frared spectrum of this CsI pellet, run in double-beam mode against an identically prepared pellet of pure CsI on a grating spectrophotometer (Perkin-Elmer model 621). Also shown is the comparable double-beam spectrum of a pair of CsI pellets, one a control and the other containing a few milligrams of sublimed sulfur (Mallinckrodt). The agreement is excellent. The bands at 3440 and 1613 cm<sup>-1</sup> in both spectra are due to bound water. The strong features near 465 and 243 cm<sup>-1</sup> are characteristic of elemental sulfur in the cyclo-S<sub>8</sub> configuration (5). Our sample was also examined by laser Raman spectroscopy (Spex model 1401; 2-watt argon irradiation at 5145 Å; 100 mw at the sample; 0.3cm<sup>-1</sup> resolution) and exhibits Raman bands at 151, 185, 217, 246, 434, and 470  $cm^{-1}$ , all corresponding (5) to  $S_8$ .

We conclude that the infrared spectrum of our powder is dominated by cyclic octatomic sulfur (with water contaminants), and that the organic molecules that we know are present have an abundance that is an order of magnitude less than that of sulfur. The spectra of Fig. 1 suggest that the S<sub>8</sub> ring vibrational features at 465 and 243 cm<sup>-1</sup> be searched for in the infrared spectra of Jupiter and other objects in the outer solar system. The only such spectra that we know of are those obtained by Houck et al. at aircraft altitudes and described in the preceding report (6). In addition to the expected J = 0 and J = 1 rotational transitions of  $H_2$ , these spectra apparently reveal an unexpected absorption feature centered near 23 µm. A comparison of the spectrum of this Jovian feature with the spectrum of the CsI pellet containing our brown precipitate, both obtained with the same flight spectrometer, is exhibited in Fig. 2. The spectrum of the precipitate has been displaced 1  $\mu$ m to longer wavelengths in the comparison. The temperature sensitivity of the 465-cm<sup>-1</sup> S<sub>8</sub> feature has apparently not been studied, but variations as much as 10 cm<sup>-1</sup> in the frequency of maximum absorption with temperature excursions over plausible Jovian regimes are known for other bands of  $S_8$  [for example, see (7)]. In addition, the absolute wavelength calibration of the spectrometer used in the comparison is uncertain to about  $10 \text{ cm}^{-1}(8)$ .

The strongest infrared absorption feature present in powders produced under simulated Jovian conditions roughly matches the most prominent unidentified infrared feature in the spectrum of Jupiter: accordingly we suggest that both are due to the same material, cyclic octatomic sulfur. However, because of the tentative nature of the announcement of the Jovian feature (6), its reality must be considered with caution. The question can be settled with 29 AUGUST 1975



60 cent)

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containing the brown polymeric material (A) as compared with the infrared spectrum of the Jovian feature at 22 to 24  $\mu$ m (B), both taken with the same flight spectrometer. The two spectra are displaced from each other by 1  $\mu$ m. Experimental errors in (B) are indicated by error bars; experimental errors in (A) are indicated by the width of the curve.

higher-resolution spectroscopy of the apparent 23- $\mu$ m feature, or by searches for the other strong infrared transitions of  $S_8$ , those at 150  $\mbox{cm}^{\mbox{--1}}$  and at 200 to 250  $\mbox{cm}^{\mbox{--1}}$ (5), if they are not obscured by Jovian  $NH_3$ and H<sub>2</sub>. That elemental sulfur might be produced on Jupiter by solar UV photolysis of H<sub>2</sub>S was proposed in 1937 by Wildt (9). In recent speculation that the optical frequency chromophores on Jupiter might be compounds of sulfur (10, 11), attention has concentrated on compounds of sulfur and NH<sub>3</sub> and not on elemental sulfur, although this possibility has been mentioned by Lewis and Prinn (11). The chromatographic fraction of our sample which is sulfur-free is nevertheless strongly absorbing in visible light, and we continue to hold that organic molecules may be the optical frequency chromophores on Jupiter. However, it is clearly prudent to consider polymeric sulfur as an additional prime candidate.

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### **References and Notes**

- C. Sagan and B. N. Khare, Science 173, 417 (1971); Astrophys. J. 168, 563 (1971).
  B. N. Khare and C. Sagan, Icarus 20, 311 (1973).
  Nature (Lond.) 232, 577 (1971). 1. C

- The elemental analysis was done at Schwarzkopf Microanalytical Laboratory, Woodside, New 4 York. Oxygen was determined by the Unzerzau-cher method, hydrogen and carbon by the Pregl method. sulfur by the ethylenediaminetetra acetic acid method, and nitrogen by the Dumas method.
- R. B. Barnes, *Phys. Rev.* **39**, 562 (1932); H. J. Bernstein and J. Powling, *J. Chem. Phys.* **18**, 1018 (1950); D. W. Scott and J. P. McCullough, *J. Mol. Spectrosc.* **13**, 313 (1964).
- J. R. Houck, J. B. Pollack, D. Schaak, R. A. Reed, A. Summers, *Science* 189, 720 (1975).
   V. D. Neff and T. H. Walnut, *J. Chem. Phys.* 35, 1723 (1961).

- D. Schak, personal communication.
  R. Wildt, Astrophys. J. 86, 321 (1937).
  T. Owen and H. P. Mason, J. Atmos. Sci. 26, 870 (1960). 10
- (1969). 11. J. S. Lewis and R. G. Prinn, *Science* **169**, 472 1970).
- We are grateful to J. Houck and R. Reed for use-12. we are grateful to J. Houck and R. Reed for use-ful discussions, to M. Marcus for assistance in obtaining Raman spectra, and especially to D. Schaak for obtaining infrared spectra of our samples with the flight spectrometer. This work was supported in part by NASA grant NGR 33-010-101 010-10

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# Sun-Tracking Solar Furnaces in High Arctic Flowers:

28

## Significance for Pollination and Insects

Abstract. Heliotropic flowers (Dryas integrifolia, Papaver radicatum) act, in sunshine, as solar reflectors, their corollas focusing heat on the sporophylls. Considerable intrafloral temperatures are generated. Winds above 3.8 meters per second and cloud abolish the effect. Insects that bask in the flowers also gain heat. The phenomena are important in maximizing the small heat budget.

In the arctic, any biotic mechanism for maximizing use of the small heat budget is advantageous. Heliotropism is such a mechanism in plants and is defined by Kevan (1) as turning to and with the sun—that is, sun-tracking. It is a manifestation of positive phototropism in which turning proceeds at a rate of 15° of arc per hour.

The flowers of two common high arctic plants (which occur widely in arctic and al-

pine regions) around Hazen Camp, Lake Hazen, Ellesmere Island, Northwest Territories, Canada (about 82°N), were found to be heliotropic under optimal conditions-Papaver radicatum Rottb. (Papaveraceae) for a possible maximum of 24 hours and Dryas integrifolia M. Vahl. (Rosaceae) for a possible maximum of about 6 to 8 hours centered about 11.00 hours solar time (Fig. 1). The possibility that this phenomenon has some thermal significance was pointed out by Hocking and Sharplin (2) and Hocking (3).

The flowers of both plants are open bowls (Fig. 2) which, in their sun-tracking movements, suggest radar antennas or radio telescopes. It is not necessary to assume a paraboloid shape, as a spherical reflector will function to concentrate, or focus, heat. Figure 2 shows a geometric diagram of each flower based on measurements of living flowers in the field. *Dryas integrifolia*, the smaller, is rendered as a parabola

$$x^2 = 4F_{\rm p}y \tag{1}$$

with  $F_p$ , the focus, at 0.30 cm, and as part of a circle

$$x^2 + y^2 = C^2$$
 (2)

with C, the center, at 1.02 cm (calculations based on measurements of 20 flowers). *Papaver radicatum* is similarly rendered, on the basis of measurements from nine flowers, to almost the same parabola  $(F_p = 0.31 \text{ cm}, \text{ the corolla merely extend$ ing beyond <math>y = 0.84 cm in *Dryas* to y =1.23 cm in *Papaver*) or to a somewhat larger circle than *Dryas*, C = 1.23 cm. All the symbols used in this report are explained in (4).

In a spherical reflector there is a plane of foci ( $F_c$ ) which is parallel to the plane of the tangent at the origin (O). This plane of foci cuts OC at the midpoint. As OC diverges (by  $\theta$ ) from parallel to the incoming rays, the focal point on  $F_c$  will move in the opposite direction by  $\frac{1}{2}OC\sin\theta$ . In a paraboloid no such plane of foci exists, there being a principal focus ( $F_p$ ). Divergence of the incoming rays away from the line  $OF_p$ will result in a shift and diffusion of the "focus." The mathematical analysis of this problem is complex and beyond the scope of this report. Nevertheless, the effect can be intuitively appreciated.

Assuming a spherical reflector, the calculations on measurements from flowers of *Papaver* indicate that as long as the flowers track the sun with no greater error than

Table 1. Examples of corolla temperature excesses ( $T_{en}$ ) or corolla temperatures ( $T_c$ ) in *Dryas* and *Papaver* and body temperature excesses of insects basking in *Dryas* flowers;  $\overline{T_a}$  is mean ambient air temperature, and other abbreviations are explained in (4).

C	N	Temperature (°C)					
Species	IN	Mean	Maximum	Minimum	$T_{a}$		
		Flowers					
Papaver							
$T_{en}$	7	5.4	7.0	4.5	7.0		
T <sub>c</sub>	12	23.0	26.8	19.0	15.8		
Dryas							
T <sub>en</sub>	4	6.8	8.3	6.0	13.0		
Ten	20	6.5	7.8	4.3	12.5		
$T_{\rm c}$	20	22.4	25.0	18.0	15.0		
		Insects					
Aedes sp.	24	10.1	16.0	3.5	14.2		
Aedes nigripes	9	5.9	6.5	5.0	10.5		
Rhamphomyia filicauda	18	6.2	9.5	4.5	12.5		
Rhamphomyia nigrita	18	12.0	16.5	8.0	15.1		
Carposcalis carinata	4	13.5	16.7	10.3	13.4		
Boreellus atriceps	4	15.4	17.4	11.3 **	17.5		

22.7°, the limits of the plane of foci ( $F_c$ ) will remain within the gynoecium. *Dryas*, however, must track exactly if the focus is to fall on the tip of the gynoecium, although the anthers would catch the plane of foci if tracking were not exact (see Fig. 2).

Assuming a parabola, in each flower the focus  $F_p$  is situated well within the gynoecium. In Dryas this would appear to be a better situation, demanding less close tolerance in sun-tracking. In Papaver, either a paraboloid or a spherical reflector can be postulated to concentrate radiation at the gynoecium, the mass and position of which would make either as effective. In both flowers, the shapes have natural irregularities which must give rise to many optical aberrations. At the same time the bulk of the sporophylls (gynoecium and androecium)-particularly in Dryas, in which they are numerous-must have considerable shading, insulating, and heat absorbing properties.

In a series of experiments designed to examine the extent and significance of the phenomena, I used small copper-constantan thermocouples (0.2 by 1 mm), one mounted within and the other outside the flower studied. The thermocouples were not blackened like those used by Hocking and Sharplin (2), because I wished to measure only temperature, rather than radiation as well. The reference junction hung in the air beside the flowers. Ambient air temperatures were measured by dial and mercury thermometers. When both thermocouples hung in ambient air and one was shaded, no consistent difference in the temperature (voltage) could be measured. For some measurements small microprobe thermistors were used. All temperature sensors were calibrated against a mercury thermometer to  $\pm 0.1$  °C in a water bath.

Measurements were made inside and

Table 2. Examples of intrafloral temperature excesses in normal, desporophyllate, and decorollate flowers of *Dryas* and body temperature excesses of insects basking in such *Dryas* flowers and in the open air,  $T_a$  is mean ambient air temperature, and the other abbreviations are explained in (4). Except for *Aedes nigripes*, insect temperature ranges are based on direct measurements with thermistors. Maximum and minimum possible ranges are calculated from maximum and minimum object temperatures and minimum and maximum ambient temperatures, respectively. Hence, they are probably more extreme than they would be if calculated from paired thermocouple temperature difference measurements. NA, not applicable.

					Tem	perature	(°C)							
Species	N		T <sub>en</sub>			T <sub>es</sub>			T <sub>ec</sub>			T <sub>ea</sub>		$\overline{T_{a}}$
		Mean	Max.	Min.										
					Flov	vers								
Dryas	5	3.9	4.3	3.3	4.0	4.3	3.8	1.5	1.8	1.3	NA	NA	NA	4.0
Dryas	20	6.5	7.8	4.3				4.0	5.3	2.5	NA	NA	NA	12.5
					Inse	ects								
Aedes sp.	10	12.9	18.3	6.3	11.6	16.3	3.5	6.4	9.0	0.0	3.4	5.0	0.0	13.9
Aedes nigripes	2	5.8	6.3	5.5	5.9	6.0	5.8	3.5	3.8	3.3	3.8*			16.0
Rhamphomyia nigrita	10	14.0	8.3	11.0	13.8	18.8	9.3	9.7	14.0	3.5	4.8	9.5	0.5	15.0
Carposcalis carinata	4	15.3	17.0	14.0	15.0	16.8	13.5	10.7	12.0	9.0	5.1	6.5	3.8	13.4
Boreellus atriceps	3	15.4	16.3	11.3	15.0	16.0	14.0	10.7	11.0	10.5	3.3*			17.5

\*N = 1.

outside both flowers pinned on a board mounted on a photographer's tripod and flowers in situ. The results clearly show the importance of heliotropism and flower shape in concentrating solar heat.

**Papaver** flowers were found to attain a temperature excess  $(T_{en})$  of up to 7°C at a mean ambient temperature  $(\overline{T}_a) \cdot of$  7°C when mounted on the board, and a  $T_{en}$  of up to 10°C at a  $\overline{T}_a$  of 15.8°C in the field (Table 1). During overcast conditions the flowers are not heliotropic, and the temperatures registered inside them were close to ambient (mean excess, 0.3° to 0°C; N = 32).

*Dryas* flowers act similarly. On various occasions of optimal conditions temperature excesses in mounted flowers were measured (Table 1). The linear relation

 $T_{\rm c} = 1.3T_{\rm a} + 2.56$ 

$$T_{\rm en} = 0.3T_{\rm a} + 2.56 \tag{4}$$

(3)

where  $T_c - T_a = T_{en}(17)$ , was derived from nine sets of experiments involving more than 100 readings from flowers mounted on boards and flowers in situ over a range of ambient temperatures from 4° to 15°C. Under cloudy conditions heliotropism and temperature excesses are abolished, as with *Papaver*.

To examine the importance of the various floral parts in contributing temperature excess, flowers of Dryas were mutilated by removal of sporophylls or petals. These were compared simultaneously with normal flowers. It was found that the temperature excess at the approximate position of the focus was the same in desporophyllate and normal flowers; for example, at  $T_a = 4.0^{\circ}$  C,  $T_{es} = 4.0^{\circ}$  C (desporophyllate) and  $T_{en} = 3.9^{\circ}$ C (normal) (P > .05). By contrast, the decorollate flowers were significantly cooler;  $T_{ec} = 1.5^{\circ}C (P < .01)$ (Table 2). Presumably the near equality in desporophyllate and normal flowers is afforded by (i) the absence of shading in the desporophyllate bowl, which thus has unimpeded focusing, and (ii) absorption of radiation by the sporophylls, which would compensate for the considerable shading of the normal bowl. Within the sporophylls temperature excesses of an additional 0.5°C could be measured, although on occasion deficits of that magnitude were measured.

One other bowl-shaped flower was examined, that of the smaller flowered *Potentilla nivea* L. s. lat. (Rosaceae). These flowers did not appear to be heliotropic, but when they were facing the sun temperature excesses of about  $3^{\circ}$ C were measured ( $T_a = 9^{\circ}$  to  $17.5^{\circ}$ C; N = 37).

Under breezy conditions, temperature excesses in flowers are reduced. From 29 AUGUST 1975



Fig. 1. Heliotropic periods for *Papaver* and *Dryas*. Data were obtained by counting the percentage of flowers facing the sun on several days [simplified from Kevan (1)].

more than 150 temperature measurements from *Dryas* flowers at various wind speeds, I determined the relation

$$\left. \frac{T_{e\alpha}}{T_{ea}} \right| = 1 - 0.75 \left( \frac{\alpha}{3.3} \right)^2 \tag{5}$$

where  $T_{e\alpha}$  and  $T_{ea}$  are the temperature excesses at wind speed  $\alpha$  and under optimal conditions (Eq. 4) or measured in flowers temporarily protected from the wind. Hence, at wind speeds above 3.8 m/sec,  $T_{en}$  is absent.

Northern Ellesmere Island lies in a belt of high incidence of sunshine (> 50 percent of that possible) (5, 6), low wind speed (June and July mean = 1.3 m/sec at a height of 20 cm) (5, 7), and short growing or active season (about 6 weeks) (5, 7). The plants must, in that period, develop flowers, undergo pollination (8) and fertilization, ripen the ovary, and develop seeds and their appendages (plumed achenes in the case of *Dryas*). These facts strengthen the inference that heliotropism and heat



Fig. 2. Geometric rendition of flowers of *Dryas* and *Papaver* showing parabola (inside cup) with principal focus  $F_p$  and circle (outside cup) with center C and plane of foci  $F_c$ . Central masses represent gynoecia; the dotted line in *Dryas* represents the position of the androecium with its many stamens.

concentration have considerable biotic importance.

Calculations (9) indicate that *Papaver* and *Dryas* flowers maintain considerable temperature excesses (6° to 8°C) for about 50 percent and 15 percent of their lives, respectively. Arctic plants characteristically grow close to the ground, where, at Hazen Camp, temperatures at flower height frequently range from 10° to 16°C (7, 10). Hence, in terms of growing degree-days, *Papaver* flowers gain at least an extra 25 percent and *Dryas* flowers at least an extra 8 percent in their short lives.

The heat gained must contribute considerably to the plants' floral metabolism and reproductive process. It may also be part of the feedback system that allows growth to proceed rapidly enough to permit heliotropism, which is presumably an auxinmediated growth response (11).

Hocking and Sharplin were specifically concerned with insects basking in the flowers (2, 3). To determine the importance of this behavior. I inserted thermocouples into the thoraxes of several specimens of living anthophilous insects, Aedes nigripes (Zetterstedt), Aedes spp. (Culicidae), Rhamphomyia filicauda Henrikson & Lundbeck and R. nigrita Zetterstedt (Empididae), Carposcalis carinata (Curran) (Syrphidae), and Boreellus atriceps (Zetterstedt) (Calliphoridae). All but the last bask in flowers. If an insect died during the experiment, observations were terminated. All the insects developed considerable body temperature excesses in flowers of Dryas (Table 1). The data do not lend themselves to absolute comparison as  $T_a$ was not constant, but in general the more robust, dark, and hairy an insect, the greater is its capacity for warming (12).

In other simulated basking experiments, the same species of insects were placed in mutilated flowers. The results (Table 2) are as expected from the floral measurements. Insect body temperature excesses are almost the same in normal and desporophyllate flowers, but drop considerably in decorollate flowers, although generally remaining higher than temperature excesses measured in insects suspended in the air.

Inasmuch as the basking insects may remain in the corollas of flowers, especially of *Dryas*, for considerable times, the extra warmth they obtain must be valuable in increasing their metabolism, hastening the maturation of ova, and giving them greater mobility by preheating them for flight. Also, while in heliotropic flowers the insects derive the benefit of abundant carbohydrate and protein (if taken as pollen, as in Syrphidae, some Muscidae, Collembola), food, warmth, and a vantage point for detecting dangers, the shadows of which [entomologists, some birds (13)] may pass across the flowers before the dangers themselves (14).

It is noteworthy that the flowers, Dryas at least, rely, in part, on the services of the basking insects (as well as others) for pollination and hence reproduction, dispersal, and colonization (8) and display the attributes of entomophily (14, 15).

Flower power, generated by the combined effects of heliotropism and radiant heat focusing, in the high arctic is important to reproduction of the plants and to the insects which visit flowers and may pollinate them. Insolation may play a role in the distribution of the high arctic fauna and flora (8, 16).

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### **References and Notes**

- P. G. Kevan, Can. Field-Nat. 86, 41 (1972).
   B. Hocking and C. D. Sharplin, Nature (Lond.) 206, 215 (1965).
   B. Hocking, Oikos 19, 359 (1968).
- Symbols used in this report are defined as follows:  $F_{\rm c}$  plane of foci for spherical section
  - $C_p$ , principal focus of paraboloid  $C_r$  center of sphere N, number of observations

  - O, origin of paraboloids and spheres
  - , ambient air temperature
  - c, temperature in corolla of whole flower c, temperature excess above ambient

  - $T_{ea}$ ,  $T_e$  in ambient air  $T_{ec}$ ,  $T_e$  in decorollate flower  $T_e$ ,  $T_e$  in whole, unmutilated flower
- $T_{en}$ ,  $T_{ein}$  in whole, unmultiated flower  $T_{esr}$ ,  $T_{ein}$  in desporophyllate flower  $T_{ear}$ ,  $T_{en}$  in wind of speed  $\alpha$  (m/sec) P, probability determined by *i*-test 5. P. S. Corbet, *Can. Def. Res. Board Dir. Phys. Res. Oper. Hazen No. 29* (1966).
- 6. M. K. Gavrilova, Radiation Climate of the Arctic

(translated from Russian) (National Science Foun-(ation, Washington, D.C., 1966); C. I. Jackson, Can. Def. Res. Board Dir. Phys. Res. Oper. Hazen Nos. 8 and 9 (1959).

J. M. Powell, Can. Def. Res. Board Dir. Phys. Res. Oper. Hazen No. 14 (1961).
 P. G. Kevan, J. Ecol. 60, 831 (1972).

- Calculations are based on the probability of sun-9 shine  $(P_s > .5)$  (5, 6), the probability of heliotro-pism operating  $(P_h = .3 \text{ for } Dryas \text{ and } 1.0 \text{ for } Pa$ paver), and the approximation that under sunny conditions the ambient air temperature at flower height is between  $10^{\circ}$  and  $16^{\circ}C$  (7, 10). From Eq. 3 Dryas flowers heat to about 1.5 times the ambient temperature, so that  $T_e \sim 0.5 T_a$ . Hence for Dryas  $P_{\rm s} \times P_{\rm h}$  = .15 is the probability of temperature excess being generated; multiplying this by 0.5 T<sub>e</sub> gives about 8 percent for the growing degree-days above 0°C. For *Papaver*,  $P_s \times P_h = .5$ , and with
- $T_e = 0.5 T_a$ , the number of growing degree-days Performance of the second seco 10. P 1973)
- 11. Phototropism and heliotropism in flowers has remained almost unstudied since the time of J. Weis-ner [*Denkschr. Akad. Wiss. Wien* **39**, 143 (1879); *ibid.* **43**, 1 (1882)] despite the wealth of information on coleoptiles of oats. P. S. B. Digby, J. Exp. Biol. 32, 279 (1955).
- P. S. B. Digby, J. Exp. Biol. 52, 219 (1955).
   Birds such as ptarmigan (Lagopus mutus rupestris), hoary redpoil (Acanthis h. hornemanni), Contraine communs), and ruddy turnstone knot (*Calidris c. canutus*), and ruddy turnstone (*Arenaria i. interpres*) have been observed eating flower visitors inside and outside flowers. One in-Hower visitors inside and outside flowers. One in-sect, *Rhamphomyia filicauda*, may prey on other flower visitors inside the flowers [J. A. Downes, *Can. Entomol.* **102**, 769 (1970)].
  P. G. Kevan, *Polar Rec.* **16**, 667 (1973); thesis, University of Alberta (1970).
  <u>Can. J. Bot.</u> **50**, 2289 (1972).
  and J. D. Shorthouse, *Arctic* **23**, 968
- 14.
- 15 16.
- (1970)
- 17. I am grateful to the late B. Hocking, who supported and encouraged my research through the Na-tional Research Council of Canada (grant NRC A-2560). I thank the Canada Defence Research A-2560). I thank the Canada Delence Research Board for financial support and for the use of Hazen Camp. I also thank my colleagues at Hazen Camp in 1966 to 1968 for their help and enthusi-asm. A. Wilkinson and P. Wilkinson, at Nuffield Radio Astronomy Laboratories, University of Manchester, Jodrell Bank, England, helped through the productive exchange of ideas.

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# **Predicting Response to Endocrine Therapy in** Human Breast Cancer: A Hypothesis

Abstract. We hypothesize that the presence of progesterone receptors in human breast tumors may be a sensitive marker for predicting response to endocrine therapy. Progesterone receptors were found in 56 percent of tumors with estrogen receptors, but were absent in tumors without estrogen receptors. Preliminary clinical correlations show that only those breast tumors with progesterone receptors regressed after endocrine therapy.

Metastatic human breast cancer has long been treated by surgical ablation of endocrine glands or by pharmacologic hormone therapy. Unfortunately, endocrine responsive tumors constitute only 20 to 40 percent of cases. The success rate can be improved to 55 to 60 percent by selecting for endocrine therapy only those patients

Table 1. Comparison of ER and PgR in 50 human breast tumors. More than 3 fmole per milligram of cytosol protein constitutes a positive assay.

	PgR +			
ER + ER-	20/36 (56 percent) 0/14 (0 percent)			

is present in malignant mammary cells, tumor growth is regulated by the hormonal environment and that a change in this environment will cause tumor regression. However, since binding to receptors is only an early step in hormone action, it is possible that in ER + tumors where endocrine manipulations fail, the lesion is at a later step. An ideal marker of an endocrine responsive tumor would, therefore, be a measurable product of hormone action rather than the initial binding step.

Because in estrogen target tissues the synthesis of PgR depends on the action of estrogen (2), we investigated the possibility that PgR might be such a marker. If so, it would be expected that PgR would be rare in tumors which lack ER. The presence of PgR in tumors containing ER would indicate that the tumor is capable of synthesizing at least one end product under estrogen regulation, and that the tumor remains endocrine responsive. Tumors with ER but no PgR would be resistant to endocrine therapy.

PgR has been found in the reproductive tracts of several species (3), but its demonstration in rats and humans has been difficult because of progesterone's predilection for binding to glucocorticoid receptors and to corticosteroid binding globulin (4). One indirect approach to this problem has been to mask the competing sites with unlabeled hydrocortisone (5).

Recently the synthetic progestational compound R5020 has been found to bind specifically to PgR in immature rat and mouse uteri ( $\delta$ ). With this progestin, the receptor sediments in the 8S region of sucrose gradients, where serum contaminants do not interfere.

We have used 8S binding of [3H]R5020 to identify PgR in human breast cancer tissue (7). Excess unlabeled progesterone or R5020 completely inhibits the binding, whereas hydrocortisone, dexamethasone, or estradiol do not compete effectively (8). We have now determined PgR and ER (9) in 50 human mammary tumors and the re-

Table 2. Comparison of ER, PgR, and tumor response to endocrine therapies in nine patients. Hx, Abbreviations: hypophysectomy; Ov. oophorectomy; A, androgen (fluoxymesterone).

ER	PgR	Re- sponse*	Ther- apy
+	+	+	Hx
+	+	+	Ov
+	+	+	Α
+	0	0	Ov
+	0	0	Ov
ò	0	0	Ov
0	0	0	Ov
0	0	0	Hx
0	0	0	Hx
	ER + + + + + 0 0 0 0	ER PgR + + + + + + 0 + 0 0 0 0 0 0 0 0 0 0 0 0	$\begin{array}{c ccc} ER & PgR & \frac{Re}{sponse}* \\ \hline + & + & + \\ + & + & + \\ + & + & + \\ + & 0 & 0 \\ + & 0 & 0 \\ + & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 &$

\*Objective remission defined as in (10).

SCIENCE, VOL. 189

whose tumors contain estrogen receptor

(ER) (1). Our concern now is to identify the 40 percent of ER + but endocrine resistant tumors, whose growth cannot be inhibited by either ablative or additive endocrine manipulation. To this end we hypothesize that when progesterone receptors (PgR) are present, tumors will be endocrine responsive and that in their absence tumors will be resistant to endocrine manipulation.

Normal target tissues for any hormone contain specific receptors for that hormone, and when malignant transformation occurs, the cell may retain all or part of its normal complement of receptors. The assumption has been implicit that when ER