early to consider clinical trials of progestin or anti-
progestin agents and that in vitro studies are a very
necessary prerequisite.

Work performed over the past 4 years by Pertuiset
and his coworkers in Paris, some of which was ex-
plained at the IXth International Congress of Neuro-
pathology and some of which has been reported, has
convinced us, however, that three-dimensional tissue
cultures (multi-cellular spheroids) may be a more profit-
able, if technically more difficult, method to more
close approximate in vivo conditions. Unfortunately,
as with the receptor assay itself, methodological differ-
ences may have a considerable effect on experimental
results. Meningiomas are particularly uncooperative in
culture!

Also, while it is indubitably true that progestin recep-
tor proteins are under the direct physiological control
of estrogen and estrogen receptors in the majority of
normal and abnormal tissues, this is not universally the
case. In certain fibroepithelial breast tumors and in
human T47D breast cancer cells in culture, assayable
progestin receptor far outweighs estrogen receptors.

Mockus, et al. have thoroughly described proges-
tin receptor in T47D breast tissue cultures that is phar-
macologically typical but completely insensitive to es-
trogen or anti-estrogens that act on the receptors located
only in the nucleus, and in small quantities even there.
They propose that these anomalous nuclear estrogen-
binding sites (similar to those in MCF-7 cells on chronic
estrogen treatment) may function as "chemically proc-
essed" partially activated estrogen receptors, resulting
in constant protein synthesis, which leads cyclically to
the very high progesterone receptor production that is
easily documented in these cells. They reviewed the
work of Garcia, et al., which demonstrates that 5-
bromodeoxyuridine can inhibit the "estrogen induc-
able" component of progestin receptor in breast cells
but has no effect on the "basal (constitutive)" levels,
and suggested that the "basal" (non-estrogen-dependent)
progesterone receptor may be genetically reset to
very high levels in these cells.

Such an arrangement may also exist in some menin-
gium cell lines. The study of "typical" meningioma
(high progesterone and low estrogen receptors) in cul-
ture should allow adequate description of similarities
and differences to the T47D breast cancer cell and may
concomitantly suggest therapeutic avenues which may
not be limited to simple hormonal administration. We
look forward to further reports from the Harvard lab-
oratories as the story unfolds on the place of receptor
theory in oncogenesis.

References
1. Garcia M, Westley B, Rochefort H: 5-bromodeoxyuridine
specifically inhibits the synthesis of estrogen-induced pro-
2. Horwitz KB, Mockus MB, Lessey BA: Variant T47D
human breast cancer cells with high progesterone-receptor
levels despite estrogen and antiestrogen resistance. Cell
28:633-642, 1982
3. Mockus MB, Lessey BA, Bower MA, et al: Estrogen-
insensitive progesterone receptors in a human breast can-
cer cell line: characterization of receptors and of a ligand
oids (MCS) of human meningiomas. Biol Cell 45:31,
1982. (Abstract)
5. Rao BR, Meyer JS, Fry CG: Most cystosarcoma phyllodes
and fibroadenomas have progesterone receptor but lack
estrogen receptor: Stromal localization of progesterone

RESPONSE: In our paper we showed that early-passage
meningioma cells were responsive to estrogen, proges-
terone, and tamoxifen. We specifically stated that we
hoped this in vitro system would provide a model for oth-
er investigations. We recognized the limitations of our
study, especially since the fetal bovine serum in the
early culture medium may contain variable amounts
of estrogen, progesterone, and other hormones, result-
ing in the possibility that during the initial growth
period a pre-selection occurred for cells responding to
these factors. Cell selection in early culture is a well
recognized phenomenon, and progressive chromosomal
changes have also been noted for meningiomas in short-
term culture. We are pleased to see that Markwalder,
et al., tested primary cultures of some meningiomas,
since our current studies are also in this area. However,
the initial results they report in their letter and the early
clinical study they mention both appear discouraging.

We agree with the comments of Drs. Cahill and
Markwalder and Zava that further in vitro studies are
necessary to elucidate the role of various hormones
and/or growth factors in the development of meningi-
omas, and that more work needs to be performed in
this area before rational clinical therapy can be planned.

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Thermistor Detection of Shunt Obstruction

TO THE EDITOR: I read with interest the article by
Dr. Chiba and his colleagues on obstructed ventriculo-
peritoneal shunts. (Chiba Y, Ishiwata Y, Suzuki N,
et al: Thermosensitive determination of obstructed
sites in ventriculoperitoneal shunts. J Neurosurg 62:
363-366, March, 1985). In the description of the rec-
tording technique, the authors mention a "siphoning
effect" to explain the downward deflection recorded in
cases of shunt patency. This requires clarification. The
authors observed an increase in temperature in 27 pa-
tients with distal obstruction, as shown by an upward
deflection in the recordings. Their explanation for this

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The phenomenon is that the abdominal muscles contract and compress the shunt tube when the patient sits up from the supine position, causing reflux of "warm" cerebrospinal fluid (CSF) "inside" and "outside" the tube.

When a person sits up, the rectus abdominis muscle is primarily brought into play, although the oblique muscles also contract. Once the patient is in the upright position, the muscles are no longer in a fully contracted state (unless the patient strains, as during defecation). Therefore, the act of sitting up causes at most a momentary compression of the tube and not continuous compression lasting more than 2 minutes as shown in the recordings in Figs. 1c and 3c.

Even assuming that compression of the tube does take place, the reflux is inexplicable. No reflux of CSF can occur inside the tube, even in the presence of a distal obstruction, because there is a valve in the upper end of the tube that is intended to maintain a unidirectional flow in a downward direction (from the ventricular end to the abdominal end). Reflux can occur only if the valve is not functioning, which can be confirmed by trying to propel a saline solution in the distal to proximal direction in any shunt tube with a valve.

Regarding reflux outside the tube, the authors’ hypothesis is highly imaginative. First, do they propose that this reflux of fluid along the “outside” of the shunt tube carries the CSF all the way up to the chest where the sensors (thermistors) are located? If this were true, a patient with a pseudocyst would develop a boggy fluid collection along the tube if he sits up a couple of times a day. How often has anyone seen this in practice? On the contrary, the commonest cause of fluid collection in the tube is drainage of CSF along the tube from the upper ventricular end. Furthermore, the shunt tube passes through three layers of muscle and a layer of peritoneum before it is positioned in the abdomen. All of these layers are usually well approximated and the tube is anchored. Within a week of operation, the healing process completely seals the tube within these layers.

Even if the reflux happens as suggested, why should the “reflux fluid” be warm rather than of normal body temperature? Do the authors propose that the act of sitting up produces sufficient heat to warm the reflux fluid and thereby cause the thermistor to show an upward deflection? In addition, it is stated in the Discussion that “reflux of warm fluid, either inside or outside the catheter causes the upward deflection seen on the recording, with the degree of deflection being proportional to the amount of reflux.” I would like to remind the authors that the sensor (thermistor) will respond only to changes in temperature and not to the amount of fluid reflux.

Another serious problem with the paper concerns the experimental model. The authors observed that “when the distal end of the catheter was both clamped and compressed, a gradual upward deflection occurred,” as shown in their Fig. 3c. There was no explanation of the temperature increase, but, as if to justify the rise in temperature, the authors have gone a step further and devised another experiment to demonstrate the upward movement of an oil-water border. Once again they seem to be confused. They appear to have forgotten that the sensors (thermistors) can only detect temperature changes and not movement of fluid. It is stressed that, in the experimental model also, which is a system with a valve in the proximal end, the fluid column cannot move upward if the valve is functioning.

In both the model and the clinical study, temperature increases have been reported but no reasonable explanation of the source of heat has been furnished. In the absence of a convincing answer for this, there is every reason to suspect that what the authors have recorded are errors of measurement, making it impossible to arrive at any conclusion regarding malfunction or blockage at the lower end of the shunt tube as claimed in their paper.

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Response: I appreciate Dr. Viswanathan’s questions on our recent article. Concerning the siphoning action we described, a similar action was reported by Fox, et al., in 1973. They demonstrated a remarkable negative cerebrospinal fluid (CSF) pressure when patients with shunts are in the upright position. This means that, when the shunt is functioning and the patient assumes the sitting or upright position, CSF in the shunt catheter flows faster than when the patient is in the supine position. Hence, several anti-siphon valves have been designed to prevent the overdrainage of CSF. We have always observed a downward deflection of the recording trace in patients with functioning shunts who are in the sitting position.

With regard to the reflux of CSF and warm fluid, it seems that Dr. Viswanathan does not understand our thermosensitive method for determining CSF shunt patency. As mentioned in our previous paper, the equipment is composed of a pair of thermistors; one is a measuring thermistor and the other a reference thermistor. When they are balanced at the same temperature, the indicator points to the center of the scales, producing a flat-line recording. When the measuring thermistor detects a drop in temperature, the indicator is deflected and the recording trace drops. When the measuring thermistor detects an increase in temperature, an upward deflection of the trace is shown. In patients with a patent shunt, a downward deflection of the recording trace occurs, with the degree of deflection becoming pronounced when the patient changes from the supine to the sitting position. Upward deflection of the recording trace is found in cases of malfunction or blockage of the distal end of the abdominal catheter. Theoretically, upward deflection of the recording trace
indicates that the measuring thermistor detects a higher temperature than the reference thermistor. When an ice cube in a vinyl sac is applied to the skin, the area of conduction in the surrounding skin is concentric. When both thermistors are applied on the skin at the same distance from the cooling, they record the same temperature (that is, a flat-line trace). The fact that the measuring thermistor records the higher temperature after cooling indicates a reflux of non-cooled fluid (warm fluid) due to some cause. As an upward deflection of the recording trace was always observed after patients assumed the sitting position, it appears that reflux of warm fluid was produced by an action of the abdominal muscles. When the distal end of the abdominal catheter malfunctioned, we frequently revised only its distal part. At operation we sometimes observed a fluid collection around the catheter because of pseudocyst formation, even when this fluid collection around the catheter had not been observed or palpable preoperatively. It appeared that reflux of the fluid collection occurred along the catheter when the patient changed from the supine to the sitting position.

A thermistor certainly records the changes in temperature. The temperature at the measuring thermistor changes in response to the amount of reflux fluid. Thus, cooling occurs only on the skin proximal to the thermistor, whereas the temperature of the skin distal to the thermistor is warmer than that of the skin under the thermistor.

Patients with a malfunctioning shunt are almost always inactive or lethargic and cannot sit easily unless an examiner supports their back. In that situation it appears that abdominal muscles are continuously or intermittently contracted. We attempted the same procedure in a patient with a patent shunt, but a downward deflection of the recording trace was observed in spite of the abdominal muscles being contracted.

Dr. Viswanathan questions whether there is reflux in the catheter. The Mishler dual-chamber flat-bottom flushing device has two separate interior chambers separated by a silicone septum with a miter valve. The device used in our experiment was a new one; hence, we do not believe it malfunctioned. We have since performed another experiment using the same device in order to answer Dr. Viswanathan’s questions about reflux. We filled the device with water, then injected water from the orifice of the distal catheter into the distal chamber. No reflux of water through the valve was observed, demonstrating an intact valve. However, a bulge was observed in the distal chamber due to the injected water, which had caused a proximal deviation of the septum of the device. When the proximal (ventricular) catheter was opened, water flowed back from both the proximal and distal catheters because of the proximal deviation of the septum, but no reflux occurred through the valve. When the proximal catheter was clamped, reflux of water was not observed since there was no deviation of the septum. Hence, it appeared that reflux of CSF in the catheter occurred clinically only when the distal catheter was obstructed and the patient changed position from supine to sitting.

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References