1.

QUALITATIVE AND QUANTITATIVE STUDIES ON FLUOROPYRIMIDINES CATABOLISM IN HUMAN BY ^{19}F NUCLEAR MAGNETIC RESONANCE. J. Bernadou[o], J.P. Armand[o], M.C. Malet-Martino[oo], R. Martino[oo], A. Lopez[oo], Centre Claudius Regaud, 20-24 rue du Pont Saint Pierre, 31052 Toulouse and [oo]Laboratoire des IMRCP, ERA CNRS n°264, 118 route de Narbonne, 31062 Toulouse Cedex, France.

^{19}F NMR is a convenient method for metabolism studies on fluorinated drugs. We report catabolism studies in human on 5'-deoxyfluorouridine (5'dFUrd) and 5-fluorouracile (FUra).

5'dFUrd has been investigated in human biofluids after a 6 hours infusion at 12 g/sqm :
- in blood sample we observed unmetabolized 5'dFUrd, FUra, 5,6-dihydrofluorouracile (5FUH$_2$), α-fluoro β-ureidopropionic acid (FUPA) and 'α-fluoro β-alanine (FBAL). These two last catabolites are reported for the first time. No fluorinated compound was detected after 12 h. 5'dFUrd was found at t = 1, 3, 6 h with a maximum at 3 h. FUra was observed in plasma only in the first hour (in the limit of our NMR method sensitivity). 5FUH$_2$ was detected at t = 1 and 3 h. FBAL was the major catabolite formed from t = 1 to t = 12 h with a maximum at t = 6 h. FUPA was present in samples at t = 3 and 6 h.
- in urine unmetabolized 5'dFUrd and FBAL were the main catabolites. FUPA and an unidentified catabolite were detected at a very low level.
- in bile collected from a patient with external bile derivation, the main catabolite was FUPA with small amounts of 5'dFUrd and FBAL.

In FUra treated patient (1 g in a 1 h infusion), a large amount of FBAL and few FUra and FUPA were identified in urine.

^{19}F NMR, even with its limit sensitivity (about $10^{-5}M$), is a privileged technics for analysis of fluorinated drugs. It allows, without any extraction or derivatization, direct and simultaneous analysis and dosage useful to pharmacokinetics and metabolism studies.

2.

DIAGNOSIS OF CENTRAL NERVOUS SYSTEM INVOLVEMENT IN LYMPHOPROLIFERATIVE DISEASE.

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31 Patients with lymphoproliferative disease and central nervous system involvement(CNSI)were retrospectively analysed.4 had acute lymphocytic leukemia,26 Non-Hodgkins lymphoma(NHL),one chronic lymphocytic leukemia.7,8% of our NHL patients from 1979-1982 had evidence of CNSI.NHL patients with CNSI mostly had stage IV disease,big retroperitoneal tumor masses and progressive systemic disease.The following clinical symptoms were observed:Cranial nerve palsies(48%)paresthesias(35%),pareses of peripheral nerves(32%),behavior changes(29%),headaches(26%). Their first spinal tap showed positive cytology in 52%;91% had elevation of protein content over 0,3gr /1,68% an elevation over 0,5gr/1 in their spinal fluid.Computed tomography brain scans(CT) were positive in 56%,negative in 38% and unclear in 6% of the examinations.Spinal involvement was suspected in 16%,leptomenigeal disease was suggested in 50% and in 34% intracerebral disease was thought to be present.
In summary,CNSI is accompanied by a wide variety of clinical symptoms.Most patients present with elevated protein levels,half of them have a positive cytology on their first spinal tap.Intracerebral disease is not infrequently found in CNSI,the role of CT and implications for therapy willbe discussed.

3.

RECENT ADVANCES IN DIAGNOSTIC TECHNICS FOR ROUND CELL BONE SARCOMAS. A.Mazabraud*, A.Aurias**, D.Barres***, J.Dumont*, B.Perdereau* et C.P.Thiery*.
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Pathologists often encounter difficult problems in the diagnosis of round cell bone sarcomas. Even in cases where samples are substantial and technics adequate, precise diagnosis may be difficult, due to the undifferentiated pattern of the cells. Four recent technics have proven very useful in such cases : 1 - Chromosomal analysis was performed on 5 fresh biopsies of Ewing's sarcoma, morphologically similar to a previous series of 40 cases. In all 5 cases, a constant translocation t (11;22) was found, which was also present in

cell cultures and after transplantation of the tumor on nude rats. 2 - From a series of 45 cases identified as bone lymphomas, membrane markers were studied whenever possible on cell suspension, to identify the E-rosettes or immunoglobulin receptors. In 5 out of 7 fresh biopsies, a monoclonal light chain of immunoglobulin was found on tumoral cells. In the 2 other cases, E-rosettes and immunoglobulin receptors were not present. Histiocytic markers were found in one of these 2 cases. 3 - If the conditions required for the above technics do not exist, an isotopic test may be performed on the patient, to compare the strontium metabolism of the tumoral bone with that of the symetrical healthy bone. Characteristic curves are thus obtained for the 3 main types of round cell sarcomas : steeply rising for bone lymphomas (17 cases), horizontal for Ewing's tumors (45 cases), and descending for anaplastic sarcomas (23 cases out of 90 osteogenic sarcomas). 4 - Finally, from fixed material, morphometry provided a more precise classification, based on the size distribution of the cells : in lymphomas, 88% had a diameter of less than 5μ, wheras such small cells represented 53% of the total in Ewing's tumors, and 41% in anaplastic sarcomas.

4.

UNPROVEN DIAGNOSTIC TESTS FOR CANCER. A REVIEW. S.P. Hauser, Swiss Cancer League, Berne and Department of Internal Medicine, Division of Oncology, University Hospital, CH-8091 Zürich.

The Swiss Cancer League is a private society (politically and confessionally neutral) whose aim is to overcome cancer on the basis of scientific research and practical medicine, and to educate the public about cancer. A Working Group on Unproven Methods of Cancer Management was constituted in July 1982.
At the moment a great number of unproven diagnostic tests for precancerous and cancerous conditions can be found. The different kinds of tests can be divided into 4 subgroups — which are more characterised by the archetype of the promotors than by a scientific background:

1. Magical and chamanic methods:
   Astrology, Radiasthesia, Pars-pro-toto physical tests (Iridology, Chirology etc.), Capillary dynamic reaction (KAELIN) etc.

2. Bio-electronic methods:
   Bio-electronic test (VINCENT), Electro-Acupuncture (VOLL) etc.

3. Search for carcinogenic microorganisms:
   Endobiont, Viromycet, Carcinom-Protozoan, Polyoma microbico etc.

4. Pseudo-scientific methods:
   hematological, serological, biochemical, urinary tests etc. (more than 40)

5.

PROGNOSTIC SIGNIFICANCE OF NUCLEAR PARAMETERS IN INVASIVE BREAST CANCER. Ch. Umbricht, R. Gschwind *, M. Oberholzer, J. Torhorst, Department of Pathology, Kantonsspital, CH 4003 Basel, * Department of Scientific Photography, Institut of Physical Chemistry, University of Basel, Switzerland

The identification of nodal negative breast cancers which will recur is an important goal because 20-40 % do so up to 10 years after diagnosis. Early identification of these patients should lead to early therapy and eventually to prevention of recurrence. In a retrospective analysis 15 breast cancers in post-menopausal women (pT1,2, pN0, invasive duct NOS) were observed until detection of recurrence or for a period of 9-14 years after operation without recurrence. The following nuclear parameters were analysed by computer assisted morphometry: nuclear area , roundness (FOFA: circumference normalized for area =C 2/4piA), ellipticity (ELFOUR: based on fourier analysis; ELPROJ:ferret-diameters;ELMOI: principal moment of inertia; ELFITT&PDAF: non-linear least square fit methods), concavity (PCAF: total convex deficiency of a contour in % of area; and PARIS: total length of concave contour elements in % of circumference), and bending energy (BEND: integrated sum of squared curvature). Significant differences were found by non-parametric statistical analysis for following factors:FOFA, ELPROJ, ELMOI, PDAF, PCAF, PARIS, BEND. By stepwise discriminant analysis 3 shape factors (PARIS, PCAF, PDAF) were found which achieved 100 % separation of the 2 prognostic groups. Application of the "leaving one out method" showed correct classification in 6 of 8 recurrent cases and in 7 of 7 non-metastasizing cases.