glial cell" (*9*); and in well-defined areas of the diencephalon such as the nucleus arcuatus, the pars lateralis of the nucleus ventromedialis, the nucleus preopticus medialis, the nucleus stria terminalis interstitialis, and others, but was absent in such areas as the nucleus supraopticus, the nucleus suprachiasmatis and the mamillary nuclei (*10*). Glial cells were also unlabeled (*10*).

Therefore the important question arises: Are these conflicting results indeed authentic, that is, related to differences in dose, time, or individual animals; or are they artifacts to varying extent, that is, related to different and possibly invalidating technical steps employed during the preparation of tissue sections and autoradiograms?

Evidence has accumulated by centrifugal fractionation that estradiol is concentrated and retained for several hours in cell nuclei of tissues, such as uterus and induced mammary tumors of different mammalian species (*11, 12*). Although some cytoplasmic binding of estradiol is also found in such tissues, its extent is limited to only between 20 and 30 percent of the total uptake in vivo in immature and mature castrated animals (*13*). The nuclear ^{3}H-estradiol complex is unstable at *p*H's below 5.0 and above 10.0 (*11*), and if homogenization and fractionation are performed at room temperature the nuclear binding of the labeled hormone decreases, indicating its reversible nature.

Considering these biochemical data, it is likely that estradiol can be removed from its original binding sites by such histological procedures as liquid "fixation," embedding, wet section mounting, or the use of liquid emulsion at 40°C. Agreement exists between the biochemical data and the autoradiographic results only when all fluid treatments are excluded during the preparation of the tissue sections and the autoradiograms (*6*).

Diffusion, redistribution, and leaching of the label have been determined in our own autoradiographic studies with six different methods (*14*), using two diffusible compounds, ^{3}H-estradiol and ^{3}H-mesobilirubinogen. The extent of translocation artifacts was dependent upon employing such technical steps as liquid fixation, embedding, liquid emulsion coating, or thawing of frozen sections. For instance, in these experiments, diffusion of the labeled material into the epoxy resin could be demonstrated by liquid scintillation counting and by simultaneous photographic exposure of embedding material and tissue sections (*14*). The results obtained with each individual method were reproducible, although they deviated from each other. In autoradiography, reproducibility and minimum variability have been invoked to support authenticity of the results (*9*). If the data are reproduced by the same technique, however, this conclusion is unjustified (reproducibility pitfall) (*15*). With ^{3}H-estradiol, the divergent results obtained in these comparative studies were similar to those reported by the different investigators as already cited.

In the autoradiography of diffusible substances careful investigators have demonstrated radioactive material in all of the fluids used for tissue treatment. It is well established now that liquid "fixatives" not only extract varying amounts of tissue constituents but may also produce artificial binding of molecules which were previously unbound *in situ* (*16*). While diffusion artifacts are probably the most frequent and severe artifacts in autoradiography, many other artifacts are possible. The "estradiol story"—only one example of the many that could be quoted—may caution investigators in the use of autoradiographic techniques and the interpretation of the data derived from them and also arouse the attention of journal editors and referees.

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Serum Copper and Oral Estrogen

In their article on serum copper alteration after ingestion of an oral contraceptive (*1*), O'Leary and Spellacy state that "the mechanism of action of this increase is unknown but may represent a variation in the plasma proteins that bind the various metals." The effect of the principal steroidal constituents of the oral contraceptive used, mestranol and norethynodrel, as described by these authors is neither unexpected nor unique. The effect of estrogens on serum copper and ceruloplasmin has been recognized for over a decade, after a two- to threefold increase in serum copper and ceruloplasmin during pregnancy was reported in 1947 by Holmberg and Laurell (*2*). For example, Russ and Raymunt (*3*) found that serum copper and ceruloplasmin in a variety of patients was increased two to three times after the administration of 0.25 to 1.0 mg of ethinylestradiol per day for 3 to 4 weeks, an effect exceeding that noted by O'Leary and Spellacy. It has been postulated that this estrogen action is mediated through increased biosynthesis or secretion of ceruloplasmin or both by the liver. Thus, the changes in serum copper and presumably ceruloplasmin appear to represent a typical response to moderate estrogen or steroid treatment, an effect well known in the literature.

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Models of Pulsating Radio Sources

Linear polarization of signals from the pulsating radio star CP 0950 on 3 April 1968 indicates Faraday rotation of about 4 rad at 150 Mhz (*1*). This value "is comparable with the total rotation expected from the ionosphere" and sets an extremely sensitive upper limit on the weighted magnetic field through interstellar space. Smith comments "that there can be no appreciable Faraday rotation within the source of