INVESTIGATION OF THE RADIO SOURCE 3C 273 BY THE METHOD OF LUNAR OCCULTATIONS

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THE, observation of lunar occultations provides the most accurate method of determining the positions of the localized radio sources, being capable of violding a positional accuracy of the order of 1 sec of arc. It has been shown by Hazard¹ that the observations also provide diameter information down to a limit of the same order. For the sources of small angular size the diameter information is obtained from the observed diffraction effects at the Moon's limb which may be considered to act as a

straight diffracting edge.

The method has so far been applied only to a study of the radio source 3C 212 the position of which was determined to an accuracy of about 3 sec of arc1,2. However, 3C 212 is a source of comparatively small flux density and although the diffraction effects at the Moon's limb were clearly visible the signal-to-noise ratio was inadequate to study the pattern in detail and hence to realize the full potentialities of the method. Here we describe the observation of a series of occultations of the intense radio source 3C 273 in which detailed diffraction effects have been recorded for the first time permitting the position to be determined to an accuracy of better than 1" and enabling a detailed examination to be made of the brightness distribution across the source.

The observations were carried out using the 210-ft. steerable telescope at Parkes, the method of observation being to direct the telescope to the position of the source and then to record the received power with the telescope in automatic motion following the source. Three occultations of the source have been observed, on April 15, at 410 Me/s, on August 5 at 136 Me/s and 410 Me/s, and on October 26 at 410 Me/s and 1,420 Mc/s, although in October and April only the immersion and emersion respectively were visible using the Parkes instrument. The 410 Mc/s receiver was a double-sided band receiver, the two channels, each of width 10 Mc/s, being centred on 400 Me/s and 420 Me/s, while the 136 Me/s and 1,420 Me/sreceivers each had a single pass band 1.5 Me/s and 10 Mc/s wide respectively.

The record of April 15, although of interest as it represents the first observation of detailed diffraction fringes during a lunar occultation, is disturbed by a gradient in the received power and is not suitable for accurate position and diameter measurements. Therefore, attention will be confined to the occultation curves recorded in August and October and which are reproduced in Fig. 1. It is immediately obvious from these records that 3C 273 is a double source orientated in such a way that whereas the two components passed successively behind the Moon at both immersions, they reappeared almost simultaneously. The prominent diffraction fringes show that the angular sizes of these components must be considerably smaller than 10", which is the order of size of a Fresnel

zone at the Moon's limb.

The most interesting feature of Figs. 1(e) and 1(f) is the change in the ratio of the flux densities of the two components with frequency. The ratio of the flux density of the south preceding source (component A) to that of the north following source (component B) is 1:0.45 at 410 Me/s and 1:1.4 at 1,420 Me/s, indicating a striking difference in the spectra of the two components. If it be assumed that the flux densities of 3C 273 at 410 Mc/s and 1,420 Me/s are 60 and 35 Wm-2 (c/s)-1 and that over this frequency-range the spectrum of each component may be represented by $S\alpha f^n$, then the above ratios correspond to spectral indices for components A and B of -0.9 and 0.0 respectively. The spectral index of A is a representative value for a Class II radio source; but the flat spectrum of B is most unusual, no measurements of a comparable spectrum having yet been published. If the spectral indices were assumed constant down to 136 Me/s then at this frequency component A must contribute almost 90 per cent of the total emission, a conclusion which is confirmed by a comparison of the times of immersion at 136 Me/s and 410 Me/s on August 5.

It has been shown by Scheuer⁴ that it is possible to recover the true brightness distribution across the source from the observed diffraction pattern, the resolution being subject only to limitations imposed by the receiver bandwidth and the finite signal to noise ratio and being independent of the angular scale of the diffraction pattern. However, in this preliminary investigation we have not attempted such a detailed investigation but based the analysis on the calculated curves for uniform strip sources of different widths as published by Hazard¹. Ās a first step in the investigation approximate diameters were estimated from the intensity of the first diffraction lobe and the results corresponding to the three position angles defined by the occultations and indicated in Fig. 2 are given in Table 1.

As already indicated here, the 136-Mc/s measurements refer only to component A and hence no diameter measurements are available for B at this frequency. The 410-Me/s observations of the August occultation are the most difficult to interpret owing to the components having both comparable flux density and small separation relative to the angular size of the first Fresnel zone. At immersion the widths were estimated by using a process of curve fitting to reproduce Fig. 1(d); at emersion (position angle 313°) the diameter of component B was assumed to be 3" as indicated by the estimates at position angles 105° and 83°. The individual measurements at each frequency are reasonably consistent but there is a striking variation of the angular size of component A with frequency and evidence of a similar variation for component B. As at the time of the August occultation the angular separation of the Sun and the source was about 50° and hence coronal scattering of the type observed by Slee⁵ at 85 Mc/s is not likely to be significant, this variation in size suggests that the model of two uniform strip sources is inadequate.

Therefore, a more detailed analysis was made of the intensity distributions of the lobe patterns given in Figs. 1(c) and 1(f), and it was found that in neither case can the pattern be fitted to that for a uniform strip source or a source with a gaussian brightness distribution. The 1,420-Mc/s observations of component B can be explained. however, by assuming that this source consists of a central bright core about 0.5" wide contributing about 80 per cent of the total flux embedded in a halo of equivalent width of about 7". Fig. 1(b), where component A predominates, suggests that this source has a similar structure

Table 1. Effective Width of Equivalent Strip Source (Sec. of arc)

Frequency	Component A Position angle			Component B Position angle		
Mc/s	106°	313°	84°	105°	314°	83°
136	6.4	6.4			_	
410	3.1	4·2 † 2 (6) *	4.2	3.1	3.0†	2.7
1,420			2.9			$\frac{2\cdot 1}{0\cdot 5}$ (7)

^{*} Estimated from an analysis of the whole diffraction pattern. † Component B assumed to have width of 3".

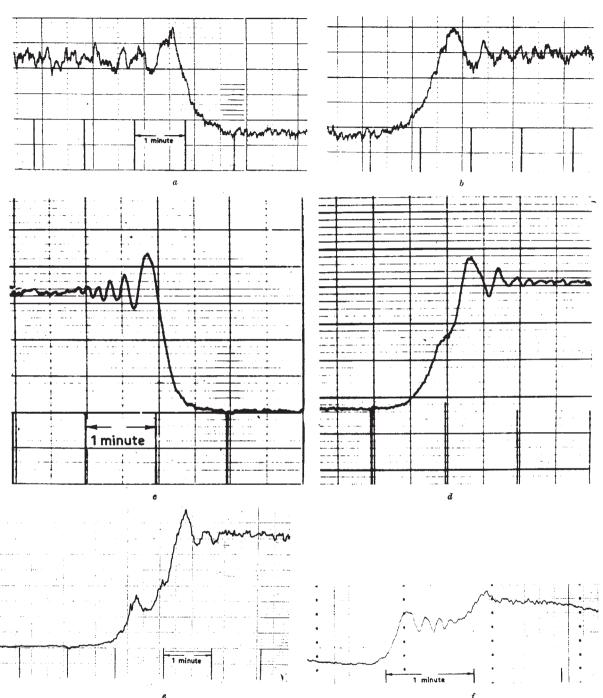


Fig. 1. Facsimiles of records showing occultations on August 5 and October 26, 1962, at different frequencies. (a) Emersion of August 5, 1962, at 136 Mc/s; (b) immersion of August 5, 1962, at 136 Mc/s; (c) emersion of August 5, 1962, at 410 Mc/s; (d) immersion of August 5, 1962, at 410 Mc/s; (e) immersion of October 26, 1962, at 410 Mc/s; (f) immersion of October 26, 1962, at 1,420 Mc/s.

Abscisse, U.T.; ordinates, flux density

but with a core of effective width about 2" at 410 Mc/s and a halo of width 6". It therefore seems that the overall extent of both components are comparable but that the emission is more highly concentrated to the nucleus in B than in A. The close agreement between the halo size of A and its effective diameter at 136 Mc/s suggests that the observed variation of effective size with frequency may be due to a difference in the spectra of the halo and central regions. This would imply that the spectrum becomes steeper in the outer regions of the sources, that is, in the regions of lower emissivity. It is of interest that the integrated spectral indices of the two components

show an analogous effect. Thus the spectrum of B, where most of the emission arises in a source about 0.5'' wide, is markedly flatter than that of A, where it arises in a source about 2'' wide.

The analysis is not sufficiently accurate to reach any reliable conclusions on the ellipticity of the individual components of 3C 273, but allowing for the uncertainty in the estimated widths and position angle 314° , the 410-Me/s observations indicate that both components may be elliptical with A elongated approximately along the axis joining the two components and B elongated perpendicular to this axis.

The position of each source was calculated from the observed times of disappearance and reappearance, which were estimated from the calculated flux density at the edge of the geometrical shadow and, where possible, from the positions of the diffraction lobes; these times are given in Table 2. In estimating the values of T_D^A and T_{R^A} from the 136-Me/s records a small correction was applied for the effects of component B, this correction being estimated by comparison with the 410-Mc/s records. The corresponding times for B were estimated from the 410-Mc/s observations using the estimated position of component A and the known flux density ratio of the two components. For each component the times and associated errors given in Table 2 define three strips in each of which the source should lie; the centre lines of these strips represent the limb of the Moon at the time of observation and define in each case a triangular-shaped area. In principle, the position of the source lies in the area common to the three associated strips but it was found that for each component, and in particular for component A, that the size of the triangles defined by the Moon's limb was larger than would be expected from the estimated timing errors. This suggests that errors in the positions of the Moon's limb are more important than the estimated timing errors, and possibly that the effective position of the source varies slightly with frequency. The position of each source was therefore assumed to be given by the centre of the circle inscribed in the triangle defined by the Moon's limb at the relevant times. Dr. W. Nicholson of H.M. Nautical

Almanac Office has kindly carried out these calculations and the estimated positions are as follows:

$\pm 0.03s$
1.5"
± 0.02s 0.5″
-

The average positions of the two sources given here represent the most accurate determination yet made of the position of a radio source. The quoted errors were estimated from the size of the triangles defined by the Moon's limb at the times of disappearance and reappearance, for the method is not subject to uncertainties introduced by refraction in the Earth's ionosphere or troposphere and is also free from the effects of confusion. A comparison of the times of disappearance and reappearance at different frequencies indicates that there is also no significant source of error due to refraction in either the solar corona or a possible lunar ionosphere; any refraction appears to be less than 0.3" even at 136 Mc/s. This may be compared with the upper limit of 2" at 237 Me/s and 13" at 81 Me/s as estimated by Hazard¹ and Elsmore⁶ respectively, and allows a new limit to be set to the density of the lunar ionosphere. Thus, from his observations at 81.5 Mc/s, Elsmore has set an upper limit to the electron density of 10³ cm⁻³; and it follows that the present measurements set a limit of about 10² cm⁻³. Similarly, Buckingham⁷ has estimated that at

Table 2. Observed Occultation Times of the Two Components of $3C\ 273$

m; c.1.	Component A (U.T.)	Component B (U.T.)		
Time of disappearance August 5, 1962 Time of reappearance	$07h~46m~00s~\pm~1s$	$07h~46m~27{\cdot}2s~\pm~0{\cdot}5s$		
August 5, 1962 Time of disappearance	$09h~05m~45.5s~\pm~1s$	$09h~05m~45\cdot7s~\pm~1\cdot5s$		
October 26, 1962	02h 55m 09·0s ± 1s	$02h \ 56m \ 01.5s \ \pm \ 0.4s$		

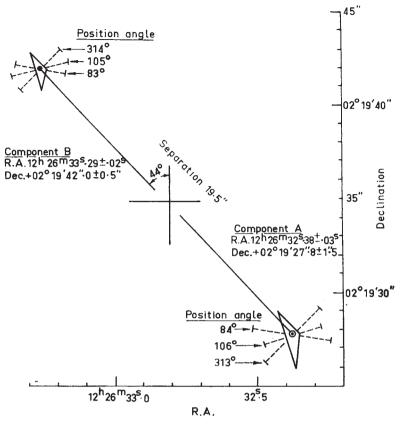


Fig. 2. Diagram of the radio source 3C 273. The sides of the full line triangles represent the positions of the limb of the Moon at the times of occultation. The broken lines represent the widths of the equivalent strip source as measured at 410 Mc/s for each of three position angles indicated

50 Me/s a ray passing at 50° to the Sun would be deviated by 1" if the electron density in the solar corona at the Earth's distance from the Sun is 100 cm⁻³. The present observations at 136 Me/s and 410 Me/s on August 5 indicate that at 50 Mc/s the deviation is less than 2" at this angle, setting an upper limit to the electron density of about 200 cm⁻³, which may be compared with an upper limit of 120 cm⁻³, set by Blackwell and Ingham⁸ from observations of the zodiacal light.

In a preliminary examination of a print from a 200" plate it was noted that the position of component B agreed closely with that of a thirteenth magnitude star. understand that the investigations by Drs. A. Sandage and M. Schmidt of the Mount Wilson and Palomar Observatories have revealed that this star and an associated nebulosity is very probably the source of the radio emission.

We thank Mr. J. G. Bolton for his interest in this work. and his assistance, with that of the staff at Parkes, in ensuring the success of these observations. We also thank Dr. W. Nicholson, who calculated the positions of the sources, for his valuable co-operation and interest in the occultation programme. One of us (C. H.) thanks Dr. E. G. Bowen for his invitation to continue occultation work at Parkes as a guest observer from the Narrabri Observatory of the School of Physics of the University of Sydney.

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3C 273: A STAR-LIKE OBJECT WITH LARGE RED-SHIFT

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THE only objects seen on a 200-in. plate near the positions of the components of the radio source 3C 273 reported by Hazard, Mackey and Shimmins in the preceding article are a star of about thirteenth magnitude and a faint wisp or jet. The jet has a width of 1''-2'' and extends away from the star in position angle 43° . It is not visible within 11'' from the star and ends abruptly at 20'' from the star. The position of the star, kindly furnished by Dr. T. A. Matthews, is R.A. 12h 26m $33\cdot35s \pm 0\cdot04s$, $Decl. +2^{\circ}$ 19' $42\cdot0'' \pm 0\cdot5''$ (1950), or 1'' east of component B of the radio source. The end of the jet is 1'' east of component A. The close correlation between the radio structure and the star with the jet is suggestive and intriguing.

Spectra of the star were taken with the prime-focus spectrograph at the 200-in. telescope with dispersions of 400 and 190 Å per mm. They show a number of broad emission features on a rather blue continuum. The most prominent features, which have widths around 50 Å, are, in order of strength, at 5632, 3239, 5792, 5032 Å. These and other weaker emission bands are listed in the first column of Table 1. For three faint bands with widths of 100–200 Å the total range of wave-length is indicated.

The only explanation found for the spectrum involves a considerable red-shift. A red-shift $\Delta\lambda/\lambda_0$ of 0·158 allows identification of four emission bands as Balmer lines, as indicated in Table 1. Their relative strengths are in agreement with this explanation. Other identifications based on the above red-shift involve the Mg II lines around 2798 Å, thus far only found in emission in the solar chromosphere, and a forbidden line of [O III] at 5007 Å. On this basis another [O III] line is expected at 4959 Å with a strength one-third of that of the line at 5007 Å. Its detectability in the spectrum would be marginal. A weak emission band suspected at 5705 Å, or 4927 Å reduced for red-shift, does not fit the wave-length. No explanation is offered for the three very wide emission bands.

It thus appears that six emission bands with widths around 50 Å can be explained with a red-shift of 0·158. The differences between the observed and the expected wave-lengths amount to 6 Å at the most and can be entirely understood in terms of the uncertainty of the measured wave-lengths. The present explanation is supported by observations of the infra-red spectrum communicated by

Table 1.	WAVE-LENGTHS	AND IDE	ENTIFICATIONS	
λ	λ/1-158	λ	0	
3239	2797	279	98 Mg II	
4595	3968	397		
4753	4104	410		
5032	4345	434	10 Ηγ	
5200-5415	4490-4675			
5632	4864	486		
5792	5002	500	07 [O III]	
6005-6190	5186-5345			
6400-6510	5527-5622			

Oke in a following article, and by the spectrum of another star-like object associated with the radio source 3C 48 discussed by Greenstein and Matthews in another communication.

The unprecedented identification of the spectrum of an apparently stellar object in terms of a large red-shift suggests either of the two following explanations.

(1) The stellar object is a star with a large gravitational red-shift. Its radius would then be of the order of 10 km. Preliminary considerations show that it would be extremely difficult, if not impossible, to account for the occurrence of permitted lines and a forbidden line with the same redshift, and with widths of only 1 or 2 per cent of the wavelength.

(2) The stellar object is the nuclear region of a galaxy with a cosmological red-shift of 0·158, corresponding to an apparent velocity of 47,400 km/sec. The distance would be around 500 megaparsecs, and the diameter of the nuclear region would have to be less than 1 kiloparsec. This nuclear region would be about 100 times brighter optically than the luminous galaxies which have been identified with radio sources thus far. If the optical jet and component A of the radio source are associated with the galaxy, they would be at a distance of 50 kiloparsecs, implying a time-scale in excess of 10⁵ years. The total energy radiated in the optical range at constant luminosity would be of the order of 10⁵⁹ ergs.

Only the detection of an irrefutable proper motion or parallax would definitively establish 3C 273 as an object within our Galaxy. At the present time, however, the explanation in terms of an extragalactic origin seems most direct and least objectionable.

I thank Dr. T. A. Matthews, who directed my attention to the radio source, and Drs. Greenstein and Oke for valuable discussions.

ABSOLUTE ENERGY DISTRIBUTION IN THE OPTICAL SPECTRUM OF 3C 273

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THE radio source 3C 273 has recently been identified with a thirteenth magnitude star-like object. The details are given by M. Schmidt in the preceding communication. Since 3C 273 is relatively bright, photoelectric spectrophotometric observations were made with the 100-in. telescope at Mount Wilson to determine the absolute distribution of energy in the optical region of the spectrum; such observations are useful for determining if synchrotron radiation is present. In the wave-length region between 3300 Å and 6000 Å measurements were made in 16 selected 50-Å bands. Continuous spectral scans with a resolution of 50 Å were also made. The measurements were placed on an absolute-energy system by also observing standard stars whose absolute energy distributions were known¹. The accuracy of the 16

selected points is approximately 2 per cent. The strong emission features found by Schmidt were readily detected; other very faint features not apparent on Schmidt's spectra may be present.

The source $3\hat{C}$ 273 is considerably bluer than the other known star-like objects 3C 48, 3C 196, and 3C 286 which have been studied in detail². The absolute energy distribution of the apparent continuum can be accurately represented by the equation:

$$F_{\nu} \propto \nu^{+0.28}$$

where F_{ν} is the flux per unit frequency interval and ν is the frequency. The apparent visual magnitude of 3C 273 is +12·6, which corresponds to an absolute flux at the Earth of 3·5 \times 10⁻²⁸ W m⁻² (c/s)⁻¹ at 5600 Å. At

radio frequencies³ the spectral index is -0.25 and the flux at 960 Mc/s is 5.0×10^{-25} W m⁻² (c/s)⁻¹. Between 6000 Å and 10,250 Å, eleven 120-Å bands were

Between 6000 Å and 10,250 Å, eleven 120-Å bands were measured with an accuracy of 10 per cent. These measures indicate that the relatively flat energy distribution given in the equation here applies as far as 8400 Å. Beyond 8400 Å the flux may increase significantly. Between 3300 Å and 8400 Å the energy distribution cannot be represented, even approximately, by the flux from a black-body or a normal star. At least part of the optical continuum radiation must be synchrotron radiation.

During the course of the infra-red observations a strong emission feature was found near 7600 Å. Further observations with a 50-Å band-width placed the emission line at 7590 Å with a possible error of about 10 Å. The emission profile was found to be similar to that of the emission line at 5632 Å. Using this line and others

in the visual spectrum Schmidt has shown that the most prominent emission features are Balmer lines and that the line at 7590 Å is $H\alpha$. Using Schmidt's red-shift $\Delta\lambda/\lambda_0$ of 0·158, $H\alpha$ should appear at 7599 Å; this is in satisfactory agreement with observation, when it is recalled that the atmospheric A band absorbs strongly beyond 7594 Å. It is possible that the [NII] lines which have unshifted wave-lengths of 6548 Å and 6583 Å can contribute to the emission feature identified as $H\alpha$. A large contribution. however, would shift the line significantly towards the red. The relative positions of $H\alpha$, $H\beta$, $H\gamma$, and $H\delta$ cannot be produced by applying a red-shift to any other hydrogen-like ion spectrum.

Further observations, particularly in the infra-red. will be made in the near future.

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RED-SHIFT OF THE UNUSUAL RADIO SOURCE: 3C 48

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THE radio source 3C 48 was announced to be a star¹ in our Galaxy on the basis of its extremely small radio diameter², stellar appearance on direct photographs and unusual spectrum. Detailed spectroscopic study at Palomar by Greenstein during the past year gave only partially successful identifications of its weak, broad emission lines; the possibility that they might be permitted transitions in high stages of ionization could not be proved or disproved. Hydrogen was absent but several approximate coincidences with He II and O VI were suggested.

The discovery by Schmidt (a preceding article) of much broader emission lines in the apparently stellar radio source, 3C 273, suggested a red-shift of 0·16 for 3C 273 if the lines were interpreted as the Balmer series. In 3C 48 no such series was apparent; measurable lines still do not coincide with the hydrogen series. However, the possibility of a very large red-shift, which had been considered many times, was re-explored successfully. 3C 48 has a spectrum containing one very strong emission feature near λ3832 which is 35 Å wide and about 10 other weaker features near 23 Å in width. The sharper lines are listed in Table 1 in order of decreasing intensity. Some broad lines or groups of lines between 50 and 100 Å width may be red-shifted hydrogen lines.

Table 1. IDENTIFICATIONS AND OBSERVED RED-SHIFTS

wave-length				
λ*	λ lab.	Source	λ*/λ lab.	
3832.3	$2796 \atop 2803$ $\bigg\}$ 2798	Mg II	1.3697:	
4685.0	3426	[Ne V]	1.3676	
5098	$\frac{3729}{3726}$ } $\frac{3727}{3726}$	[0 11]	1.3679	
4575	3346	[Ne V]	1.3673	
5289	,3868	Ne III	1.3671	
4065.7	2975:	[Ne V]	1.3667:	

The weighted mean red-shift $d\lambda/\lambda_0$ is 0.3675 \pm 0.0003, an apparent velocity of +110,200 km/sec. The slightly discrepant value for $\lambda 2975$ of [Ne V] is compatible with the uncertainty of \pm 3 Å in the wave-length predicted by Bowen³. The Mg II permitted resonance doublet has a small additional displacement to longer wave-lengths, possibly caused by self-absorption in an expanding shell; it is the strongest emission line in the rocket-ultra-violet spectrum of the Sun. The forbidden lines are similar to those in other intense extragalactic radio sources.

So large a red-shift, second only to that of the intense radio source 3C 295, will have important implications in

cosmological speculation. A very interesting alternative, that the source is a nearby ultra-dense star of radius near 10 km containing neutrons, hyperons, etc., has been explored and seems to meet insuperable objections from the spectroscopic point of view. The small volume for the shell required by the observed small gradient of the gravitational potential is incompatible with the strength of the forbidden lines.

The distance of 3C 48, interpreted as the central core of an explosion in a very abnormal galaxy, may be estimated as $1\cdot 10 \times 10^9$ parsecs; the visual absolute magnitude is then $-24\cdot 0$, or $-24\cdot 5$ corrected for interstellar absorption. The minimum correction for the effect of red-shift is of the order of $2\ v/c$ and a value between 4 and 5 times v/c is probable for a normal galaxy. The absolute visual magnitude of 3C 48 is then brighter than $-25\cdot 2$ and possibly as bright as $-26\cdot 3$, 10-30 times greater than that of the brightest giant ellipticals hitherto recognized, which are near $-22\cdot 7$ and another factor of five brighter than our own Galaxy, near $-21\cdot 0$.

As a radio source at a distance of $1\cdot 1\times 10^9$ parsecs 3C 48 is not markedly different from other known strong radio sources like 3C 295 or Cygnus A. The one feature in which it does differ from most sources is in its high surface brightness. This is partially due to its extremely small radio size of ≤ 1 sec of arc². The optical size is comparable, being also ≤ 1 sec of arc⁵. At the assumed distance such angular sizes indicate that both the optical and radio emission arise within a diameter of ≤ 5500 parsecs. The radio diameter might even be comparable with or less than that of 3C 71 (NGC 1068) the diameter of which is about 700 parsecs. However, 3C 71 has 5 orders of magnitude less radio emission.

If we determine the integrated radio emission of 3C 48 from the observed spectral index of the radio spectrum, and correct for the red-shift, we find that 3C 48 is comparable with 3C 295, emitting 4×10^{44} erg/sec of radio-frequency power. The cut-off frequencies were 7×10^7 c/s and 10^{11} c/s. The lower limit is indicated by the observed radio spectrum and the upper limit is an assumed one.

The absolute magnitudes of the galaxies connected with 3C 295 and Cygnus A, corrected for interstellar absorption. are $M_v = -21.0$ and -21.6 (using a red-shift correction of $2 \ v/c$) or $M_v = -22.4$ and -21.8 (using a correction

of 5 v/c) respectively. Thus 3C 48 radiates about 50 times more powerfully in the optical region than other more normal but intense radio galaxies. In contrast, the absolute radio luminosity of 3C 48 is the same as that of Cygnus A and 3C 295. The unusually strong optical radiation may be synchrotron radiation as suggested (for other reasons) by Matthews and Sandage⁵.

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HUMAN CANCER: MENDELIAN INHERITANCE OR VERTICAL TRANSMISSION?

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THE purpose of this article is to consider whether the I familial tendency to malignant disease should be attributed to genetic inheritance or to the transmission of an oncogenic virus from either parent to offspring ('vertical' transmission'). It will be shown that this is one of those situations, rare in cancer research, where the available evidence is adequate to allow almost unambiguous conclusions to be drawn about an issue of fundamental importance.

Following many demonstrations of the vertical transmission of leukæmogenic viruses in mice, Gross² has recently stated: "... one could therefore regard the development of cancer, leukæmia, or that of any other [the printed form is not 'any other' but 'another': it is presumed that 'any other' is intended] malignant tumour, as the result of an activation, frequently merely accidental of an oncogenic agent, hitherto masked, and carried by the host since birth. . . . Oncogenic agents carried in descendants of certain families, in humans as well as in other species, may have a higher pathogenic potential and be more readily activated than those carried in other families. . . . Thus cancer, leukæmia, or other malignant tumours would develop more frequently in members of certain families than in others". Elsewhere it is made clear that the 'oncogenic agent' is a virus.

This authoritative and influential working hypothesis inspires much contemporary cancer research, and is supported by an enormous volume of experimental evidence obtained from chickens, mice and rats.

Nevertheless, it was claimed recently³, in harmony with previous conclusions⁴⁻⁶, that the 'inheritance factor' in human leukæmias usually takes the form of an apparent dominant 'predisposing' mutation of incomplete penetrance; furthermore, the several ætiologies of the various forms of this neoplastic disease are all polygenic in nature³. Haldane⁷ in 1938 arrived at a similar conclusion with respect to cancer in general on the basis of Little's⁸ statistical investigations of cancer inheritance. In rare families, but especially in those where the parents are consanguineous, childhood leukæmias and lymphomas can exhibit apparent recessive inheritance, 10.

I have deduced^{3,11} that malignancies in adult human beings generally develop from one or more cells containing a total of four specific (nuclear) gene mutations, one of which is often inherited, the remainder originating in one or more somatic cell lines.

The incompleteness of the penetrance of the inherited mutation arises because the probability of a somatic cell accumulating the fourth and final 'carcinogenic mutation' within the normal life-span is less than unity.

The evidence from families where the parents are consanguineous9,10 indicates that two out of the four 'carcinogenie' mutations affect both homologous genes at a particular locus. More indirect evidence and arguments12 are consistent with the view that the remaining two mutations affect both homologous genes at another locus. The

ætiology of many childhood and adolescence malignancies3 should involve a primarily non-genetic 'stress' factor such as (1) a hormonal stimulus; (2) a pyogenic infection (notably pneumonia^{6,18}); or (3) infection, by 'horizontal' transmission, with an oncogenic virus. Direct epidemiological support for (3) has lately been obtained in the ætiology of a malignant lymphoma in children living in certain regions of Africa14.

Familial Leukæmia and Mutation Frequency

By calculating (1) the size of (genetic) carrier subpopulations; (2) the 'penetrance' of an inherited mutation in the phenotypic form of a childhood leukemia, the approximate frequency of childhood leukæmia in multiple sibs⁶ can be accounted for³. Using Haldane's¹⁵ "indirect method" for the calculation of mutation frequencies (where approximate genetic equilibrium is assumed) the derived values for the mutation frequencies of 'leukæmogenic' genes are closely comparable with known frequencies at other loci^{3,11}. They lie at the upper end of the normal range¹⁶ for dominant and sex-linked loci; but they include some effects attributable to gross chromosomal changes. Thus, trisomy for chromosome 21 (mongolism, or Down's syndrome) is associated with a very high leukæmia incidence in childhood^{6,17,18}, and the discovery of the Ch¹ chromosome by Gunz et al. 19 shows that the inheritance of a chromosome 21 from which a portion of the short arm has been either deleted or translocated, predisposes to chronic lymphatic leukæmia.

There is another source of uncertainty that could introduce an overestimation of the mutation frequency. It is assumed that only two major 'leukæmogenic' loci are implicated with respect to each of the two groups of genetically related leukæmias3. Although immunological evidence indicates that one specific structural locus may be involved in the ætiology of many carcinomas12, and although the phenomena of the Ph^1 and Ch^1 chromosomes 19,20 are consistent with specific loci being associated with leukæmogenesis, the possibility cannot be dismissed that there may be several loci of similar phenotypic expression. It is evident from the calculated mutation frequency that the number of major 'leukæmogenic' loci cannot be high, but it could be greater than two. (Other loci will undoubtedly affect the phenotypic expression of the major loci through their influence on factors such as growth, or growth-rate, but their net effect on the calculated mutation frequency should in general be small.)

The measure of agreement between established mutation frequencies and those calculated for the hypothetical major 'leukæmogenic' genes is obviously of considerable theoretical significance; it is rather unlikely that it represents a mere chance coincidence.

Direct Cytogenetic Evidence for an Inheritance Factor

With regard to the theoretical ætiology of chronic lymphatic leukæmia it was stated³: "Chronic lymphatic