in the Artemis mission in the next few years and then to travel to Mars. For perspective the direct distance to the Moon is 383,000 km whilst a mission to Mars could vary between 55–400, 000, 000 km. and could take about 3-years for a return trip. Besides the technical challenges of a journey to Mars there are important medical challenges including: (1) Space radiation; (2) Micro-gravity; (3) A hostile, closed environment; (4) Isolation and confinement; and (5) Distance from Earth. Radiation is an important hazard for human inter-planetary space flight. There are potential health consequences, immediate and long-term. The immediate potential risks are: (1) Acute radiation syndromes; and (2) Neuro-ocular disturbances whereas the long-term consequences include: (1) Cancer; (2) Cardio-vascular disease; (3) Cataracts; and (4) Degenerative diseases. Sources of radiation on a journey to Mars include: (1) Trapped charged particles and high energy electrons (Van Allen belts); (2) Galactic cosmic rays; and (3) Solar events (charged particles & UV). Galactic cosmic rays include: (1) High energy/high charge ions; (2) High energy protons; (3) Secondary protons; (4) Neutrons; and (5) Fragments produced by interactions with the spacecraft shielding and human tissues. Solar particle events include: (1) Solar winds; (2) Coronal mass ejections; and (3) Low to medium energy protons. The Earth's magnetosphere protects us from much of this radiation, but this protection is lost on a journey to Mars. The Artemis-1 mission which recently circumnavigated the Moon is providing data on radiation exposure. Our normal background radiation dose on Earth is about 2.4 mSv/year whereas journey to Mar could expose astronauts to 300–600 mSv over 3-years. Concernedly, damage to DNA produced by heavy charged ions encountered in space is different and probably more dangerous than our exposure to ionizing radiations on Earth. Several mitigation measures have been developed including: (1) Spacecraft shielding; (2) Crew shielding; (3) Spacecraft positioning; (4) Mission planning; (5) Radiation storm shelters; (5) Limited spacewalks; (6) Crew selection and others. My conclusions are: (1) Radiation is an important hazard of inter-planetary travel; (2) There are immediate and long-tern consequences of high radiation exposures; (3) Interventions are needed to reduce radiation risk; (4) There are important knowledge gaps regarding long-term adverse events; and (5) We need to train a new generation of physicians to deal with these challenges.

https://doi.org/10.1016/j.htct.2025.103866

03

THE HISTORY OF CHRONIC MYELOID LEUKEMIA (CML): FROM ARSENIC TO TYROSINE KINASE INHIBITORS (TKI)

Rüdiger Hehlmann

Medizinische Fakultät Mannheim, Heidelberg University, Alemana

It took 20-years from the first description of CML in 1845 to the report by Lissauer in 1865, of an effective treatment with arsenic. After another 38-years the beneficial effect of splenic irradiation was described in 1903, and after 50 more years the palliative efficacy of the alkylating agent busulfan (Galton, 1953). Several other agents were found effective (dibromomannitol, hydroxyurea), and in 1979 first reports on the efficacy of bone marrow transplantation were published. After more than 100-years of trial and error, the observation in 1960 of the Philadelphia (Ph)-chromosome, a translocation between chromosomes 9 and 22, marked the first step to understanding the pathophysiology of CML and to a rational and causative treatment approach. The breakpoint on chromosome 9 occurred in the gene encoding the ABL-oncogene. Most of ABL was translocated to chromosome 22 next to a region called Breakpoint Cluster Region (BCR). The detection of a BCR:ABL fusion RNA in CML (R. Gale contributed), prompted transfection experiments to mice which developed CML-like phenotypes (Daley et al, Heisterkamp and Groffen, 1990). Since the ABL-oncoprotein is a tyrosine kinase deregulated by juxtaposition next to BCR, the search for an inhibitor of BCR-ABL was the logical next step. The choice of imatinib as the first BCR-ABL-TKI was fortuitous and led to a profound change of CML treatment. Other TKI followed, but none-prolonged survival of CML compared to imatinib. Still, progression to blast crisis occurred in 6%–7% of imatinib-treated cases, but CML-specific survival increased to more than 90% and survival of CML-patients diagnosed and treated in the chronic phase of CML approached that of the general population.

https://doi.org/10.1016/j.htct.2025.103867

04

MDS DIAGNOSIS? STILL BY BONE MARROW EXAMINATION?

Moshe Mittelman

Tel-Aviv Sourasky Medical Center, Tel Aviv University, Israel

The Myelodysplastic Syndromes (MDS) are a heterogenous group of clonal Bone Marrow (BM) stem cell myeloid neoplasms, characterized by BM dysplasia, macrocytic anemia or cytopenia with a tendency for leukemic transformation. The suspicion of MDS is raised by a typical but not specific clinical picture and routine laboratory findings, but the gold standard for the diagnosis of MDS is still BM examination with the presence of uni- or multi-lineage dysplasia and blast percentage, together with exclusion of other reasons. Cytogenetics is also a part of the diagnostic process. Flow cytometry and genetics are helpful but are not always mandatory for the diagnosis of MDS. We will summarize the current steps in the diagnostic approach for a patient suspected of having MDS. I will also describe new concepts that use non-invasive diagnostic technologies, especially digital methods as well as peripheral blood genetics. The hope is that one day these will mature, be introduced into clinical practice, and perhaps in many cases even replace the invasive BM biopsy.

https://doi.org/10.1016/j.htct.2025.103868