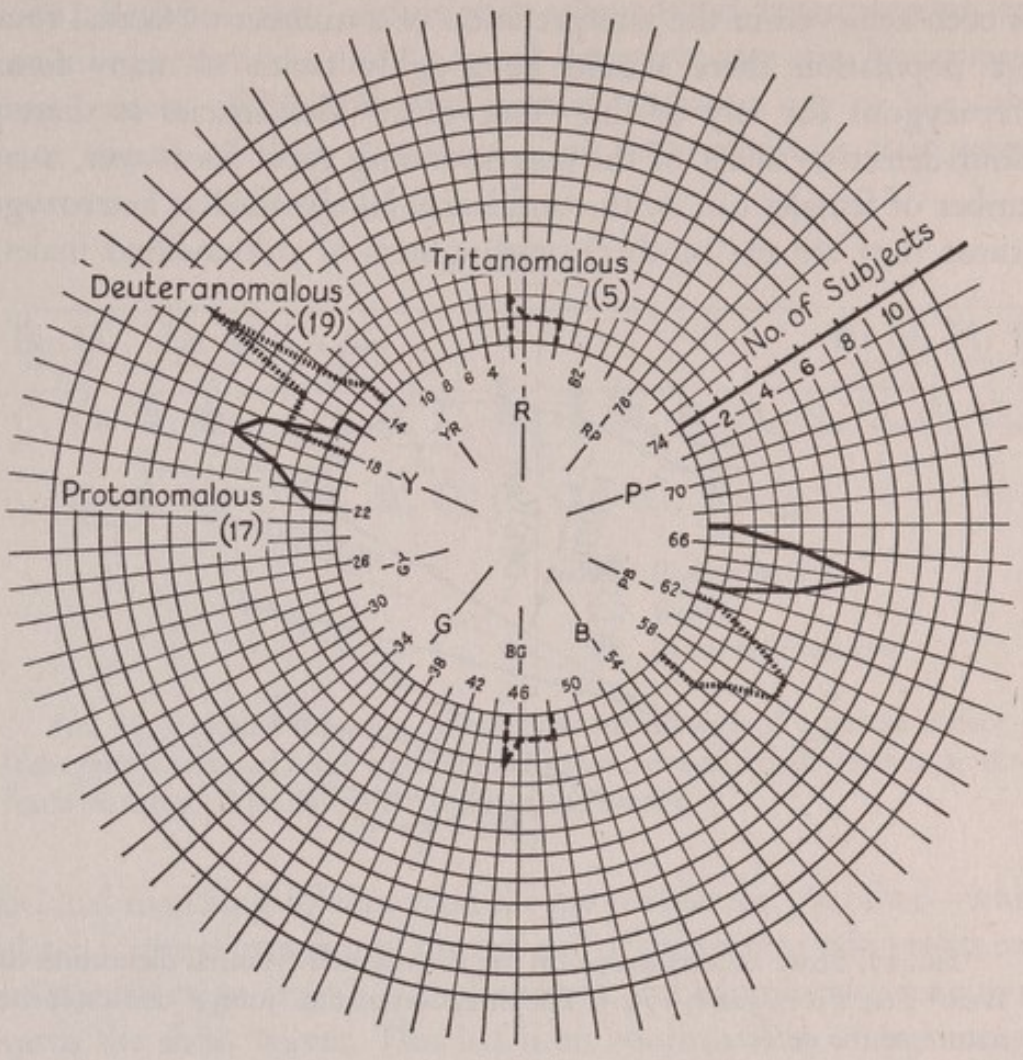

FIG. 16. Distribution on the Farnsworth–Munsell diagram of the axes of maximum error among 41 anomalous trichromats, whose deficiency was sufficiently pronounced for identification. Combined data of Farnsworth and the author.

though it is only a useful screening device and not a reliable diagnostic test. It can be administered and scored in less than 5 minutes. Fifteen caps which are much more widely "spaced" than in the full test are arranged in one rack. A preliminary diagnosis of colour defects is possible by inspection of the scoring sheets (Fig. 17).

A comparison of the efficiency of this screening test with lantern, anomaloscope and chart tests has been published by Farnsworth, Sperling and Kimble (1949).

DETECTION OF SIMPLE HETEROZYGOTES

The heterozygous manifestation of sex-linked colour vision deficiency has been the subject of many investigations, but no unanimity

has been achieved in the interpretation of a number of factual results. In a population there should be roughly twice as many females heterozygous for any of the "four great" deficiencies as there are colour-defective males of the corresponding type. Moreover, a large number of females can, with confidence, be classified as heterozygous because they are the mothers or daughters of colour-blind males or

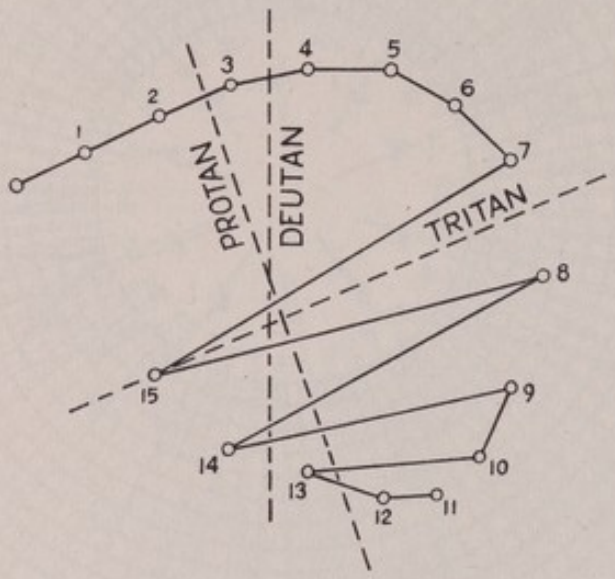

FIG. 17. Score of a tritanope on the Farnsworth–Munsell dichotomous B-20[9] Test (from Judd, 1950). The direction of the "jumps" indicates the nature of the defect.

females, the sisters of colour-blind women or are genetically recognizable in other ways. Nevertheless the purely phenotypical diagnosis of a defect in many of these girls and women is somewhat dubious. On the one hand many heterozygotes appear individually normal, while of those not carrying an abnormal colour vision gene some show similar slight deficiencies. Collectively, however, differences between groups of such heterozygotes and "normal" controls could sometimes be established. The latest papers dealing extensively with this problem are by Walls (1952) and by Pickford (1959), and there is no doubt that occasionally heterozygotes suffer from fully manifest colour blindness. A well-documented example is the daughter in the pedigree of Vanderdonck and Verriest (1960) illustrated on p. 65. An old example is a pedigree by Reber (1895) containing six colour-blind women in two generations. In common with other students of defective colour vision the author has also seen such females. The pedigree of a family containing several such individuals is shown in

Fig. 18. Between such exceptional colour-blind heterozygotes and the to all appearances colour-normal heterozygotes, can be arranged a great variety of heterozygous women showing one or the other sign or stigma of their condition. One such symptom is a greater

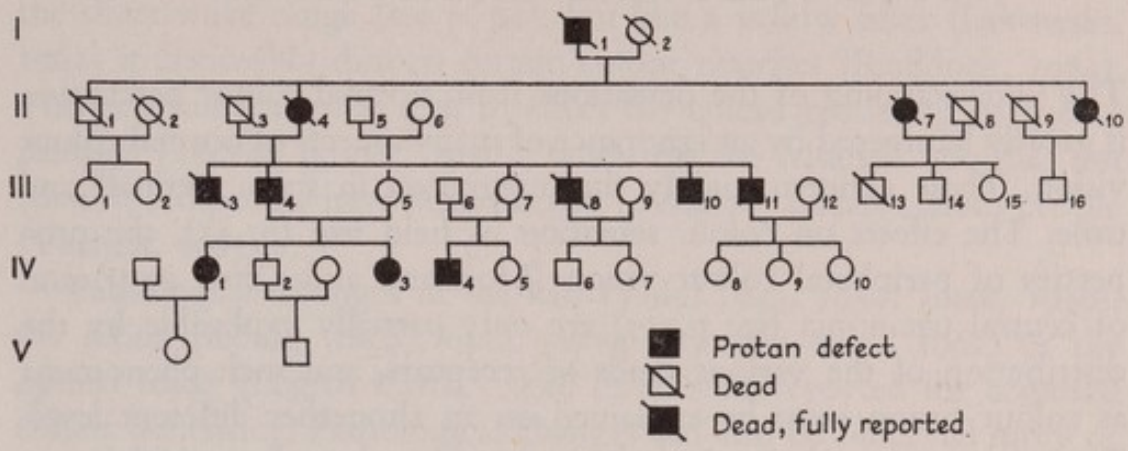

FIG. 18. Pedigree showing an irregular inheritance of a protan defect. If the trait is assumed to be sex-linked recessive, several female heterozygotes must be assumed to have married into the family.

individual matching tolerance on the anomaloscope. Another—which is related to the shortening of the red end of the spectrum in protanopes—is Schmidt's sign (1934), a displacement of the luminosity maximum towards the short waves. This has been confirmed by many investigators.

However, Schmidt (1955) herself, who later investigated 35 such defectives, was unable to discover in them any other anomaly. Nothing of the sort occurs in the heterozygotes in the deutan series.

A difficulty in the discovery of "carrier" heterozygotes for any type of sex-linked colour deficiency is the frequent occurrence of mimicking minor deviations in genotypically "normal" people.

CHAPTER VIII

HYPOTHETICAL PATHOLOGY*

THE understanding of the deviations from normal colour perception is greatly hampered by an ignorance of many aspects of normal colour vision. These concern mainly the integration in space (retinal) and time. The effects on colour sensation of field size (p. 45), the properties of peripheral colour vision (Moreland and Cruz, 1959) and of central tritanopia (see p. 55) are only partially explicable by the distribution of the various kinds of receptors, and such phenomena as colour fusion must be explained on an altogether different level. This phenomenon is particularly impressive when the retinal image is stabilized (Ditchburn, 1961). In such conditions colour sensation, together with many other features of normal vision, tends periodically to disappear, leading one to conclude that much of the normal colour perception is activated by the scanning of the borders between colours through slight involuntary eye movements. Another idea suggested by these observations and supported by electrophysiological observation is that colour sensations are transmitted by signals, the time characteristics varying according to the hues of the light used as stimulus. These as yet badly understood integrative powers of the retina are also a great hindrance in the interpretation of any effects which retinal mosaicism (see p. 83) might be expected to produce.

As yet, however, these physiological complexities are little understood and the grosser defects of colour vision can only be interpreted by the older and obviously inadequate ideas concerning the mechanisms of colour perception. Other contrast phenomena are probably partially responsible for the colour appearance of objects in their natural settings (see p. 11) which follows quite different rules from those observed when using colour matching instruments (Land, 1959).

Defective colour vision may be caused on the one hand by a breakdown of existing structures through age, trauma, toxic or bacterial agents and genetical conditions of late onset (see p. 15). Or on the other hand by non-development or malformation of such visual structures again through environmental or genetical causes.

* Compare also with p. 14.

Age hardly affects the retinal components of colour perception—as evidenced by the aphakic eye—but is accompanied by the deposition of yellow-brownish pigment in the lens (Judd, 1952; Wright, 1952; Said and Weale, 1959). This process which progresses rapidly in middle age does not greatly impair colour discrimination—except in the short wave range (see p. 95), but like a yellow filter (Lakowski, 1962) it noticeably distorts certain colour matches (Ruddock, 1964). This can sometimes be seen to affect the colour rendering of ageing painters (Trevor Roper, 1956). Based on the Munsell 100 hue test (p. 47), old people have been likened to slightly tritanomalous people (Verriest, 1963).

Pathological changes in the lens (Judd, 1943, 1950; Ishak, 1940), the retina (König, 1894), optic nerve (Francois *et al.*, 1961) or the optical tracts (Legros Clark, 1900) have been reported for acquired colour deficiency. Pathological changes can also be observed more or less regularly in those hereditary diseases in which the defective colour vision is only a minor or initial symptom as happens in certain forms of optic atrophy, ocular albinism, retinitis pigmentosa and others (see p. 15).

Little is known concerning the abnormal developmental processes, which result in any of the stable hereditary forms of defective colour vision.

Absence of one of the cone pigments in the protanopic retina, as described by Rushton (1955, see p. 29), is so far the only fully objective feature correlated to any of the hereditary defects of colour vision. In deutans no such difference has been found and in tritans so far no attempt has been made to show it. Nobody has yet succeeded in demonstrating any peculiarity in histological sections of a colour-defective eye though a few attempts have been made. Therefore most of the following brief deliberations are hypothetical and provisional; nevertheless they are necessary for any attempt at understanding defective colour vision. The scheme of branched pathways, which is based on Walls (1955), is a graphic representation of such a hypothesis and not an anatomical model (Fig. 19).

Abnormal colour sensations can in principle arise from the malfunctioning of one or several structures, for instance a discoloration of the lens, lack or maldistribution of one or several cone pigments or of pigmented cones and rods, faulty neural connections in the retina or the primary and secondary visual centres. Any of these faults may result in an individual's loss of brightness or of "colour" dis-

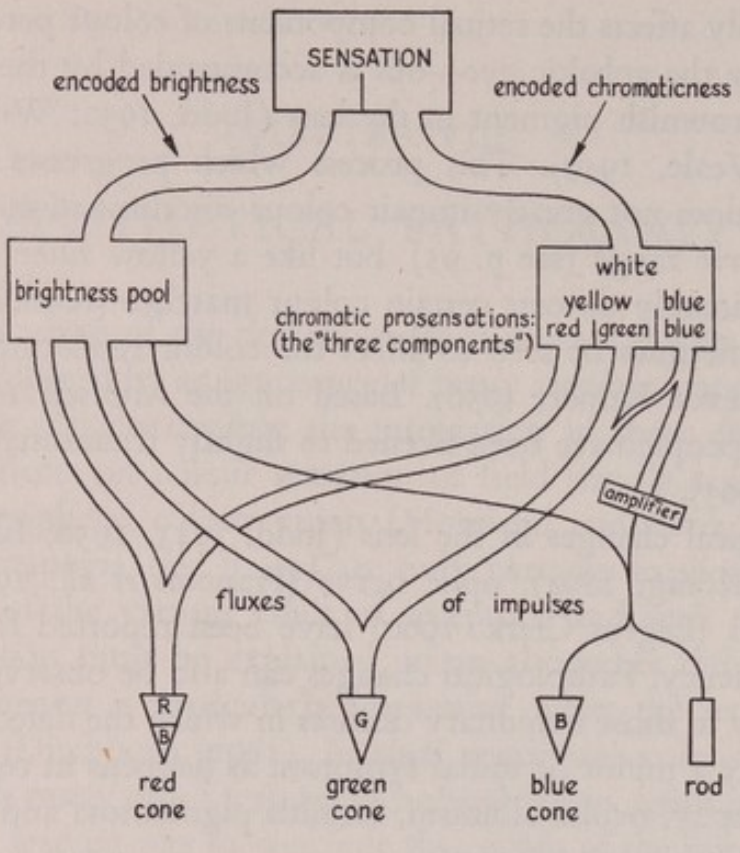

FIG. 19. Hypothetical pathways for colour and brightness perception in the normal light adapted eye (after Walls, 1955).

In *protanopes*, who do not experience redness, the *red cones*—containing red absorbing pigment and some blue absorbing pigment—may be *missing* and contribute neither to the brightness pool nor to the chromatic system.

In *deuteranopes*, who perceive only yellow and blue, *red* and *green* cones are probably *identical* both containing red absorbing pigment and probably no green absorbing pigment. Contribution to the brightness pool is nearly normal.

In *tritanopes* the *blue* cones are *missing* (hereditary) or out of action (acquired).

The defects of anomalous trichromats, monochromats and "atypically" colour-blind people can also be expressed by deletions in the diagram.

crimination—usually in both. While several of the possibilities mentioned above and derivable from Fig. 19 probably exist, we are in most specific cases reduced to guessing. It must also be borne in mind that, as a consequence of the complexity of the visual system, a defect of one kind of structure or at a particular level is very likely to produce collateral secondary deficiencies of structure and of function.

TRITAN DEFECTS

Though probably rare and the latest to be extensively explored (König, 1897; Engelking, 1925; Jaeger, 1951; Judd *et al.*, 1950; Wright, 1946; and Kalmus, 1955) these defects are the easiest to explain in terms of objective changes. As shown by König (1894), Willmer (1944) and Willmer and Wright (1945), the foveal vision of normal eyes is tritanopic. This can easily be demonstrated by viewing appropriate confusion charts (p. 39) or the matching field in a colorimeter from far away so that the relevant areas subtend an angle between 30 minutes and one degree, roughly corresponding to the retinal area occupied by the fovea centralis. Foveal tritanopia may be mimicked by heavy macular pigmentation (Judd, 1950; Ishak, 1940), but is usually explained by the lack of the "blue cones". Rods* also are not found in the fovea centralis of most people (Stiles, 1946). Figure 19 indicates the possible sites for inherited and acquired tritan defects.

Extrapolating from this situation we can derive a good model for the tritanopic and tritanomalous eye by assuming that the retinal area free from blue cones in such eyes is considerably larger than in normal eyes, where it coincides with the fovea centralis. Whether this is in fact so is still an open question.

In certain pedigrees of night blindness, defective blue vision has been described in the affected individuals (p. 20). This indicates a possible connection of the rods with blue perception (Willmer, 1955) as indicated in Fig. 19. However, typical tritans are not night blind and absence of blue cones best explains their colour vision. It is uncertain whether the blue cones are just missing or replaced by the other two types of cones. No statement can be made of whether autosomal tritanopia and sex-linked tritanomaly have similar developmental effects.

Certain rare peculiarities of colour vision, which have some resemblances to trito defects, are by some authors—mostly exponents of a "four-colour theory" (p. 4)—described as *tetratanopia*. A man described by Walls (1955) could not see any "blueness" in blue objects but described them as intensely white, in fact whiter than white objects presented simultaneously. Obviously this cannot be explained by any peculiarity of receptors but must be ascribed to a peculiarity in pathways.

* The shape of both the rods and the cones in different regions of the mammalian retina varies a great deal.

PROTAN DEFECTS

Protanopia can be explained by a similar total, or near total, lack of the "red" cones in the central areas of the retina, a point of view supported by the objective findings of Rushton (1955) mentioned on p. 29. Absence of red cones can explain not only the absence of a red sensation in protanopes but also their loss of brightness, which is particularly marked at long wavelengths. The only colour sensations experienced by protanopes are thus yellow and blue—separated on the colour chart or on a continuous spectrum by a grey region.

Protanomaly could on the same lines be explained by a partial loss, from the central retinal areas, of the red cones. But it must be stressed again that we do not have enough knowledge to exclude quite different alternative hypotheses.

DEUTAN DEFECTS

Neither deuteranopia nor deuteranomaly can be explained by a total or partial loss of a class of cones. Rather, one might assume that they possess a common class of cones, possibly carrying only one kind of pigment, instead of the separate classes of red and green cones characteristic of normal retinae; or that red cones and green cones though separate are faultily connected to the bipolar cells of the retina. Both assumptions would explain why for the deuteranopes red and green stimulation always occurs in a fixed ratio (perhaps even in a 1: 1 ratio). Also why they have no loss of brightness when compared with colour-normal people and why, like the protanopes, they cannot generally distinguish between red and green and the only hues which they perceive are yellow and blue (Fig. 6).

The common lack of red–green discrimination was responsible for the former description of the protan and deutan defects as red–green blindness. But though we cannot be sure what the differences are, it is now fairly clear that the protan series and the deutan series of alleles produce primary defects at different levels of retinal organization and altogether of a different kind.

It now remains to consider the sites of anatomical anomalies that might conceivably account for the sensations of the heterozygotes (women) and of the totally colour blind. These defects can be expected to be slight in the heterozygotes, when compared with those of affected hemizygotes, but rather severe in the monochromats. Many women, heterozygous for protanopia, show Schmidt's (1934) sign (Walls and

Mathews, 1952), a dimming of yellow, orange and particularly red (spectral) light (see p. 51). This is taken to indicate that the brightness branch of the "red" cone path is impaired, rather than that anything might be wrong concerning the number or quality of the "red" cones. The observational fact that the colour vision of women showing Schmidt's sign differs in some respects from protanomalous individuals supports this assumption. In developmental terms, this implies that the differentiation of some retinal pathways and the differentiation of the receptors are interdependent processes. At present we do not, however, know what the implied interactions are.

Bearing in mind how variable the effects of single colour blindness genes are in simple heterozygotes, one may be critical of *ad hoc* explanations of mosaicism (difference between left and right eye, p. 12) and of colour perception differences between female identical twins. Somatic mutation and possibly Lyon's (1962) hypothesis (p. 83) may also account for some such situations.

Female compound heterozygotes for a protan and a deutan gene (usually discovered in repulsion) have as a rule fairly normal colour vision; and this is the main reason for accepting the 2-loci hypothesis (see p. 63). But one such woman (Hylkema, 1943) was totally colour blind (Walls, 1955) of the rare cone type, having perfect visual acuity and no photophobia as the rod monochromats have. The most plausible interpretation of the colour vision of this woman would be that her pathways for both red and green sensation—but not for those for her brightness sensation—are non-functional. Thus it is not profitable to propose any general anatomical hypotheses to explain the subjective phenomena of compound heterozygotes by assuming the existence of one compound lesion or by two developmentally independent lesions. *Ad hoc* explanations on those lines are also available for individuals combining protan and deutan defects of varying degrees. Whether a similar explanation applies to certain cone monochromats cannot at present be decided (see Fig. 11). There is, however, little doubt that not many cone monochromats are compounds combining a protan with a deutan gene in their X-chromosomes, but that other aetiologies usually apply. In cases where cone monochromatism is genetical in origin, combinations of one of the sex-linked defects, either protan or deutan, with autosomal tritanopia seem most probable. However, there may exist special genes for monochromatism. As cone monochromats are exceedingly rare it is not surprising that nothing concrete is known concerning the anatomical or histochemical basis of this deficiency.

CHAPTER IX

GENETICS I—THE INDIVIDUAL GENES

RECENT advances in general human genetics, in sense physiology and in the history of the subject, have resolved some of the puzzles which have obscured the traditional and simple genetics of colour blindness. But they have also posed new problems and have, by their rapid progress, made an up-to-date exposition more difficult.

The solution of some of these problems depends on the recognition of the interactions between different colour vision genes and of the resulting compound types of colour blindness.

(a) *Autosomal Tritanopia*

The characteristics of tritanopia have been described on p. 55. Genetically it has been shown to be an autosomal dominant, showing incomplete manifestation (Kalmus, 1955) (Fig. 20). Though not quite

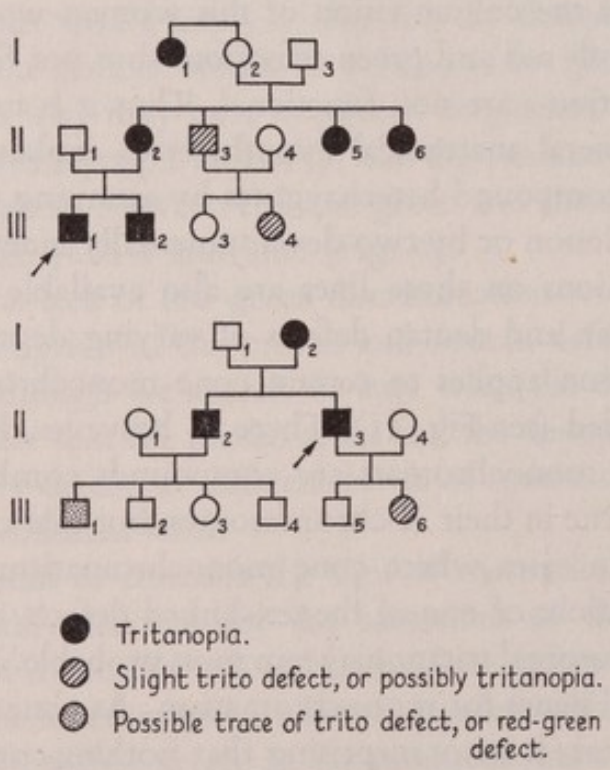

FIG. 20. Two tritanopia pedigrees (from Kalmus, 1955).

as rare as formerly supposed it still is not frequent. The minimum frequency in Great Britain has been estimated as between 1 in 13,000 and 1 in 65,000, but its real frequency is probably somewhat higher. The phenotypical results of the interactions, both in males and females, of the tritanopia gene with several of the sex-linked colour deficiency genes are discussed on p. 23. Possibly some such combination can produce cone monochromatism.

THE SEX-LINKED GENES

(b) *Sex-linked Tritanomaly*

This has been described on p. 21. There is little doubt that this lesser deficiency of the "blue sense" may be caused by a sex-linked gene (Engelking, 1925; Oloff, 1935; Meitner, 1941; Jaeger, 1955). It is certainly less frequent than the common forms of sex-linked colour blindness of the protan and deutan series, but how frequent is not known. This ignorance is mainly due to the scarcity of diagnostic tools for the detection of trito defects, which in turn is a consequence of their lesser practical importance in signalling and in traffic when compared with the red–green deficiencies. The possible properties of some compounds for tritanomaly and other colour vision genes are discussed on p. 23; other genetical complications may exist.

Sex-linked Colour Deficiencies of Higher Frequency

As Maupertuis has pointed out in 1752 (Glass, 1947), the probability of two rare and similar hereditary disabilities in two or more members of a family, being caused by two or more "different" mutant genes of separate origin, is small; and one usually assumes that such variations of manifestation between relatives are caused either by the environment or by other accessory, secondary genetical differences, such as sex modifying genes or the "genetical background". The inferred morbid genes are assumed to be the same in all affected members of such a family and the type of the affection with its limits of variation is sometimes said to be genetically "pure". In the study of rare metabolic diseases this approach has been of great value, but it has its limitations.

Historically defective colour vision was approached as a unitary genetical problem and as indeed the majority of pedigrees are "pure" in the sense described, and as all the more frequent deficiencies happen

to be sex linked and usually recessive, the basic mode of inheritance of all of them was not difficult to discover. In retrospect, one can now deduce from the first description of colour blindness (Huddart, 1777, see also p. 2) that the condition is recessive sex-linked protanopia, while the second family described by Sçott (1778) (Fig. 21) is also recessive sex linked and shows pseudo-paternal inheritance,*

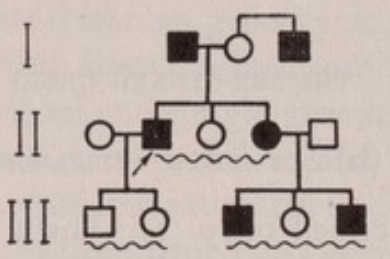

FIG. 21. Scott pedigree. The Scott pedigree also called the Whisson and Lort pedigree, the oldest pedigree of protanopes (1718), showing pseudo-paternal inheritance in a woman of the second generation.

the defect—presumably protanomaly—being introduced through the father and the mother. But at the time no such conclusions were, of course, drawn. The first to recognize the mode of inheritance was Horner (1876), who stated that the rule of transmission established for haemophilia (Otto, 1803; Nasse, 1820) also applies to colour blindness; Horner's law was mainly based on a family containing 14 colour-blind males—but no females—in four generations and is a purely formal statement to the effect that colour blindness only shows in males, is inherited through an unaffected mother but not through an affected father, though as we have just described pseudo-paternal inheritance occasionally occurs (Fig. 22).

In Horner's lifetime a proper genetical interpretation of his empirical rules was impossible and Horner's law remained an isolated oddity. But in 1911 Wilson drew attention to the fact that the transmission of defective colour vision in man fully accorded with the transmission of several sex-linked (X-borne) recessive characters in the fruit fly *Drosophila melanogaster*, as described by Morgan (1910); and soon afterwards it became clear that the colour vision genes must be localized on an X-chromosome, and incidentally that man and *Drosophila melanogaster* have a similar mechanism of sex determination based on X-bearing and Y-bearing spermatozoa.

* Pseudo-paternal is a term better suited to a sex-linked recessive gene than pseudo-dominant, which should be confined to autosomal recessives.

In respect of any single type of sex-linked colour defect six matings are possible, which together with the possible types of offspring are listed below (Table 6).

TABLE 6. COLOUR VISION OF THE CHILDREN FROM THE SIX PARENTAL UNIONS POSSIBLE IN RESPECT OF A PARTICULAR NEAR-RECESSIVE SEX-LINKED COLOUR DEFICIENCY

		mother		
		cv^+cv^+, normal	cv^+cv, carrier, usually normal	cv cv, colour deficient
father	cv^+, normal	cv^+ sons, normal	$\frac{1}{2}cv^+$ sons, normal. $\frac{1}{2}$cv sons, colour deficient	cv sons, colour deficient
		cv^+cv^+ daughters, normal	$\frac{1}{2}cv^+$ daughters, normal. $\frac{1}{2}$cv cv daughters, carriers, usually normal	cv^+cv daughters, carriers, mostly normal
	cv, colour deficient	cv^+ sons, normal	$\frac{1}{2}cv^+$ sons, normal. $\frac{1}{2}$cv sons, colour deficient	cv sons, colour deficient
		$cvcv^+$ daughters, carriers, usually normal	$\frac{1}{2}cv^+cv$ daughters, carriers usually normal. $\frac{1}{2}$cv cv daughters, colours deficient	cvcv daughters, colour deficient

In this table the frequency of unions decreases from left to right and from top to bottom.

MIXED PEDIGREES

With the comparatively frequent hereditary defects in colour perception, it is not always safe to assume that only one kind of morbid gene occurs in a family and that for instance "colour-blind" brothers must always carry the same gene. In a European population about one of 17 of the colour-blind brothers of a man with a protan

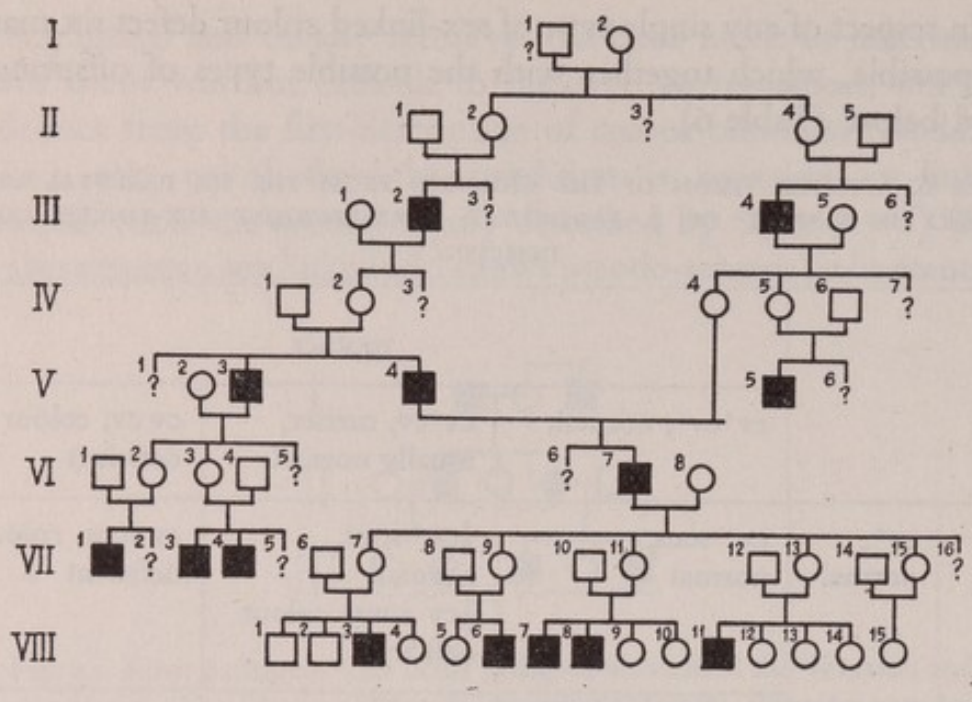

FIG. 22. Horner's (1876) original pedigree of deuteranopes (from Bell, 1926).

defect will be of the deutan type; and one out of about 50 colour-blind brothers of deutan males will be protans. Families containing members showing different defects of colour perception are in fact the most interesting ones. Pseudo-paternal inheritance of colour blindness occurs with a frequency of about one in 12 in European populations. In this situation a son's colour-blindness gene is not derived from his father's colour-blindness gene, though in the case of the father and mother being consanguineous the paternal and filial genes may be descended from a common ancestral mutant. In this latter case, or if by chance the paternal and maternal abnormal genes are of the same kind, paternal inheritance may be wrongly inferred (see Fig. 21). If, on the other hand, two or more different genes causing defective colour vision occur in a family, father and son may be of a different type. Most males in such families belong to two or more phenotypically clearly distinct groups, while others, together with the females, may be fairly atypical. This latter finding is indicative of a compound genetical constitution (p. 23).

Females homozygous for the same gene within a family are probably rather similar to each other, but pedigrees containing several such women are rare. The defects of such homozygotes closely resemble those of their sons. The deficiencies in colour vision of female heterozygotes may vary a great deal within one and the same family,

but they tend to be rather more similar. The properties of compound heterozygotes and of the still hypothetical compound homozygotes and hemizygotes are discussed on pp. 25 and 61.

ALLELISM

Families containing several types of colour defectives provide an opportunity of considering the problems of the allelism of the various colour vision genes.

No allelism is, of course, possible between autosomal and sex-linked genes. Whether autosomal tritanopia is always caused by mutation in the same locus, or even the same chromosome, cannot at present be decided, nor do we know if there exist minor trito defects caused by alleles of autosomal tritanopia.

Not much more is known about the localization of the rare sex-linked tritanomaly (see p. 21) and whether it might not be allelic with the protan or the deutan defects. Concerning the allelism of these more common deficiencies, complete unanimity has as yet not been reached.

ONE-LOCUS OR TWO-LOCI

Whether the several genes responsible for the protan and deutan defects represent one common series of alleles on the X-chromosome or two separate series has been debated for a long time. At present the 2-loci hypothesis seems better supported, and in fact an attempt has been made (Kalmus, 1962) to estimate the distance (recombination fraction) between the protan locus and the deutan locus.

It is rather difficult to decide what should be considered evidence for the joint localization of the protan and the deutan alleles. One might suggest that females carrying a protan gene on one X-chromosome and a deutan gene on the other, should not as a rule have a normal colour vision—but many have (see p. 23). A 1-locus hypothesis would require the absence of any crossover cases between protan and deutan genes, a negative which it is difficult to prove and which furthermore seems now disproved (see p. 65). On the other hand proof for the separate localization on the human X-chromosome of the protanopia–protanomaly alleles and of the deuteranopia–deuteranomally alleles ideally requires the demonstration of (1) non-allelic compound hemizygotes (males) which in conditions of equi-

librium in a European population should occur about once among about 800 men (once in 67 colour-blind men), and of (2) normal crossover males descended from women combining both classes of defect.

An assessment of the existence and frequency of the various compound hemizygotes (p. 27) depends on the kind of colour vision ascribed to them, mainly on whether one expects complementation or not; some of these double hemizygotes could be *sui generis*, others difficult to distinguish from deutans, protans or even normals. Walls and Mathews (1952) consider two brothers, each combining protanopic and deuteranopic features, as slightly different compounds, though Stern (1958) prefers to consider them as bearers of a new allele at a single locus. Men combining features of "red" and "green" blindness have also been described in the older literature (see Bell, 1926) and more recently by Jaeger (1951); they are indeed familiar to careful investigators. On the other hand, some such compounds may be placed among the pure protans or deutans by insufficient testing, while others may have a sufficiently balanced colour vision to pass an anomaloscope test or may be sufficiently different from the ordinary run of colour-blind people not to fail on pseudo-isochromatic charts. These uncertainties would explain why so few protan–deutan hemizygotes have so far been described.

Until recently no crossover between a protan gene and a deutan gene has been reported. But two or possibly three crossovers between the deuteranopia and the protanomaly genes occur in a pedigree by Vanderdonck and Verriest (1960). The family consists of the offspring from a protanomalous wife (daughter of a deuteranopic man and a normal woman) and a normal husband (son of a normal man and a woman of unknown colour vision). This union produced two deuteranopic, one protanomalous and two normal sons, as well as one protanomalous and one normal daughter (Fig. 23). The colour vision of the members of this family has been expertly investigated and their nuclear sex shown to agree with apparent sex. We may thus consider the two normal sons and possibly the normal daughter as recombinants from the X-chromosomes of their mother, one of which carries a protanomaly gene, probably with heterozygous manifestation, and the other a deuteranopia gene.

Before attempting an estimate of the recombination fraction between the protan and deutan genes one may ask why, in spite of prolonged attempts (Francescetti and Klein, 1956), recombination has

not been previously found. Women heterozygous for protan and deutan genes are rare (about one in 250), and having either near normal or atypical colour vision (Jaeger, 1951; Walls and Mathews, 1952) they can only be discovered through having a protan and a deutan son. At least a third son is needed to show recombination but his chance to do so is less than a half. Fewer than a handful of such families has been previously described (Francois, 1961) and as no recombinants had been found, it was concluded that the two colour vision loci are likely to be closely linked (Renwick, 1961). This conclusion is no longer warranted.

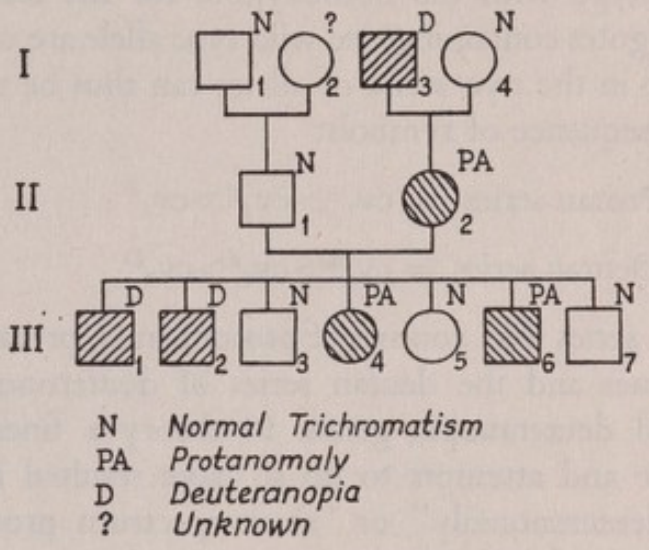

FIG. 23. Pedigree showing free recombination of protan and deutan alleles (from Vanderdonck and Verriest, 1960).

Some idea concerning the distance between protan and deutan genes may be derived from a linkage study including colour blindness and G6PD deficiency. Porter, Schulze and McKusick (1962) recently estimated the recombination fraction between the gene responsible for this deficiency and that for deutan defects as 0·05 (between 0·009 and 0·18 at 90 per cent confidence level) and the 90 per cent probability of recombination between the G6PD gene and a protan gene as less than 0·2; they thought their result insufficient to decide between the 2-loci and 1-locus hypothesis. However, considering Vanderdonck and Verriest's pedigree, it is at present reasonable to assume that the protan locus and the deutan locus are not very close, possibly some 10–20 recombination units apart and that perhaps the locus for

G6PD deficiency lies between them, probably nearer to the deutan locus (Kalmus, 1962). (See also pp. 72 ff.)

DOMINANCE RELATIONS (SEE PP. 17, 19)

While the controversy concerning the number of sex-linked colour vision loci has not been quite firmly settled, there is fair agreement concerning the dominance relations within the protans and deutans. In conformity with other similar situations, such as the white locus in several *Drosophila* species, heterozygotes combining a more severe defect in one X-chromosome with a lesser defect in the other agree in their phenotype with the homozygote for the lesser deficiency, while heterozygotes containing one wild type allele are usually normal.

Dominance in the two series of alleles can thus be represented by the following sequence of symbols:

$$\text{Protan series} = cv_1^{+} > cv_1^{P} > cv_1^{P}$$

$$\text{Deutan series} = cv_2^{+} > cv_2^{d} > cv_2^{D}$$

The protan series then consists of protonormal, protanomalous and protanopia genes and the deutan series of deuteronormal, deuteranomalous and deuteranopia genes. In theory a finer classification could be made and attempts to do so have resulted in such classes as "extreme deuteranomaly" or "short spectrum protanopia". The difficulty lies in the fact that recombinations in human material cannot be experimentally produced and that chance combinations are comparatively rare. A mixed protan pedigree and a mixed deutan pedigree are reproduced in Figs. 24 and 25.

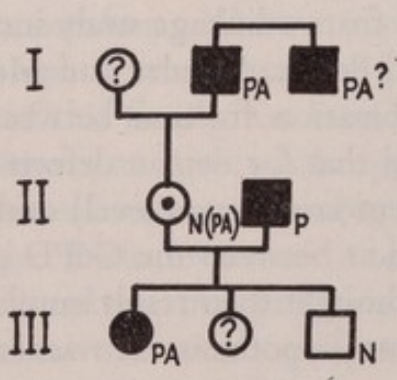

FIG. 24. Pedigree containing several protan defectives. P = protanopia, PA = protanomaly (after Pickford, 1950).

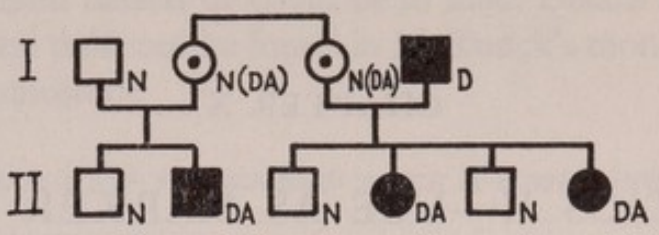

FIG. 25. Pedigree containing several deutan defectives. D = deuteranopia, DA — deuteranomaly (after Francescetti, 1928).

CHAPTER X

GENETICS II—USE AS MARKER GENES

LINKAGE

THE association in some individuals of a population of two mutant characters both determined by one and the same gene (allele) is called *pleiotropism;* one speaks of *linkage* when two characters are determined by two separate genes (alleles) at two chromosomal loci not too far apart on the same chromosome. Two linked mutant characters—or their "wild type" (normal) opposites—may be inherited either together, a situation called "coupling", or separately, "repulsion", while as a rule repulsion ought not to be observed if two characters are determined by the pleiotropic gene. However, when dealing with a "new" combination of characters in a single family or small tribal group it is sometimes difficult to distinguish between very close linkage in the coupling phase and pleiotropic association, and if the manifestation of two pleiotropic characters is incomplete a situation indistinguishable from repulsion may occur. But, if coupling predominates in some families and repulsion in others, or if crossing over is observed between two characters each showing full manifestation, one ought to speak of linkage. The linkage relations between the protan and deutan genes have been discussed on p. 65 in connection with their relative position to the G6PD locus.

Linkage data combining sex-linked defects in colour vision with other sex-linked characters ought to be separated in those concerning protan defects and those concerning deutan defects. Such a procedure will not only contribute to a decision between the 1-locus and 2-loci hypothesis (p. 63) but will also remove some uncertainties from the linkage maps of the human X-chromosome thus giving more consistent and convincing results. Unfortunately this distinction has not been made often in the past and is still not universal. We are thus in the unfortunate position of inferring linkage estimates from the older data that have lost a great deal of their value while only rarely being able to supersede them by better information. Table 7 lists sex-linked characters which either have been used in linkage studies

with colour vision defects or could be so used. Details and references concerning these traits can be found in McKusick's monograph (1962) on the X-chromosome.

TABLE 7. SOME TRAITS AND SYNDROMES IN WHICH X-BORNE GENES ARE INVOLVED*

A. Principally X-borne conditions

1. Partial colour blindness, deutan series
2. Partial colour blindness, protan series
3. Tritanomaly
4. Glucose-6-phosphate dehydrogenase deficiency
5. Xg blood group system
6. Muscular dystrophy, Duchenne type, autosomal recessive mimic
7. Muscular dystrophy, Becker type
8. Haemophilia A
9. Haemophilia B, Christmas disease
10. Agammaglobulinaemia
11. Hurler syndrome (gargoylism), recessive autosomal mimic more severe
12. Late spondylo-epiphyseal dysplasia, similar to the autosomal Brailsford–Morquio syndrome
13. Aldrich syndrome
14. Hypophosphataemia
15. Hypoparathyroidism of early onset, later autosomal form
16. Nephrogenic diabetes insipidus
17. Neurohypophyseal diabetes insipidus, autosomal mimics

B. Conditions to which X-borne genes make a small contribution

18. Oculo-cerebro-renal syndrome of Lowe
19. Hypochromic anaemia (Cooley–Rundles–Falls type) rarely X-borne
20. Angiokeratoma diffusum corporis universale
21. Dyskeratosis congenita
22. Dystrophia bullosa hereditaria, typus maculatus
23. Keratosis follicularis spinulosa cum ophiasi
24. Ichthyosis vulgaris
25. Anhidrotic ectodermal dysplasia
26. Amelogenesis imperfecta, hypomaturation type
27. Amelogenesis imperfecta, hypolastic type
28. Absence of central incisors
29. Congenital deafness
30. Progressive deafness
31. Mental deficiency
32. Börjeson syndrome
33. Spinal ataxia
34. Cerebellar ataxia with extrapyramidal involvement
35. Spastic paraplegia
36. Progressive bulbar paralysis

*After McKusick, 1962, where detailed information is available

37. Charcot–Marie–Tooth peroneal muscular atrophy
38. Diffuse cerebral sclerosis (Pelizaeus–Merzbacher)
39. Diffuse cerebral sclerosis (Scholz)
40. Hydrocephalus
41. Parkinsonism
42. Ocular albinism
43. External ophthalmoplegia and myopia
44. Microphthalmia
45. Microphthalmia, with digital anomalies
46. Nystagmus
47. Megalocornea
48. Hypoplasia of iris with glaucoma
49. Congenital total cataract
50. Congenital cataract with microcornea
51. Stationary night blindness with myopia
52. Choroideremia
53. Retinitis pigmentosa
54. Macular dystrophy
55. Retinoschisis
56. Pseudoglioma
57. Van den Bosch syndrome
58. Menkes syndrome

MAPPING THE X-CHROMOSOME

The protan and deutan genes are potentially useful as indicating the probable presence or absence in an individual of a morbid gene closely linked to one of them; in combination with other sex-linked genes they are now used for constructing a linkage map of the X-chromosome (Steward, 1962; McKusick, 1962; Race and Sanger, 1963). The state of this linkage map is at present rapidly changing as research progresses and thus too much reliance ought not to be put on the detailed results presented below. Of more lasting value might be the description of the general approach.

Estimates of the length of the human X-chromosome vary between 5·8 per cent and 6·8 per cent of the length of the haploid autosomal complement. Ford and Hamerton (1958) found on the average 56 chiasmata per primary spermatocyte metaphase. If chiasmata occur in both males and females with the same frequency, and in autosomes and X-chromosomes, 60 chiasmata should occur during oogenesis corresponding to 3000 centimorgans; the map length of the X-chromosome should be about 150 centimorgans of which about 54 would be on the short arm and 96 on the long.

ISOCHROMOSOMES

The normal human X-chromosome consists of a short and a long arm, which can be easily distinguished. Very occasionally, however, individuals are found who, either in all cells or in some* of them, carry chromosomes which are either composed of two short arms or two long arms. These are called presumptive iso-short-X-chromosomes and presumptive iso-long-X-chromosomes. It is clear that in females a defective cv gene in a normal X-chromosome will be left partnerless by the absence of a cv locus in a long arm iso-X-chromosome, so that the former will show in such more or less female individuals.

Evidence is accumulating that the deutan locus, at least, is localized in the short arm and such a case is illustrated in Fig. 26 and Fig. 27.

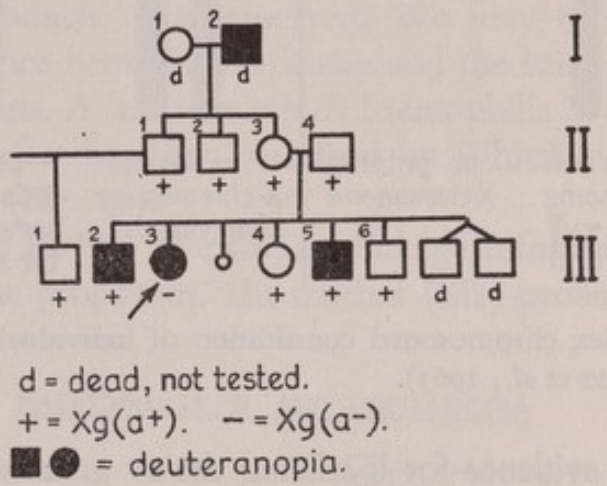

FIG. 26. Pedigree of a woman lacking the short arm of an X-chromosome showing segregation of the Xg(a) traits and of deuteranopia (from Lindsten *et al.*, 1963).

Cell cultures from the proposita in the pedigree shown in Fig. 26, who is mainly of female appearance, were of two kinds; the majority, with a count of 46, showed two sex chromosomes, one X-chromosome of normal appearance and the other apparently consisting of two long arms (Fig. 27, right); the minority showed cells with a count of 45 containing only one normal X-chromosome (Fig. 27, left). As neither of these constitutions provides a paternal short arm which could carry the normal deutan allele, we can understand why this individual, in common with two of her brothers, is manifestly deuteranope. The linkage relation of the deuteranopia and the Xg-loci is discussed

* The mosaicism in the tissue cultures from such individuals are often difficult to interpret and deductions from such findings are sometimes dubious.

below (Lindsten *et al.*, 1963). As the average number of chiasmata in this short arm is very nearly 1, any other gene localized on the short arm ought to show some degree of linkage with the deutan locus.

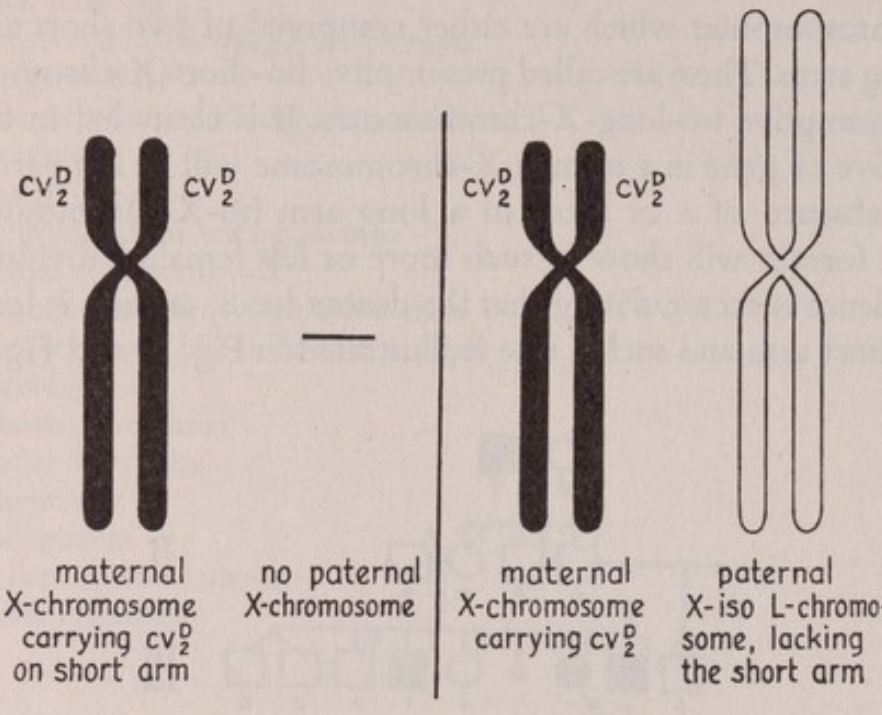

FIG. 27. Sex chromosomal constitution of individual III3 in Fig. 26 (from Lindsten *et al.*, 1963).

Additional evidence for localizing the cv genes on the short arm is as follows. (1) The locus for G6PD deficiency, a gene causing primaquine sensitivity favism and other abnormal reactions and quite frequent in some Mediterranean and African peoples (Tarlov, Brewer, Carson and Alving, 1962), shows close linkage with the protan and deutan loci (McKusick and Renwick, 1961) and is some 25 centimorgans from the Xg-locus, the alleles at which determine a serological character (Adam, Sheba, Race, Sanger, Tippett, Hamper and Gavin, *Lancet*, 1963). (2) From the testing of families of females with part of one of their chromosomes visibly missing (see, for instance, Fig. 26) it has been concluded (Race and Sanger, 1962; Lindsten *et al.*, 1963; Fraccazo and Lindsten, 1963) that Xg is on the short arm. If one provisionally assumes that the Xg-locus is near the end of the short arm rather than near the centromere, both cv loci would be somewhere near the middle of the short arm.

The linkage relations between the G6PD gene and the cv_1 and cv_2 genes have been discussed on p. 65. Which of the cv loci is on

the terminal side and which on the centromere side of G6PD must at present remain open.

Older linkage data concerning the 2 cv loci and haemophilia suffer from the circumstance that protan and deutan loci were then not distinguished and that Christmas disease (haemophilia B) had not been separated from classical haemophilia (haemophilia A). Haldane and Smith (1947) estimated that recombination frequency between "colour blindness" and "haemophilia" as 9.8 per cent. From their paper it seems probable that this estimate is based on 16 deutan families and one small protan pedigree and most likely most of the haemophilia was of the classical A type.

This probably also applies to an extensive Japanese pedigree (Murakami *et al.*, 1951) in which a crossover between "haemophilia" and "colour blindness" was observed. We may thus provisionally redraw the distance between the deutan and the haemophilia A locus as 10 centimorgans. A family in which haemophilia B occurs together with a protan defect has been described by Whitaker, Copeland and Graham (1962) (Fig. 28).

The pedigree in Fig. 28 provides linkage information mainly in the sibship of the propositus. His mother (III2) probably carried the

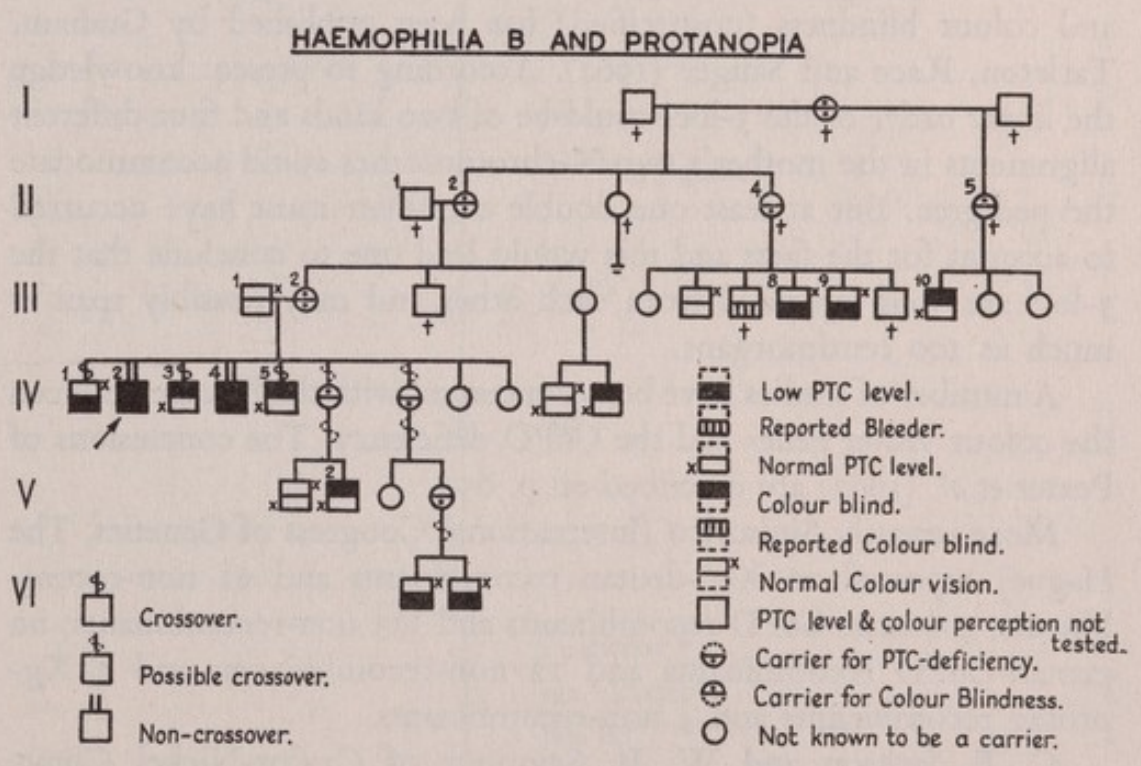

FIG. 28. Segregation of haemophilia B (Christmas disease) and protanopia (from Whitaker *et al.*, 1961).

protan gene and the haemophilia B gene in coupling, in which case three of her five sons would be crossover products (if the mother carried the two mutant genes in repulsion two of her sons would be crossovers). This and the occurrence of at least two crossovers in the female lines indicates very free recombination, probably 50 per cent, i.e. absence of any linkage and a map distance of 50 centimorgans or more, i.e. haemophilia B might be localized in the long arm.

In the same paper Whitaker *et al.* also describe a more extensive pedigree of deuteranopia and haemophilia A, which they found linked having a recombination frequency of 12 per cent (not 6 per cent as erroneously stated).

Yet another sex-linked gene which has been found linked with one of the colour-blindness genes—one of the anomalous trichromasies—is that responsible for the Duchenne type of muscular dystrophy. Philip and Walton (1956) reported a family containing five crossover individuals out of 20, giving a recombination fraction of 25 per cent. The distance of this muscular dystrophy gene from the Xg–locus has been estimated at more than 50 centimorgans (Clark *et al.*, 1962), and we may conclude that this would put the Duchenne gene somewhere on the long arm of the X-chromosome. A pedigree containing three sex-linked genes, mainly those responsible for Xg, haemophilia B and colour blindness (unspecified) has been published by Graham, Tarleton, Race and Sanger (1962). According to present knowledge the linear order of the 3-loci could be of two kinds and four different alignments in the mother's two X-chromosomes could accommodate the pedigree. But at least one double crossover must have occurred to account for the facts and this would lead one to conclude that the 3-loci are well separated from each other and may possibly span as much as 100 centimorgans.

A number of studies have been concerned with the linkage between the colour vision genes and the G6PD deficiency. The conclusions of Porter *et al.* (1962) are described on p. 65.

More recently Siniscalco (International Congress of Genetics, The Hague) reported 26 Xg^a-deutan recombinants and 61 non-recombinants; 4 deutan-G6PD recombinants and 133 non-recombinants; no protan-G6PD recombinants and 12 non-recombinants; and 2 Xg-protan recombinants and 4 non-recombinants.

C. E. Jackson and W. B. Seymour of Caylor-Nickel Clinic, Bluffton, Indiana, deduce (unpublished) from extensive family material of Xg and colour-blindness data, that the protan and deutan loci cannot

be very far apart and are both about 32 centimorgans from the Xg-locus. They consider the G6PD locus to be in between, about 5 centimorgans from the colour vision loci, and the haemophilia A locus to be on the other side about 12 centimorgans away.

Before attempting to draw a recombination map some curious findings ought to be mentioned, mainly the lack of recombination between G6PD and cv in Sardinian families (Siniscalco, Motulsky *et al.*, 1960) where both coupling and repulsion occur, and the strong preponderance of repulsion of the two characters in Israel (Adam, 1961), again with the absence of recombinations. These findings are not easily reconciled with a simple situation and suggest the possibility of some crossover suppressor—perhaps an inversion—near the G6PD locus and the colour loci (see p. 65). Figure 29 summarizes

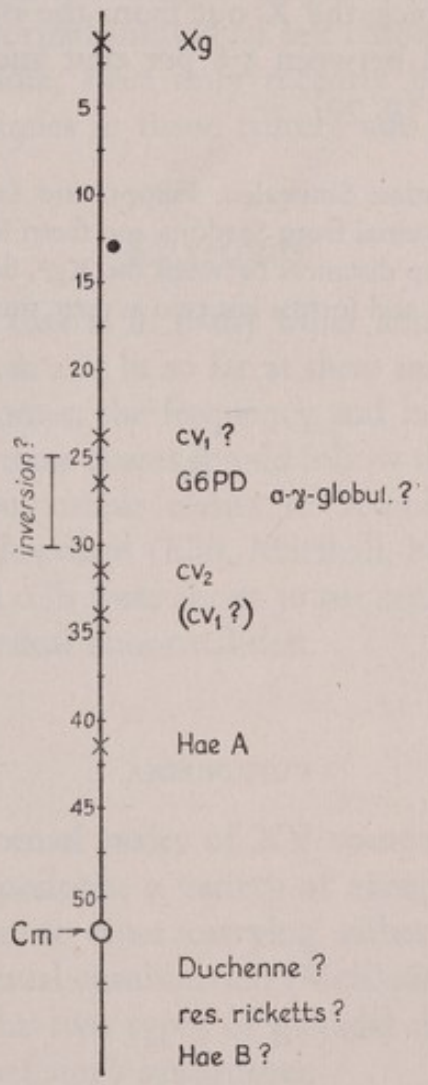

FIG. 29. Hypothetical map of the short arm of the human X-chromosome. Cm = Centromere. Combined from various data.

the findings described in this chapter and others in an attempt to draw a provisional map of the short arm of the human X-chromosome.*

Before entering into a discussion of this map, certain technical difficulties are worth pointing out because they affect the certainty and reliability of some of the results and conclusions described in this chapter.

In metaphase plates of specially treated mitotically dividing human cells, for instance in leucocytes or cells from the bone marrow, one can distinguish seven groups of chromosomes. The most numerous one consists of six autosomes and the X-chromosome, all of which are metacentric and of medium length. The two arms of these vary in relative length between 1 : 1·6 and 1 : 3·1. If measurements from different nuclei are considered, the asymmetry of the X-chromosome itself is almost as variable as that of the whole group and this often makes it difficult to pick the X out from the others. Its total length is variously estimated between 5·8 per cent and 6·8 per cent of the haploid autosomal set (p. 70).

* In a recent publication Siniscalco, Filippi, and Latte (1964) suggest two different maps for the material from Sardinia and from Israel and Greece. For the first they estimate the map distances between the Xg^a, deutan, G6PD and protan loci as 0.40, 0.04 and 0.05 and for the last two as 0.27, unstated and 0.03.

CHAPTER XI

GENETICS III—CHROMOSOMAL PECULIARITIES AND DEFECTIVE COLOUR VISION

THE sex-linked colour vision genes can be implicated in many abnormalities involving the sex chromosomes and in particular the X-chromosome.

Deviations from the normal groupings of the human sex chromosomes as well as abnormal individual sex chromosomes, though suspected for a long time, have only recently been demonstrated by means of new techniques in tissue culture and haematology.

POLYPLOIDY

It is just possible that as in many other animals several classes of human polyploids exist and in so far as these may contain three, four or more X-chromosomes, the frequency and inheritance of defective colour vision among these classes should follow the same rules of distribution as in the comparable classes of X-polysomics (see p. 80). Recently a girl was described (Ellis, Marshall, Normand and Penrose, 1963) whose cultured cells were about 50 per cent triploid. She showed mild mental and physical abnormalities.

ANEUPLOIDY

In addition to normal males of XY composition and to normal females of XX composition, a variety of exceptional individuals are produced from time to time carrying either fewer or more sex chromosomes or unusual combination (McKusick, 1962). Of these the most common are the two types of gonadal dysgenesis described as Turner's and as Klinefelter's syndromes.

Individuals suffering from Turner's syndrome are of general female

appearance and show sexual underdevelopment, hyperextensibility of joints and a webbing of the neck. Their most usual chromosomal constitution is X, or as is sometimes written XO, i.e. they lack a second sex chromosome, an X if considered female, a Y if considered male (Jacobs and Strong, 1959). A "Turner" may inherit an X-born colour deficiency from either its mother or its father.

People showing Klinefelter's syndrome are of male appearance, have small testes lacking in spermatogenesis and show endocrine peculiarities. Their most usual chromosomal constitution is XXY (Ford, Jones, Miller and Polani, 1959; Ford and Briggs, 1959), that is they have either an additional X-chromosome if considered male, or an extra Y-chromosome if considered female. As "Klinefelters" have a male appearance, though they frequently show gynecomastia and lack spermatogenesis when adult, while "Turners" have a rather infantile female appearance, one must conclude that in the human species a male habitus is mainly dependent on the presence of a Y-chromosome and a female habitus on its absence. This contrasts with the situation in *Drosophila* and many other animals where the Y-chromosome is less important for sexual development than the number of X-chromosomes in relation to the number of autosomes.

Individuals of Caucasian origin showing Turner's syndrome, most of whom despite their female appearance carry one X-chromosome only, will contain the high male proportion of colour defectives (8 per cent). The more male looking "Klinefelters" on the other hand, the majority of whom have an XXY constitution, only show a low frequency of sex-linked colour defects comparable to that found in normal females.

The figures in Table 8 are in agreement with those expected from the chromosomal findings.

The female appearance of patients suffering from Turner's syndrome will on occasion increase the frequency of defective colour vision among "female" samples, while the opposite effect of "Klinefelters" will usually be negligible.

Walls (1959) has suggested that an investigator finding an "irregular" defect of colour vision in an apparently female patient, should be alert to the possibility that "she" may in fact be an XO individual—though he need not in many circumstances let anybody suspect this. Conversely confronted with a colour-blind "Turner" it is worthwhile to investigate the colour defect in detail to see whether it is irregular.

Combinations of more than two X-chromosomes and/or possibly

TABLE 8. FREQUENCIES OF COLOUR DEFECTIVES IN TURNER'S AND KLINEFELTER'S SYNDROMES

	Sex chromosomes	Colour defectives	Exp. approx. frequency	Ref.
Turner's syndrome	XO	4 out of 26	8%	Bishop, Lessof and Polani (1960)
Klinefelter's syndrome	XXY	nil out of 73*	0·4%	Polani, Bishop, Lennox, Ferguson, Smith, Stewart and Prader (1958)
Klinefelter's syndrome	?	3 out of 34†	?	Novakowski, Lenz and Parada (1959)

* Originally 55.

† Abnormal gamete formation in a colour-blind mother and other types of non-disjunction leading to various chromosomal combinations may be responsible for this high value.

more than twoY-chromosomes are very rare. Their origin by various mechanisms of non-disjunction has been extensively discussed (Stewart, 1962) but would not concern us here. Development without the presence of at least one X-chromosome seems to be impossible.

Assuming that the dominance relationships (p. 66) and the manifestations of non-allelism in gonadal dysgenesis are the same as in normal people, we would expect the individual defects of colour vision to be roughly distributed with the following frequencies.

XY normal male	q
XO Turner	q
XX normal female	q^2
XXY Klinefelter	q^2
XXYY	q^2
XXX	q^2 to q^3*
XXXX	q^2 to q^3
XXXY	q^2 to q^3
etc.	

The segregation of colour blindness in families containing XO and XXY individuals can be used to determine the sex chromosome contribution of father and mother to those individuals. A maximum likelihood method for this purpose has been published by Fraser (1963).

Nuclear sex. Drumsticks

A phenomenon closely related to sex chromosomal constitution and also affecting sex-linked colour blindness is nuclear sex.

The number of X–chromosomes in a person's cell nuclei as found during mitosis† is correlated to the presence or absence of certain Feulgen-positive structures (chromatin bodies, Barr bodies) in the "resting" nuclei of several tissues. In individuals having two X-chromosomes, i.e. in normal females and "Klinefelters", a proportion of nuclei contain these bodies, which the nuclei of the cells of males and of "Turners" always lack (Barr and Bertram, 1949). It is widely believed that each "sex chromatin" body is a single heteropycnotic, perhaps encapsulated, X-chromosome or at least part of it. If that is so one

* According to the type of non-disjunction producing the particular abnormality.

† Most chromosome counts are made on cells from tissue culture, derived from skin or blood.

X-chromosome only would be chemically active during interphase (resting stage) in any cell, whether female or male. This interpretation is in agreement with the postulate often made, that a method of close compensation must exist to allow the double number of sex-linked genes in the female complement to do the same work as the single complement in the male. Somewhat akin to the Barr bodies are the "drumsticks", small projections from the nuclei of polymorphic blood leucocytes, which occur in a small percentage of female cells but never in male cells (Davidson and Smith, 1959).

Occasionally individuals occur some of whose nuclei contain not one but two chromatin bodies and some of whose leucocytes occasionally contain two drumsticks. These may, for instance, be "double chromatin positive" males of the constitution XXXY or "double chromatin positive" females of the constitution XXX. Individuals showing mosaicism in respect of sex chromatin also exist.

The frequencies of sex-linked colour defects among the chromosomal classes of people ought to be correlated to the maximum number of their Barr bodies or drumsticks in the same way as to the number of X-chromosomes, except that the individual's number of Barr bodies and drumsticks are one less than the number of X-chromosomes.

ISO-X-CHROMOSOMES

The role of iso-X-chromosomes in the determination of an individual's colour vision has been discussed on p. 71.

INVERSIONS, DELETIONS, TRANSLOCATIONS

The existence of an inversion or inversions near the cv loci in some X-chromosomes has been variously suspected and may perhaps account for some of the inconsistencies in the linkage data concerning the two cv loci, the G6PD locus and others (Siniscalco *et al.*, 1960; Adam *et al.*, 1961). However, it may well be that these difficulties will be resolved in other ways.

Small deletions of part of an X-chromosome may, in the female, sometimes mimic one of the recessive mutations. In males they might possibly be responsible for some cases of achromatism.

Fragments of various sizes of an X-chromosome attached to autosomes or the Y-chromosome (translocations) and carrying one of the

loci responsible for defective colour vision can also be expected to interact with their normally located allele or alleles. This may probably account for some anomalous pedigrees. Recently a ring X-chromosome has been described and this possibility must also be taken into account when one considers linkage with colour blindness.

In a number of experimental animals translocations between the X- and Y-chromosomes have been observed and thus it might be possible that a segment of the X-chromosome carrying one or both cv loci could become attached to the Y-chromosome.

During oogenesis chiasmata are found between the two X-chromosomes and crossing over thus occurs in the female, but it is very doubtful whether X- and Y-chromosomes ever pair during human spermatogenesis, or in other words whether the X- and the Y-chromosomes have a common (homologous) segment where crossing over could take place. Statistical evidence for the existence of partially (sometimes called incompletely) sex-linked genes, first collected by Haldane (1936), may thus be a sampling artifact. So far defective colour vision has to our knowledge never been associated with any part of the Y-chromosome.

MOSAICS

Mosaicism involving the X-chromosomes may be of manifold origin, involving many Karyo-types (see p. 80). The mosaics may arise from normal cells, when they will have partly normal and partly abnormal constituents. Part of a woman's body may carry two X-chromosomes and be heterozygous for one of the cv genes, whereas the other part may, through the loss of one X-chromosome, be of the XO constitution and only carry the morbid gene. If the XO part of the body comprises one eye of such a woman, she may be colour blind in this eye only (see p. 12) (also for other possibilities p. 71).

Other types of mosaics consist of two abnormal parts which may be the more or less complementary products of an abnormal mitotic division during embryogenesis. In this way composites of XXX and XO, or of XX and XO, or others may originate. These types too may occasionally result in individuals having one colour defective and one normal eye. As mentioned above, abnormality of the sex chromosomes is frequently of the mosaic type. It is, however, important to consider in this particular instance to what extent mosaicism

observed in the tissue culture from an individual is a reflection of mosaicism in its body.

NUCLEAR BODY AND MOSAICISM

A different kind of mosaic from those just described could arise according to the Lyon hypothesis.

Acceptance of the theory, that the nuclear bodies are single heteropycnotic X-chromosomes without metabolic function (Ohno and Hauschka, 1960), has led Lyon (1962) to formulate the hypothesis that in some sizeable cell genealogie of a mammal's body it is the maternal X-chromosome, in others the paternal X-chromosome, which is in this way functionally eliminated; certain mottlings of coat colours in laboratory mice can be reasonably explained along these lines, and other more or less plausible examples have been quoted, among them ocular albinism in the human retina. Concerning colour blindness, expectations derived from the "Lyon-hypothesis" depend entirely on the time and place of "fixation", that is when and where and how frequently either the paternal or the maternal chromosome is inactivated and how extended the different parts are which result from this sort of dichotomy. Thus a woman, heterozygous for a type of colour blindness, may be colour blind in one eye only but not in the other. A number of such women have in fact been described, and at first glance there seem to be rather more of them than one would expect, considering the low frequency of colour defect in females. On the other hand quite a number of men who are colour blind in one eye only have also been described and these cannot be explained by Lyon's hypothesis. And, of course, differences in colour vision between the left and right eyes of women can arise by other mechanisms (pp. 12, 57).

If the retinal mosaic is finer, that is if only small areas of the retinae are homogeneous for an X-chromosome, it would be difficult to detect this. The retina is a highly integrative system and one would not ordinarily expect such a mosaicism to show subjectively, e.g. by anomaloscope measurement. It is just conceivable that methods comparable to those used by Stiles (1956) for the demonstration of "rod-invasion" might succeed in the discovery of finer mosaicism in one or the other of female colour vision heterozygotes. Should the inactivation of one or the other of the X-chromosomes in neighbouring cones be quite fortuitous, one might not expect to discover anything

beyond the well-known fact that most women heterozygous for one of the colour vision genes are more or less normal, but that a few tend to be mildly affected.

There is some evidence that in females carrying structurally abnormal X-chromosomes, these are more likely to be "put away" in the nuclear body than are their normal counterparts. If that were so, certain deductions could be drawn and verified for the occurrence of colour blindness in such women.

CHAPTER XII

GENETICS IV—FREQUENCY OF DEFECTIVE COLOUR VISION IN DIVERSE GROUPS

GENERAL CONSIDERATIONS

One of the purposes of this monograph is to provide anthropologists with common techniques for the ascertainment and classification of defective colour vision. Unfortunately so many different methods have been applied in the past, often with insufficient knowledge of the subject, that detailed comparisons of the quite extensive frequency data from the literature (Kherumian and Pickford, 1959; Post, 1962) must necessarily be of a tentative nature. A few figures which it is hoped are representative are nevertheless presented in the following table.

While little can be done to improve the primary data collected in the past, the following general points may be useful for an assessment of their value and for future investigators (see p. 41).

1. In some investigations the sex of the individual is not mentioned. This unfortunately appears to have happened in Nelson's (1940) anomaloscopy data. Population frequencies for rare sex-linked recessives must be based on male samples.

2. *Classification.* The deutan defects, in many groups the most common colour vision deficiencies, as well as the protan defects, are graded in severity and are presumably each caused by a series of polyalleles (p. 63). It is thus not surprising that by the use of different techniques, and even by different investigators using the same tests, slighter degrees of these conditions may be classified as anomalous in one instance and as normal in another; significantly different frequencies are thus recorded not only of these two classes of trichromasy, but of the overall frequency of "colour blindness". This has apparently happened in two recent investigations of immigrant groups into Israel, in one of which the author was associated (Kalmus, Amir, Levine, Barah and Goldschmidt, 1961; Adam *et al.*, 1961; Goldschmidt, 1963) and which produced quite similar relative frequencies in the samples,

TABLE 9. OCCURRENCE OF DEFECTIVE COLOUR VISION IN MALE POPULATIONS. RANGE OF PERCENTAGES IN DIFFERENT SAMPLES*

Europe:	per cent
English	6·8 – 9·5
Scots	7·5 – 7·7
French	6·6 – 9·0
Belgians	7·5 – 8·6
Germans	6·6 – 7·8
Swiss	8·0 – 9·0
Norwegians	8·0 –10·1
Czechoslovakians	10·5
Russians	6·7 – 9·6
Jews (Russian)	7·6
Finns (Leningrad)	5·7
Turks (Istanbul)	5·1

Asia:	per cent
Tatars	5·0 – 7·2
Chinese	5·0 – 6·9
Japanese	3·5 – 7·4
Indians (caste Hindu)	0 –10·0
Indians (tribal)	0 – 9·0
Israelis	2·1 – 6·2
Druses (Israel)	10·0
Filipinas	4·3
Fiji Islanders	0 – 0·8
Polynesians (Tonga)	7·5
Africa:	
Bechuanas	3·4
Bugandans	1·9

	per cent
Bahutus	2·7
Batutsi	2·5
Congolese	1·7
North America:	
U.S. Whites	7·2 – 8·4
U.S. Negroes	2·8 – 3·9
Amerindians	1·1 – 5·2
Eskimoes	2·5 – 6·8
Canadian Whites	11·2
Mexicans (urban)	4·7 – 7·7
Mexicans (tribal)	0 – 2·3

South America:	per cent
Brazilindians	0 – 7·0
"White" Brazilians	6·9 – 7·5
"Dark" Brazilians	8·8
Brazilian Japanese	12·9
Australia:	
Whites	7·3
Aborigines	2·0
Mixed	3·2

*Compiled from Kherumian and Pickford (1959), Post (1962) and Kalmus *et al.* (1964), where details and further data can be found.

but somewhat different absolute frequencies. The simplest explanation is that the criteria for a positive diagnosis were applied with different stringency. Even more variable frequencies of colour blindness have been reported by the local recruiting boards for some remote areas of Scandinavia (unpublished). Very great changes in these sizeable samples of populations hardly affected by migration were recorded from year to year, probably caused by changes in testing personnel.

Different techniques might also be responsible for the exceptionally high frequencies (up to 15 per cent) of colour defectives reported by Jonkheere (1962) for the age groups 20–40 years.

Ideally, therefore, statistical comparisons ought to be made testing the scoring efficiency of the investigators concerned before a comparison of these results is attempted. This is hardly ever done.

Population frequencies of colour blindness are often derived from data collected for specific, usually practical, purposes such as applicants for jobs in transport, volunteers for the air force or navy, recruits in peace or wartime, etc.; such data must be always suspect of bias. Even schoolboys may not provide suitable material, e.g. in countries with a rigid social and/or racial stratification (Kalmus, DeGaray and Rodarte, 1964). In small tribal or religious groups even total ascertainment may be of little use for purposes of comparison, not only as a consequence of size but also because of inbreeding (see Post, 1962). For other kinds of bias, see p. 97.

Probably the most important factor in the evaluation and planning of population studies is sample size. The collection of too few data does not produce significant results and is thus usually a waste of time, but so is the collection of too many data. In addition, large bodies of data tend to suffer from heterogeneity. However, the following calculations of minimum sample size are based on the assumption of rather ideal random conditions, such as are rarely encountered in colour vision testing. Somewhat larger numbers should therefore be tested as a rule.

SAMPLE SIZES

The confidence we have in an empirical frequency such as that of colour defectiveness depends on its magnitude and on sample size. The standard error of a percentage is given by $\sigma_p = \sqrt{pq/N}$ when p is the percentage of colour-defective men (or of protanopes, deuteranopes, etc.) q is the percentage of colour-normal men and N is the number of men tested in a particular group.

Figures 30 and 31 give the confidence limits of 5 per cent and 1 per cent for empirical percentages of colour defectives in sample populations of a specified number. It appears that samples of several hundred

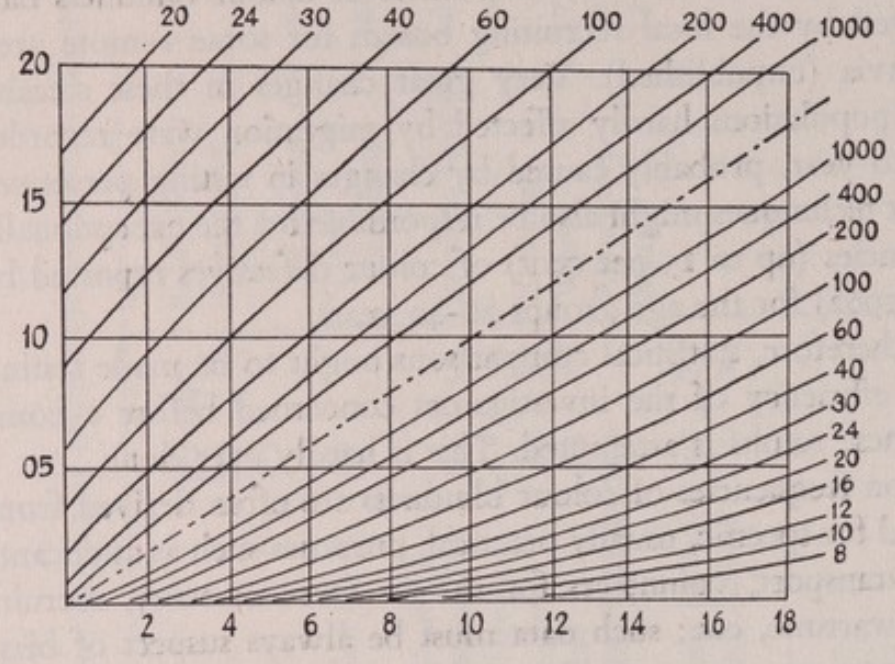

FIG. 30. Confidence belts for empirical percentages of colour defectives in sample populations. A vertical line is drawn through the point on the interrupted line corresponding to the found percentage. The ordinates of the points of intersection of this vertical with the curves for the given sample size above and below indicate with probability $P = 0{\cdot}95$, the limits between which the true population percentage lies (partly redrawn from *Biometrical Tables for Statisticians*, Cambridge University Press, 1956).

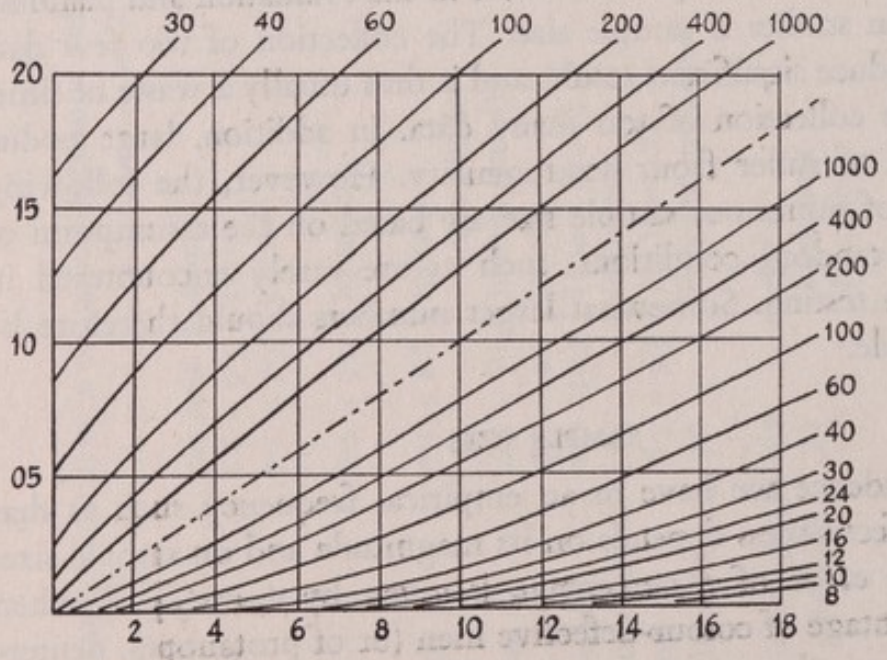

FIG. 31. Same as Fig. 30, but $P = 0{\cdot}99$.

men are necessary to make one confident of the accuracy of small percentages.

The significance of a difference in percentage between samples from different groups such as ethnic groups also depends on the magnitude of these percentages and the size of the samples.

Table 10 indicates the sample sizes necessary to establish significant

TABLE 10. MINIMUM NUMBERS $n = 9pq/d^2$ IN EACH OF 2 EQUAL SAMPLE POPULATIONS A AND B, NECESSARY TO ESTABLISH PERCENTAGE DIFFERENCES ($P = 0{\cdot}98$)*

Percentage difference $d = p_1 - p_2$	Average percentage $p = (p_1 + p_2)/2$							
	1	2	3	4	5	7	10	15
0·5	3564	7056	10,476	13,824	17,100	23,436	32,400	45,900
1·0	891	1764	2619	3456	4275	5859	8100	11,475
1·5	346	783	1163	1534	1898	2601	3596	5095
2·0	223	441	655	864	1069	1465	2025	2869
3	–	196	291	384	475	650	899	1274
5	–	–	105	138	171	234	324	459
10	–	–	–	–	43	54	57	115

differences in the percentage of colour-defective males at various percentage levels, assuming both samples are of equal numbers. It appears again that very considerable numbers of men—more than are usually tested—are necessary to demonstrate minor differences of percentage.

A useful example of how to conduct such an investigation might be a paper by Francois, Verriest, Mortier and Vanderdonck (1957).

INTERPRETATIONS OF POPULATION DIFFERENCES

Reported frequencies of defective colour vision in general, and of the various types in particular, differ considerably between various populations. A recent paper by Post (1962) summarizing the results of more recent and fairly comparable sample studies shows overall percentage for colour blindness ranging from 0·00 per cent among

* For $P = 0{\cdot}95$ about half these numbers are required.

200 males from Fiji Islands to 10·5 per cent among 656 males from Czechoslovakia.

Bearing in mind what has been said on p. 85 concerning the uncertainties arising from comparisons of material collected by different investigators using different methods, it is still possible to draw three tentative conclusions from a survey of colour vision frequencies. (1) The incidences of defective colour vision in populations that have only "recently" been separated are similar: this means that selection has not as yet acted very strongly in respect of the colour vision genes, and that their frequencies are suitable for the assessment of special historical relations between populations, such as migration, mixture or drift. (2) Surveying humanity in its entirety no very clear ethnic pattern emerges. High frequencies of colour blindness are found among some Indian (Brahmin), Arab (Druses), Chinese and most European samples, while low frequencies occur in Amerindian, Negro or Polynesian samples. But there are numerous exceptions. (3) As proposed by Post (1962) it is possible to see a correlation between the frequency of colour blindness and the distance in time of any population from the hunting phase of human existence. Samples from people still living as hunters or not too long removed from this state are as a rule poor in colour-blind individuals, while samples from populations which have long subsisted by agriculture or urban pursuits have many colour blind. Post suggests that when agriculture became the prevalent mode of subsistence, which occurred for various peoples' ancestors 3000–5000 years ago, the selection against the genes concerning defective colour vision was suddenly relaxed to zero. These genes, which had in the previous hunting state been eliminated, then started to increase by unchecked mutation. Considering the mutation of the wild type alleles for protan defects ($cv_1^+ \rightarrow cv_1^p$) and for deutan defects ($cv_2^+ \rightarrow cv_2^d$) separately, one might assume that within the time span indicated, that is since neolithic times, the frequency of the protan genes has increased from about 0·005 to 0·02 and that of the deutan genes from 0·016 to 0·06. If one assumes that this increase can be attributed solely to the net mutation rates (=frequency of mutation minus frequency of back mutation) these rates might be estimated as follows (Table 11).

The above mutation rates are somewhat high but not impossible.

From these estimates of the protan and deutan mutation rates one can derive an idea of the intensity of selection which had maintained the prae-neolithic frequencies of the two kinds of mutant genes (0·005

TABLE 11

	Increase of gene frequency		Time (years)	Approx. number of generations	Net mutation rate (mutation per gene per generation)
	from	to			
Protan genes	0·005	0·020	3000 4000 5000	120 160 200	$12{\cdot}5 \times 10^{-5}$ $9{\cdot}375 \times 10^{-5}$ $7{\cdot}5 \times 10^{-5}$
Deutan genes	0·015	0·060	3000 4000 5000	120 160 200	$37{\cdot}5 \times 10^{-5}$ $28{\cdot}13 \times 10^{-5}$ $22{\cdot}5 \times 10^{-5}$

and 0·015). Applying the formula $S=3\mu/q$ for the coefficient of selection operating only for the hemizygous* sex, we can estimate the losses of males per generation. Substituting arbitrarily 10^{-4} and 10^{-5} for μ we arrive at the values for S (Table 12).

TABLE 12

	q = gene frequency	Mutation rate $\mu = 10^{-4}$	Mutation rate $\mu = 10^{-5}$
Protan genes	0·005	$S = 0{\cdot}06$	$S = 0{\cdot}006$
Deutan genes	0·015	$S = 0{\cdot}02$	$S = 0{\cdot}002$

These values mean that between 3 and 30 "genetical deaths" occur per 100,000 males per generation, corresponding to between 0·2 per cent and 6 per cent of the corresponding colour-blind men. These seem quite reasonable results.

It must, of course, be pointed out that direct proof for the past operation of selection of this kind or for its subsequent relaxation is entirely missing. In fact it would be difficult to establish the working of such small selective forces in a primitive society even if they were operative at the present time.

* By omitting the fraction 3, Post obtained one-third of the values for S. Also his estimate of 7–200 "genetical deaths" per 10,000 persons per generation are much too high. It should be 7–200 per 10,000 *colour-blind* persons.

MODELS OF SELECTION AGAINST DEFECTIVE COLOUR VISION

Physical models, showing how such selection might operate, can be visualized and part of such action might be actually demonstrated.* Defective colour discrimination can affect primitive man in two ways, in his capacity as a hunter (or collector) and in his capacity as a prey. Either way the damage is done by gaining imperfect information concerning vital objects, but the effects will differ in intensity and distribution: failure to spot a tiger is likely to result in the death of a few individuals, but failure to spot an antelope, deer, or some ripe fruit, only in some deprivation. On the other hand the second situation, though less dangerous, might have been much more frequent. The average loss of fitness through defective colour vision might be the same in both instances.

If we consider the second situation in more detail a paradoxical conclusion has first to be discussed; namely that in a system where the coloration of a prey (e.g. a deer) has been cryptically adapted to hide it from the normal eye of a single species of predator (namely man), people with abnormal colour vision may very well be more able to detect the prey, rather than less able to do so.

This agrees with the observation made in wartime, that colour blind observers were sometimes less effectively deceived by camouflage than were observers having normal colour vision. The explanation of this curious fact is that the pigments used when imitating such objects as grass or soil are not the natural ones, and that the colour of the materials and the artificial objects are balanced for the colour-normal eye only but not for the abnormal eye. Another demonstration of this situation is the existence of those pseudo-isochromatic charts (p. 35) which the colour blind can read, but the colour normal not.

Experiments demonstrating the superiority of colour-blind men in this kind of situation could be easily made by putting stuffed specimens of deer and other prey into their natural habitats and by comparing the speed or frequency of their detection by comparable groups of colour-normal and colour-deficient men.

Overriding such special "advantages" it must still be argued that a man with abnormal colour vision will in most situations be at a disadvantage, and this for the following reasons: (1) His colour dis-

* The following speculations are based on the assumption that selection of colour vision genes is effected by selecting phenotypes according to their colour discrimination and not according to some other pleiotropic effect of the genes unconnected with colour discrimination.

crimination is impoverished so that certain shades or shade differences will escape him. This applies particularly to the perception of red (or brown) colours and to their distinction from greens. (2) The coloration of prey animals may be adapted cryptically to several predators having different colour discrimination and not to man alone.

Recently, Neel and Post (1963) have discussed and criticized some of the above points. In addition they have suggested that the possibility of positive selection during or after a critical period of transition from hunting to non-hunting should be thoroughly investigated. Sex-linked defective colour vision provides the only clear example of a simply inherited defect the frequency of which has significantly increased with the advent of civilization.

Perhaps less speculative than the discussion of the frequencies of the sex-linked colour vision genes may be a discussion of the population frequency of autosomal tritanopia. This may simply be the result of a mutation rate of one in 100,000 (a normal value) and a heterozygote fitness—irrespective of sex—of 0·8; this produces stable equilibrium at a gene frequency of 1 in 20,000, sufficiently low to enable us to ignore the fitness of homozygotes and the occurrences of back mutation; on the other hand the rare occurrence of tritanopia makes difficult a convincing demonstration of the possible 20 per cent loss in fitness of tritanopes.

CHAPTER XIII

SOME RELATED PROBLEMS AND PRACTICAL IMPLICATIONS

In this chapter some information is collected concerning various questions which people interested in human colour perception are likely to ask, or which they might ask if better informed.

COLOUR VISION AND COLOUR BLINDNESS OF ANIMALS

Two such questions are: (1) Whether "animals" are colour blind, and (2) whether animals of a particular species such as cats or cattle are colour blind. The answer to the first question is that many species of animals have been shown to possess colour discrimination and thus are not colour blind, while for others no such positive proof exists. The existence of colour perception in an animal can be inferred only from experiments demonstrating the dependence of a behavioural reaction on wavelength, as opposed to intensity. Anatomical, biochemical (retinal bleaching) or electrophysiological evidence should, of course, agree with the animal's behaviour, but is—in the absence of a generally accepted theory—not by itself conclusive.

The existence of elaborate systems of colour perception in many animals is now established beyond doubt (Autrum, 1958, 1961), as is the fact that some of these systems, e.g. that of honey bees (Daumer, 1956; Kalmus, 1960) are different from the human, whereas that of certain anthropoids and birds are fairly similar to it.

For those species which have so far not been shown to have a colour sense the question must be asked, whether this lack of discrimination is characteristic of all individuals of the species or only of some. In popular parlance we may then ask, "Are all cattle or cats colour blind?" The exact answers to these unexact questions are that so far no conclusive evidence has been produced that cattle (the "red cloth for the bull") react to colour; nor do cats, though two different cone pigments have been found in the cat's retina. In guinea pigs (Trinker and Berndt, 1957), reactions to colour could only be

demonstrated in a minority of individuals, though whether the others could or could not perceive colour cannot of course be decided. Among blowflies, most of which in some ways resemble human tritanopes, Autrum and Stumpf (1953) found individuals deviating in their spectral sensitivity, for instance that for red. It is quite possible that in other species, too, exceptional individuals will be discovered whose colour discrimination is deficient.

PIGMENTATION AND COLOUR VISION

Ocular albinism, as mentioned on p. 14, is frequently accompanied by apparent defects of colour vision. This deficiency is the consequence of inadequate "fovealization", and the nystagmus associated with it. It is unlikely to be directly caused by any lack of the yellow macular pigment. Curious defects in colour perception have also been found by the author when investigating the vision of children carrying genes responsible for pigment dilution. But again these phenomena seem to be associated with other grosser eye defects. Finally the question arises whether the normal variability in hair, skin and iris colour, as found in European populations, may be associated with abnormal colour perception. This has been claimed by Vernon and Straker (1943) who, in a nationwide survey, found that among drafts for the Royal Navy from nine major areas of Britain there was some such association (see also p. 15). However, whether this arises from the fact that the local population samples differed in frequency both in the genes responsible for defective colour vision and in the genes responsible for pigmentation, or whether some of the genes responsible for darker pigmentation are also the ones responsible for normal colour perception, remains to be seen. It is also conceivable that some sex-linked genes, which are producing defective colour vision in lightly pigmented individuals, may fail to do so in darker individuals. On the other hand dark-skinned people, like the inhabitants of Torres Straits (Rivers, 1901) or Egyptians (Rivers, 1901; Ishak, 1940; Pickford, 1959), tend to have more strongly pigmented lenses than light-skinned people. The effects on colour vision of the increase with age of lens pigmentation are described on p. 53.

DEFECTIVE COLOUR VISION IN ART AND INDUSTRY

Any assessment of the biological disability caused by defective colour

vision must be based on a study of the effects which it has in various occupations. It must, of course, be realized that while colour blindness may disqualify a man for certain occupations, for instance in professional transport and the military services, it need not in modern conditions necessarily result in a decrease of his biological fitness, but may only entail a different choice of occupation or its change. Nevertheless a consideration of the effects of defective colour vision in the arts and in some industries is interesting.

Searching pictures for evidence of colour blindness in painters, as indeed for other visual disabilities, is promising only when applied to naturalistic paintings; these have only been produced during limited periods and by a few civilizations. Trevor Roper (1957) who, in a most interesting paper, considered the influence of various eye diseases on pictorial art, states that

> The colour blind artist . . . can never have a normal evaluation of the affected hues; and it seems reasonable to accept that the majority do down-tone those colours, that they register less distinctly, while the minority may well in defiance exalt these same colours with correspondingly less attempt at naturalism. And the evidence, such as it is, does rather support this.

Total colour blindness—which is very rare—is of course incompatible with painting, but the sex-linked forms of red–green deficiency which occur in about 1/12th of our men must have occurred among the hundreds of apprentices of the mediaeval mosaic makers and illuminators as well as the Renaissance painters, yet there is no trace in such mosaics or paintings of any colour deficiency. We do not know whether this was caused by the elimination of colour-blind apprentices (colour blindness was only discovered much later, see p. 1), deflecting them perhaps into engraving, as suggested by Riddell and Trevor Roper (1959); or whether they acquired sufficient secondary critera for the aptness of their pigments. Perhaps their mistakes were corrected by their masters and colleagues.

Confusion of red and green was noted by Liebreich (1872) in certain pictures of a London Exhibition of 1872, where roof tops and oxen were depicted red on the well-lit side and green on the dark side. Defective colour vision has since been claimed more or less convincingly for artists such as Constable, Leger and many moderns, some of whom have confirmed these suspicions and have even been tested. It is quite possible that a few painters have been able to make a virtue out of necessity and have used their faulty colour systems as means of expression or as individual hallmarks.

The effects of increasing lens pigmentation on the paintings of ageing artists has been described and illustrated by Trevor Roper (1959).

Work relating to the effects which defective colour might have on industrial employment as opposed to employment in the public services is scarce. It may either refer to personnel already employed or to the selection of personnel. Investigation (Richter, 1953) of the incidence of colour blindness among textile workers (colourists) in Germany revealed no significant decrease in their percentage and this is probably true of other places. That the colour quality of the goods produced does on the whole not suffer in these industries, would indicate that colour-normal people in the groups concerned are able to correct most of the mistakes which the defectives might have made or passed. This explanation tallies with that given for the absence of colour-defective work among medieval mosaic workers and illuminations and the Renaissance paintings (p. 96).

On the other hand Lakowski (1962) has stated that the Master Printers' Association in Edinburgh accepts the advice of the Applied Psychology Unit of Edinburgh University and rejects those applicants for apprenticeship who suffer from "major" colour vision defects. They also relegate such people already in their employ to non-colour work. The more difficult selection of people of superior colour discrimination, that is the exclusion of the merely "colour weak" (p. 47), need not concern us here. Lakowski comments on the rather high incidence of major defects among the aspirants by stating that many of them are unaware of their deficiency and that other considerations —among them family ties—may be more important than colour aptitude.

The intricate problems of weak and anomalous colour vision in industry have been extensively discussed by Pickford (1955) and need not here be repeated as they are not of great genetical interest.

As stated on p. 40 all claims of curing hereditary colour blindness or of improving defective colour perception have so far proved spurious. But a great deal can nevertheless be done by the colour-defective person to help him in his everyday life—and more could be done by society—apart from keeping him away from special occupations. By looking through a green filter, for example, most deutan defectives will be able to distinguish between green objects, which will appear light, and red objects which will look dark. They will also learn that they perform better in certain kinds of illumination than in others. The colour of traffic lights can be chosen in such a

way that the red contains a good admixture of orange and the green is rather bluish, which will make the two signals sufficiently distinct. Vertical or horizontal streaks running through the lights can also be used as cues and a definite relative position such as red on top of green could universally be chosen. Finally, if we consider the ignorance of many people concerning their own deficiency (see p. 30), more thorough testing for colour blindness might be included in the physical examinations of school children and the results utilized for vocational counselling.

COLOUR AND LANGUAGE

Uncertainty in the naming of colours is frequently an indication of defective colour vision, while the use of correct colour names cannot in ordinary circumstances be taken as a proof of normal colour sense (see p. 30). This is a consequence of the traditional* use of colour names, enabling even the blind to describe the sky as blue, the grass as green, etc. By taking proper precautions, mainly by the removal of secondary cues, the verbal statements of a subject can however be quite sufficient for diagnosis and this has been discussed on p. 32.

But language affects research in colour perception at many points and levels and a short discussion of some of these should also be helpful in classifying people's colour vision defects.

The correct naming of colours presupposes a considerable degree of abstraction and verbal fluency and some children find it difficult to acquire. Infants have been shown to have a preference for red coloured objects (own observations), but it would be difficult to establish the colour blindness of a particular little boy by classic experiments. We are thus not able to say much about colour perception or colour matching before the age of 3. The degree and sophistication of a person's later colour vocabulary is, of course, a function of his occupation and general environment.

A comparison of the colour names in different languages poses some very interesting problems concerning their equivalence and mutual relation. Considering for the moment living languages only, it appears that words of common origin may describe different colours in different European languages. English "purple", French "pourple"

* These traditions may be poetic stereotypes often chosen for their evocative power or acoustic pleasantness. Or they may be religious: red for sin, black for evil, white for death.

and German "purpur" are all derived from the Latin "purpura", referring to the pigment of Mediterranean snails of the genus *Murex* and itself derived from the Greek "πόρφνρος". But nowadays, as in fact in antiquity (Andrè, 1949), these words denote different hues; "purple" for instance being much "bluer" than "pupur". If one considers the name of the group of substances called "porphyrins", many of which are blue and even green, one may see how far scientists have deviated from the original meaning of the colour name. Part of this confusion can probably be attributed to differences of the material pigments and to differences in the garments dyed with them, but similar confusion applies to other colours as well. Gold, for instance, is variously and in many languages described as red, yellow or just "bright", and the word golden and its equivalent used to describe hair, the stars, the sun, etc. These usages are, of course, very often just literary clichés, but on the other hand it must be considered that alloys of gold which contain silver are yellow, and may in fact be almost white, while the copper alloys are "red".

Difficulties of this kind are increased, when we consider the colour names of languages remote from ours, either in origin or in time. It has, for instance, been claimed that "in Homeric Greek, as well as recent Japanese and some primitive tribal languages today, there is no proper word for blue" (Trevor Roper, 1959). I am told that Welsh also lacks such an adjective. The apparent lack of distinctive colour names has been variously assumed to show that the early Greeks in common with other ancient peoples had a more "primitive" colour sense than we have, distinguishing only between warm and cold colours; and that our present colour discrimination was a new and thus, biologically, almost sudden acquisition. Such speculations are almost certainly misconceived; chimpanzee (Grether, 1940) and diurnal monkeys (Trendelenburg and Schmidt, 1930) apparently have colour systems very similar to ours, and even bees possess a fairly fine colour discrimination, though they "divide" the spectrum quite differently into primary regions (see p. 94). Subdivisions of the spectrum into regions radically different from ours have been claimed for various Amerindian tribes (Kay, 1953), for the Arabic peoples and others (le Blane, private communication; Hess, 1920), but such radical differences are difficult to accept (Table 13). Nevertheless it is worth considering that our basic colour qualities (blue, green, yellow and red) may be less firmly established in human nature than is commonly thought, and that, for instance, early experience may affect an in-

TABLE 13. SUB-DIVISION BY VARIOUS AMERINDIAN TRIBES OF THE SPECTRUM. THE WORDS USED CAN BE SEEN IN RAY, 1953.

	Wave-length	English Northwest U.S.	Salish Sanpoil	Sahaptin Tenino	Chinook Wishram	Salish Songish	Athapaskan Chilcotin	Eskimo Atka	Athapaskan Chetco R.	Takelma Rogue R.	Kalapuya Santiam
Violet–red	comp 5600										
Red	6571	red									
Orange–red	6340										
Red–orange	6230										
Orange	6085	orange									
Yellow–orange	5390										
Orange–yellow	5870										
Yellow	5793	yellow									
Green–yellow	5710										
Yellow–green	5600										
Green	5164	green									
Blue–green	5050										
Green–blue	4985										
Blue	4695	blue									
Violet–blue	4455										
Blue–violet	4350										
Violet	4210	violet									
Red–violet	comp 4990										
Violet–red	comp 5600										

dividual's exact dividing line between two spectrally adjoining colours. An example of this mentioned on p. 31 may be the fact that some people call certain turquoises blue while others call them green, a widespread difference of naming that has nothing to do with tritanopia (author's observation). On the other hand Pickford (1951) deduced from anomaloscope findings that people who call blue "green", violet "blue" or purple "violet" usually are slightly deficient in blue sensitivity. It is very interesting though that he found a normal girl using these descriptions apparently under the influence of her blue-deficient sister.

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